

16.1.9 Documentation of Statistical Methods

16.1.9.1 Statistical Analysis Plan

Statistical Analysis Plan

A Longitudinal Ambulatory Study to Assess Changes in Cigarette Consumption Behavior and Biomarkers of Exposure during a 6-Week Switch to Very Low Nicotine Cigarettes

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Statistical Analysis Plan Signature Page

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1. INTRODUCTION

The following statistical analysis plan (SAP) provides the framework for the summarization of the data from this study. The SAP may change due to unforeseen circumstances. Any changes made from the planned analysis within protocol, after locking of the database will be documented in the clinical study report (CSR).

Any additional analyses not addressed within this SAP and/or driven by the data, or requested by the SPONSOR, will be considered out of scope and must be described in the CSR.

2. STUDY PURPOSE, HYPOTHESIS, OBJECTIVES AND ENDPOINTS

2.1 Study Purpose

The purpose of this study is to examine whether measures of cigarette consumption behavior (cigarettes per day and smoking topography) are changed when smokers switch from smoking conventional cigarettes to smoking cigarettes with a very low nicotine (VLN) content (0.4 mg nicotine per gram of tobacco). Secondary purposes are to examine changes in biomarkers of exposure (BoE), nicotine pharmacokinetics (PK) and subjective measures of dependence, smoking urges, withdrawal symptoms and perceived health risks, when subjects switch to smoking VLN cigarettes.

2.2 Hypothesis

It is anticipated that when adult smokers switch to smoking VLN cigarettes, after habitually consuming their usual quantity and brand of cigarettes, their daily cigarette consumption will be reduced. It is further anticipated that puffing topography parameters will be unchanged following smoking VLN cigarettes for 6 weeks (i.e. no smoking compensation will occur).

2.3 Objectives

Primary objectives:

1. To characterize cigarette consumption behavior (cigarettes per day and puffing topography) before, during and after a switch from usual brand (UB) to VLN cigarettes for 6 weeks.

Secondary objectives:

1. To evaluate changes in tobacco-related biomarkers of exposure (BoE) before, during and after a 6-week switch from UB to VLN cigarettes.
2. To evaluate nicotine PK before, during and after a 6-week switch from UB to VLN cigarettes.
3. To evaluate changes in subjective effects before, during and after a 6-week switch from UB cigarettes to VLN cigarettes.

2.4 Endpoints

Product Use Endpoints (Primary Objective 1):

- Cigarettes smoked per day (CPD). Both compliant and non-compliant smoking captured in the electronic diaries (e-diaries).
- Number of collected used cigarette butts (apparent compliant, apparent non-compliant, and total)
- Puffing topography parameters (puff duration, puff volume, peak puff flow rate, average flow rate and inter-puff interval)

BoE Endpoints (Secondary Objective 1):

- In urine:
 - Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL; 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone [NNK] biomarker)
 - Total N-Nitrosonornicotine (NNN)
 - 3-hydroxypropylmercapturic acid (3-HPMA; acrolein biomarker),
 - S-phenylmercapturic acid (S-PMA; benzene biomarker),
 - 1-hydroxypyrene (1-OHP; hydroxypyrene biomarker)
 - Total nicotine equivalents (Tneq)
 - Creatinine concentration (for normalization of urinary BoE endpoints)
- Carboxyhemoglobin in blood
- Cotinine in plasma

Nicotine PK Endpoints (Secondary Objective 2)

- Nicotine PK parameters will include C_{max}, AUC₀₋₁₈₀ and T_{max}

Subjective Effects Endpoints (Secondary Objective 3)

- Fagerström Test for Cigarette Dependence (FTCD)
- Brief Questionnaire of Smoking Urges (QSU-Brief)
- Minnesota Nicotine Withdrawal Scale - Revised (MNWS-R)
- Perceived health risk scale
- Safety endpoints will include adverse events (AEs).

3. STUDY DESIGN

This is an open-label, randomized, forced-switching study to be conducted at multiple study sites. Seventy (70) self-affirmed exclusive filtered non-mentholated cigarette smokers and 70 self-affirmed exclusive filtered mentholated cigarette smokers will be enrolled and begin the study at Week -1.

All potential subjects will provide informed consent and successfully complete the Screening procedures prior to participation in the study. Subjects will also engage in a

brief product trial with the VLN cigarettes. Subjects who react negatively (i.e., unwilling to use and/or cannot tolerate the product [experience AEs that will prevent them from continuing to use the product as judged by the Investigator]) to the VLN cigarettes during the product trial period will not continue in the study.

At the start of Week -1, all subjects will be asked to smoke their UB cigarettes as per their usual daily consumption for the following week. Subjects will receive an e-diary to record daily cigarette use (CPD). Training in completion of the e-diary will be provided at the visit at the start of Week -1.

Subjects will return at the end of Week -1, at the time indicated by the clinical research unit (CRU), for collection of blood and 24-hour urine samples for baseline BoE assessments. Subjective questionnaires for dependence, withdrawal symptoms, urges to smoke, and perceived health risk will also be completed at scheduled times. A randomly-selected subset of 18 non-menthol and 18 menthol smoker subjects will complete an assessment of puffing topography with their UB cigarettes during this visit. A further subset of 12 of the non-menthol and 12 of the menthol smoker subjects who complete the topography assessment will also complete a nicotine PK assessment at the end of this visit. Subjects who undergo topography and PK assessments will be assigned to switch to smoking VLN cigarettes.

On Day -1 of Week 1, subjects will be randomly selected to either remain smoking their non-menthol (20 subjects) or menthol (20 subjects) UB cigarettes, or to switch to smoking non-menthol (50 subjects) or menthol (50 subjects) VLN cigarettes as per their UB cigarette flavor. Subjects will return at the end of Weeks 2 and 6, at the time indicated by the CRU, for collection of blood and 24-hour urine samples for BoE assessments. Subjective effects questionnaires will also be completed at scheduled times. Subjects will continue recording their CPD in their e-diaries. The same subset of 18 non-menthol and 18 menthol smoker subjects selected to complete a puffing topography assessment with their UB cigarette on Week-1, will complete an assessment of puffing topography with the VLN cigarettes at these visits, and a further subset of 12 non-menthol and 12 menthol smoker subjects will also complete an assessment of nicotine PK at the end of these visits. Subjects undergoing topography and PK assessments will have been assigned to switch to smoking VLN cigarettes.

Additionally, all subjects will visit the clinic at the end of Week 4 to receive further supplies of cigarettes (if assigned to the VLN groups) and to complete subjective effects questionnaires.

Subjects randomized to the VLN groups will be provided with a supply of VLN cigarettes at each visit, which will be 150 % of their usual daily consumption as reported during Week 1. If a subject runs out of cigarettes between clinic visits, they may visit the clinic to receive additional test cigarettes. All subjects will be asked to smoke their cigarettes *ad libitum*, recording their actual daily consumption in their e-diaries. Non-compliant nicotine product consumption should also be recorded. Used

cigarette butts will also be collected during ambulatory periods to verify product use and/or assess compliance. During Week 1 (all subjects) and all subsequent weeks (subjects randomized to continue smoking UB cigarettes) subjects will be asked not to change their UB cigarette brand or flavor.

The CRU will attempt to contact all subjects who participated in the study (including subjects who terminate the study early) using their standard procedures approximately 7 days after the last contact to determine if any AE has occurred since the last study visit.

4. SAMPLE SIZE ESTIMATION

4.1 Cigarette Consumption

An intended sample size of 50 subjects in each of the two groups who switch from smoking usual brand to VLN cigarettes has been set for this study. This is based on powering the primary objective of a within-group comparison of cigarette consumption at baseline and end-of-study. The calculation was based on the number of pairs required to perform a one-tailed paired t-test with 80% power and an alpha level of 0.05 for a decrease in cigarette consumption of 3 CPD compared to available historical consumption data. The sample size was determined to be adequate based on potential non-compliance with the use of VLN cigarettes. A lower number (20) of smokers will be randomized to the continue-to-smoke usual brand groups, given the lower variability in consumption data and lower non-compliance anticipated in these groups. This will provide sufficient power for the secondary objective of between-group comparisons in cigarette consumption.

4.2 Puffing Topography

An intended sample size of 12 subjects in each of the two groups who switch from smoking usual brand to VLN cigarettes has been set for this study. This is based on powering the primary objective of a within-group comparison of puffing topography parameters at baseline and end-of-study. The calculation was based on the number of pairs required to perform a two-tailed paired t-test with 80% power and an alpha level of 0.05 to detect significant differences between UB and VLN cigarettes and is based on available puffing topography data (5). This sample size will also provide sufficient power to detect differences in nicotine PK between UB and VLN cigarettes.

5. ANALYSIS POPULATIONS

The statistical analysis will be based on separate, hierarchically organized, analysis populations defined as the following:

Safety population: All enrolled subjects who smoked at least one cigarette of any type. This population will be used for safety analysis.

Intent-to-treat (ITT) population: All subjects who had at least one valid recording of cigarette consumption (a period of one week of >70% completion of their e-diary).

Per-protocol (PP) population: All subjects who had valid recording of cigarette consumption and completed the study according to the protocol. Data will be excluded from this population:

- If a subject self-reports smoking a significant number of cigarettes other than those which they have been assigned according to the protocol, or if this is apparent following checking of their collected used cigarette butts
- If there is a significant discrepancy between the self-reported number of cigarettes smoked per day and the number of used cigarette butts collected
- If a subject is non-compliant based on a published method of assessing compliance. After switching, subjects will be deemed non-compliant if their ratio of [plasma cotinine/CPD VLN]/[plasma cotinine/CPD baseline] exceeds 0.2.

If it is determined that a subject is pregnant during the study, the pregnant subject's data will be listed but excluded from all PK parameter summaries.

PK Population: Subjects in the PP or ITT population who have at least one PK blood draw resulting in at least one quantifiable plasma nicotine concentration. This population will be used for PK analysis (secondary endpoint analysis) and all available data will be included in the concentration and PK parameter tables to the extent possible.

5.1 Preliminary Analyses

Topline preliminary reports will be prepared using final PK and puffing topography data. The PK and puffing topography TFLs listed in [Section 13](#) will be included in the topline reports.

6. PRODUCT DESCRIPTION

The following investigational products will be used during this study:

Product	Short Description	Long Description
Non-mentholated VLN cigarette	VLN non-mentholated	Non-mentholated VLN cigarettes
Mentholated VLN cigarette	VLN mentholated	Mentholated VLN cigarettes
UB non-mentholated cigarette	UB non-mentholated	Subjects' UB non-mentholated filtered cigarettes
UB mentholated cigarette	UB mentholated	Subjects' UB mentholated filtered cigarettes

For the PK and safety text and analysis, table and listing headers, and AE (on rare occasion this may also apply to additional safety endpoints), the product will be described using the short description.

For figures, listings, and footnotes, the long description will be used, wherever feasible.

7. PRODUCT USE

7.1 Product Use Measurements and Collection Schedule

7.1.1 Product Use History

Subjects will be required to report previous tobacco- and nicotine-product use histories to satisfy the study inclusion and exclusion criteria. In addition, the subject will be asked if he/she is planning to quit smoking within the next 3 months. Those planning to quit will be excluded from participating in the study.

The subjects' tobacco use and smoking history (including a color photocopy of their UB cigarette package along with a ruler) will be recorded at Screening. Verification of the subject's UB cigarette brand will be made at the end of Week -1 clinic visit.

7.1.2 Product Use Recording

Subjects will be provided with e-diaries to record their daily cigarette consumption, both when in clinical confinement during study visits and during ambulatory periods. Subjects will be instructed to record both compliant and non-compliant (if any) daily numbers of cigarettes smoked. Non-compliant consumption in the subjects randomized to smoke VLN cigarettes is defined as nicotine product consumption other than their UB cigarettes during the baseline period (Week -1) or VLN cigarettes following switching (Weeks 1 to 6). Non-compliant consumption in the subjects randomized to continue to smoke their UB cigarettes is defined as nicotine product consumption other than their UB cigarettes between Week -1 and Week 6. For the purposes of data analysis, the e-diary record of cigarette consumption will be used as the primary variable.

Subjects will be provided with metal canisters in which to store their used cigarette butts during the ambulatory study periods. This is for the purposes of assessing both compliance with the study requirements and the accuracy of their self-reported (electronic diary) cigarette consumption. Subjects will be requested to collect butts of all cigarettes smoked, both compliant and non-compliant.

At the end of each collection period, the total number of butts in the canisters for the whole of that period will be counted and recorded. The number of each type of cigarette (study cigarette and non-study cigarette) will also be recorded. The cigarette butt count will be reconciled against that subject's e-diary record of cigarette consumption.

7.1.3 Puffing Topography

At clinic visits at the end of Weeks -1, 2 and 6, a randomly-selected subset of 18 non-menthol and 18 menthol smoker subjects will complete a puffing topography evaluation session with either their UB (Week -1) or the VLN (Weeks 2 and 6) cigarettes. These subjects will be/have been assigned to switch to smoking VLN cigarettes. These assessments will only be performed at a single clinical site (Lincoln) and will take place during the 24-hour confinement period.

During the puffing topography assessment, subjects will engage in a 1 hour ad libitum smoking session with their UB (Week -1) or the VLN (Weeks 2 and 6) cigarettes. In these sessions, subjects will smoke cigarettes with the mobile smoking puff analyzer (SPA-M; Sodim). The topography device will be monitored to ensure the device is actively recording during each session.

Topography assessments will be started at least one hour following either the subject's breakfast or lunch. The puffing topography session for each subject at Weeks 2 and 6 should be within ± 2 hours of the time of their Week -1 session. Additional details and instructions for puffing topography procedures will be provided separately.

The following topography parameters will be assessed:

- Puff duration
- Puff volume
- Peak puff flow rate
- Average flow rate
- Inter-puff interval

7.2 Data Summarization and Presentation of Primary Endpoints

Study product use (study product, CPD and cigarette butts) will be listed by subject and study week. CPD and cigarette butts will be summarized by study week and study product using descriptive statistics (number of observations [n], arithmetic mean [Mean], standard deviation [SD], coefficient of variation [CV%], standard error of the mean [SEM], minimum, median, and maximum). The total duration of the product use (sum of the duration of each product use) will also be summarized. The descriptive statistics will be presented for both PP and ITT populations.

Topography parameters (puff duration, puff volume, peak puff flow rate, average flow rate, and inter-puff interval) will be listed by subject and summarized by study product and time point (Week -1, 2, or 6).

7.3 Statistical Analysis of Primary Endpoints

Paired t-tests will be used to compare cigarette consumption (CPD) and puffing topography parameters at the Week 2 and Week 6 time points with the baseline (Week -1) values. This analysis will be conducted on the evaluable subjects in the PP population. If data are unexpectedly found not to be normally distributed, an appropriate non-parametric test will be performed. Differences will be considered statistically significant at an alpha level of 0.05. Means, difference of means, 90% confidence interval for difference, and p-value will be presented.

The following SAS codes will be used for the analysis:

```
Proc ttest data=< >;  
  By product_group;  
  Paired week_X*baseline;  
Run;
```

Where week_X will be either Week 2 or Week 6. Product Groups are VLN non-mentholated, VLN non-mentholated, and VLN combined which pooled non-mentholated and mentholated groups. The primary analysis will be based on the VLN combined product group.

In addition, a linear mixed model analysis of variance will be used to compare the between product group differences in the absolute change from baseline values of the consumption and puffing topography parameters. Product group, week, and product group by week interaction will be the fixed factors in the model. A restricted maximum likelihood estimation method with an unstructured (UN) covariance structure will be applied. If the model does not converge, the first order autoregressive AR(1) and/or compound symmetry CS covariance structures will be tested as alternatives. The least-square mean difference, 95% confidence interval and p-value will be provided for the product group difference. The pairwise comparisons (VLN non-mentholated versus UB non-mentholated, VLN mentholated versus UB mentholated, and VLN combined versus UB combined) will be performed at week Week 2 and Week 6. Least-square means (LSMeans), difference of LSMeans, 90% confidence interval for difference, and p-value for difference will be presented.

The following SAS codes will be used to perform the analysis.

```
Proc mixed data=< >;  
Class subject product_group week;  
Model response = product_group week product_group*week /ddfm=kr;  
Repeated week/type=<type> subject=subject;  
LSmeans product_group*week/CL alpha=0.05 CL pdiff;  
Run;
```

The primary analysis will be the pairwise comparisons of VLN combined versus UB combined (pooled non-mentholated and mentholated groups).

8. BIOMARKERS

8.1 Urine Biomarkers

8.1.1 Urine Biomarkers Measurements and Collection Schedule

Urine will be collected over 24-hour periods for urine BoE measurements, during the clinic visits at the end of Weeks -1, 2 and 6. The urine samples collected during a single 24-hour period will be pooled together and weighed. The total weight of all urine collected over each 24 hour period will be documented. Concentrations of the following biomarkers will be measured: total NNAL, total NNN, 3-HPMA, S-PMA, 1-OHP, and Tneq. Creatinine in urine will also be measured and used to report BoE as amount per unit of creatinine.

8.1.2 Bioanalytical Method

Urine concentrations will be determined using validated analytical methods at Celerion Bioanalytical Services, Lincoln, NE and Celerion, Switzerland.

Urine nicotine, cotinine, *trans*-3'-hydroxycotinine, nicotine-*N*-glucuronide, cotinine-*N*-glucuronide, *trans*-3'-hydroxycotinine-*O*-glucuronide, NNN, NNAL, 1-OHP, and creatinine concentrations will be analyzed by liquid chromatography-tandem mass spectrometry (LC-MS/MS) methods at Celerion, Lincoln, NE using validated analytical methods with appropriate quality controls according to applicable portions of Celerion Standard Operating Procedures which were written based on the FDA Guidance for Industry: Bioanalytical Method Validation (May, 2001) and the FDA Good Laboratory Practice regulations (Title 21 CFR Part 58).

Approximate lower limit of quantitation (LLOQ) values for each analyte are shown in the table below. LLOQs will be reported out to the most current validation data and included in the bioanalytical report.

Analyte	LLOQ
Nicotine	50.0 ng/mL
Cotinine	50.0 ng/mL
<i>trans</i> -3'-hydroxycotinine	50.0 ng/mL
Nicotine- <i>N</i> -glucuronide	50.0 ng/mL
Cotinine- <i>N</i> -glucuronide	200 ng/mL
<i>trans</i> -3'-hydroxycotinine- <i>O</i> -glucuronide	200 ng/mL
NNN	0.200 pg/mL
NNAL	5.00 pg/mL
1-OHP	10.0 pg/mL
Creatinine	120 µg/mL (effective LLOQ)

Urine nicotine, cotinine, *trans*-3'-hydroxycotinine, nicotine-*N*-glucuronide, cotinine-*N*-glucuronide, *trans*-3'-hydroxycotinine-*O*-glucuronide, NNN, NNAL, 1-OHP, and creatinine concentrations will be determined using validated analytical methods at Celerion, Lincoln, NE and Celerion, Switzerland.

Urine 3-HPMA and S-PMA concentrations will be analyzed by LC-MS/MS methods at Celerion, Switzerland. The analysis will be performed according to the standards described in the Swiss Ordinance relating to Good Laboratory Practice, adopted 18 May 2005 [RS 813.112.1]. This Ordinance is based on the OECD Principles of Good Laboratory Practice, as revised in 1997 and adopted 26 November 1997 by decision of the OECD Council [C(97)186/Final]. The OECD Principles of Good Laboratory Practice are accepted by Regulatory Authorities throughout the European Union, the United States of America and Japan. In addition, the analysis of clinical trial samples will be conducted in accordance with the relevant standards of Good Clinical Practice and Standard Operating Procedures based on the recommendations of the EMA 'Reflection paper for laboratories that perform the analysis or evaluation of clinical trial samples' (EMA/INS/GCP/532137/2010), the EMA 'Guideline on bioanalytical method validation' (EMA/CHMP/EWP/192217/2009) and the FDA 'Guidance for Industry, Bioanalytical Method Validation', (U.S. Department of Health and Human Services, Food and Drug Administration, CDER, CVM, May 2018).

Approximate LLOQ values for each analyte are shown in the table below. LLOQs will be reported out to the most current validation data and included in the bioanalytical report.

Analyte	LLOQ
3-HPMA	20 ng/mL
S-PMA	0.025 ng/mL

8.1.3 Urine Biomarkers Analysis

The following variables will be determined for each urine biomarker at each collection week:

- Measured concentration
- Total biomarker mass excreted per 24 hours (primary analysis variable)
- Total mass excreted per 24 hours absolute change from Baseline
- Total mass excreted per 24 hours percent change from Baseline
- Creatinine-normalized excretion level
- Creatinine-normalized change from baseline
- Creatinine-normalized percent change from baseline

Nicotine equivalents will be calculated as the molar sum of nicotine, cotinine, trans 3'hydroxycotinine and their glucuronides excreted in urine over 24 hours:

The concentration of each metabolite will first be multiplied by the 24-hour urine volume to obtain the total amount excreted in 24 hours, then divided by the molecular weight of the metabolite to obtain the total amount of each in moles. The sum in moles will then be converted to Tneq by multiplying by the molecular weight of nicotine.

Nicotine (mg/24h)	=	nicotine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Nicotine-glucuronide (mg/24h)	=	nicotine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Cotinine (mg/24 hours)	=	cotinine concentration [ng/mL] × 24h urine volume [mL] ÷ 1000 000
Cotinine-glucuronide (mg/24h)	=	cotinine glucuronide concentration [ng/mL] × 24h urine volume [mL] ÷

$$\begin{aligned}
 &1000\ 000 \\
 \text{Trans-3'-hydroxycotinine (mg/24h)} &= \frac{\text{trans-3'-hydroxycotinine concentration [ng/mL]} \times 24\text{h urine volume [mL]}}{1000\ 000} \\
 \text{Trans-3'-hydroxycotinine-glucuronide (mg/24h)} &= \frac{\text{trans-3'-hydroxycotinine glucuronide concentration [ng/mL]} \times 24\text{h urine volume [mL]}}{1000\ 000} \\
 \text{Nicotine equivalents (mg/24 hours)} &= \left(\frac{\text{nicotine [mg/24h]}}{162.23\ \text{[mg/mmol]}} + \frac{\text{nicotine-gluc [mg/24h]}}{338.36\ \text{[mg/mmol]}} + \frac{\text{cotinine [mg/24h]}}{176.22\ \text{[mg/mmol]}} + \frac{\text{cotinine-gluc [mg/24h]}}{352.34\ \text{[mg/mmol]}} + \frac{\text{trans-3'-hydroxycotinine [mg/24h]}}{192.22\ \text{[mg/mmol]}} + \frac{\text{trans-3'-hydroxycotinine-gluc [mg/24h]}}{368.34\ \text{[mg/mmol]}} \right) \times 162.23\ \text{(mg/mmol)}
 \end{aligned}$$

Urine biomarker concentration values reported as below the limit of quantitation (BLQ) will be set to one-half of the limit of quantitation prior to calculating the 24-hour mass excreted or Tneq. Total urine weight (g) will be collected during the study and converted to urine volume using the assumed density of 1 gram (g) equals 1 milliliter (mL).

Creatinine-adjusted concentrations will be calculated as shown in [Section 8.1.4](#). Absolute and percent change from baseline will be calculated as shown in [Section 8.1.5](#).

8.1.4 Creatinine Adjusted Urine Biomarker Concentrations

Creatinine concentrations will be used to adjust the concentration values of all urine biomarkers (Total NNAL, total NNN, 3-HPMA, S-PMA, 1-OHP, and Tneq) as follows:

$$\text{Urine biomarker (mass/mg creatinine)} = \frac{\text{urine biomarker (mass/mL)} \times 100}{\text{creatinine (mg/dL)}}$$

8.1.5 Change from Baseline Urine Biomarker Concentration

Urine biomarker change from baseline on Weeks 2 and 6 will be calculated as follows, where Baseline = Week -1:

$$\text{Absolute change from baseline} = \text{Post Product Use Value} - \text{Baseline Value}$$

Percent change from baseline (%) = (Post Product Use Value – Baseline Value) /
Baseline Value x 100 %

8.2 Blood Biomarkers

8.2.1 Blood Biomarkers Measurements and Collection Schedule

Blood samples for COHb in whole blood and cotinine in plasma will be collected on Weeks -1, 2, and 6. Samples will be collected at approximately 13:00, following the subject's lunchtime meal, and will be preceded by at least a 30 minute abstention from study product use.

8.2.2 Bioanalytical Method

Whole blood COHb and plasma cotinine will be analyzed by spectrophotometric measurement and LC-MS/MS, respectively, at Celerion Bioanalytical Services, Lincoln, NE, using validated analytical methods with appropriate quality controls according to applicable portions of Celerion Standard Operating Procedures which were written based on the FDA Guidance for Industry: Bioanalytical Method Validation (May, 2001) and the FDA Good Laboratory Practice regulations (Title 21 CFR Part 58). The LLOQ for COHb will be 0.2%. The LLOQ for plasma cotinine will be 1.00 ng/mL.

8.2.3 Blood Biomarkers Analysis

Absolute and percent change from baseline in blood biomarkers will be calculated as described for urine in [Section 8.1.5](#).

8.3 Data Summarization and Presentation of Biomarkers of Exposure

Blood biomarker concentrations, urine biomarker concentrations, urine creatinine concentrations, and the creatinine-adjusted urine biomarker concentrations will be listed by product, subject and week for all biomarkers. All BLQ values will be presented as "BLQ" in the listings.

Blood biomarker concentrations, blood biomarker absolute change from baseline and blood biomarker percent change from baseline as well as urine biomarker mass excreted per 24 hours, absolute change from baseline, percent change from baseline of total mass excreted per 24 hours, creatinine-normalized excretion level, creatinine-normalized excretion absolute change from baseline, and creatinine-normalized excretion percent change from baseline will be summarized by product group and week for all biomarkers using descriptive statistics (n, mean, SD, CV%, SEM, minimum, median, and maximum). The descriptive statistics will be presented for both PP and ITT populations.

8.4 Statistical Analysis of Biomarkers of Exposure

Paired t-tests will be used to compare urinary NNAL, NNN, 3-HPMA, S-PMA, 1-OHP, Tneq mass excreted, and blood COHb measures at the Week 2 and 6 time points with the baseline (Week -1) values. This analysis will be conducted on the evaluable subjects in the PP population. If data are unexpectedly found not to be normally distributed, an appropriate non-parametric test will be performed. Differences will be considered statistically significant at an alpha level of 0.05. The same SAS codes used in [Section 7.3](#) for paired t-test will be used for the analysis.

In addition, a linear mixed model analysis of variance will be used to compare the between product group differences in the absolute change from baseline values of each of the urinary and blood BoEs. The same statistical model and SAS codes used in [Section 7.3](#) for product group comparisons will be used for the analysis.

9. PHARMACOKINETIC ANALYSIS

9.1 Measurements and Collection Schedule

For a randomly-selected subset of 12 non-menthol and 12 menthol smoker subjects, PK blood sampling will occur following the completion of the 24-hour urine collection period on clinic visits at Weeks -1, 2, and 6. The selected subjects will remain in the clinic for a further night, in which they will abstain from smoking any cigarettes/using any nicotine-containing products for at least 12 hours prior to the PK assessment session. During this session, subjects will smoke a single cigarette (either their UB on Week -1 or the VLN on Weeks 2 and 6) *ad libitum* during a 5-minute period. Serial blood samples will be collected for plasma nicotine analysis at 5 minutes prior to and at 2, 5, 7, 10, 12, 15, 20, 30, 45, 60, 90, 120, 150, and 180 minutes relative to the start of cigarette smoking.

All concentration data will be included in the calculation of the individual PK parameters, the individual concentration-time plots (based on actual sample times), and in the mean concentration-time plots (based on nominal sample times). However, if there are any significant deviations from nominal sample times, some concentration data may be excluded from mean concentration-time plots and/or additional concentration-time plots of the mean data may be provided. All deviations and excluded data will be provided and discussed in the CSR.

9.2 Bioanalytical Method

Plasma concentrations of nicotine will be determined using a LC-MS/MS method at Celerion Bioanalytical Services, Lincoln, NE, using a validated analytical method with appropriate quality controls according to applicable portions of Celerion Standard Operating Procedures which were written based on the FDA Guidance for Industry: Bioanalytical Method Validation (May, 2001) and the FDA Good Laboratory Practice regulations (Title 21 CFR Part 58). The analytical range (LLOQ

– upper limit of quantitation [ULOQ]) for nicotine is expected to be 0.200 – 25.0 ng/mL.

9.3 NonCompartmental Pharmacokinetic Analysis and Parameter Calculation

9.3.1 Plasma Nicotine Pharmacokinetic Parameters

The appropriate noncompartmental PK parameters will be calculated from the plasma nicotine concentration-time data using Phoenix[®] WinNonlin[®] Version 7.0 or higher. Actual sample times will be used in the calculations of the PK parameters. Concentration data will be presented: 1) unadjusted for baseline and 2) baseline-adjusted. The baseline is the plasma nicotine concentration value obtained before the start of cigarette smoking (-5 minutes) and the adjustment will be subject-specific. For the calculation of PK parameters, plasma nicotine concentrations below the limit of quantification (BLQ) will be set to one-half (½) the LLOQ. All PK parameters included in the protocol are listed in Table 6.1 below, and are defined as appropriate for study design.

Table 6.1. Noncompartmental Pharmacokinetic Parameters to be Calculated

Parameter	Definition	Method of Determination
AUC0-180	Area under the concentration-time curve from time 0 to 180 minutes	Calculated using the Linear Trapezoidal with Linear Interpolation Method
C _{max}	The maximum observed concentration	Taken directly from bioanalytical data
T _{max}	The time to reach C _{max}	Taken from the concentration versus time data as the actual time corresponding to the maximum observed concentration

For the calculation of PK parameters, subjects must have at least 3 postproduct use data points. If the preproduct data point is missing then a value of ½ the LLOQ will be imputed. Subjects for whom there are insufficient data to calculate the PK parameters will be included in the concentration tables only.

Baseline adjustment

For PK parameters calculated using the baseline-adjusted concentrations, adjustment will be done using the reported nicotine half-life of 120 minutes (elimination rate constant, $\lambda_z = 0.0058 \text{ min}^{-1}$) with the following equation:

$$C_{t(\text{adj})} = C_t - C_0 \times e^{-\lambda_z \times t_1}$$

where $C_{t(adj)}$ is adjusted concentration, C_t is observed concentration, C_0 is the concentration at the pre-product use time point, t is actual sampling time since product administration, and t_1 is the actual sampling time since pre-product administration sample time.

After correction for pre-product use values, some concentrations may be BLQ and some may be negative values. All values obtained will be reported as is even if these values are BLQ or negative. Negative values will be assigned a value of zero in summary statistics and for PK parameter calculations.

9.4 Data Summarization and Presentation of PK Concentrations and Parameters

All nicotine PK concentrations and/or PK parameters descriptive statistics will be generated using SAS[®] and/or Phoenix[®] WinNonlin[®] as appropriate.

The plasma concentrations of nicotine will be listed by subject and summarized by study product group, time point and sex for all subjects in the PK Population. Plasma concentrations of nicotine will be presented with the same level of precision as received from the bioanalytical laboratory. Summary statistics, including n, Mean, SD, CV%, SEM, minimum, median, and maximum will be calculated for all nominal concentration time points. Excluded subjects will be included in the concentration listings, but will be excluded from the summary statistics and noted as such in the tables. All BLQ values will be presented as “BLQ” in the concentration listings and footnoted accordingly. The descriptive statistics will be presented for the PK population in both PP and ITT populations.

Mean and individual concentration-time profiles will be presented on a linear scale and semi-log scale. Linear profiles will be presented with and without SD.

Plasma nicotine PK parameters will be listed and summarized by study product group and sex for all subjects in the PK Population (from ITT and PP populations). Pharmacokinetic parameters will be reported to 3 significant figures for individual parameters, with the exception of T_{max} , which will be presented with 2 decimal places. Summary statistics (n, Mean, SD, CV%, SEM, minimum, median and maximum), will be calculated for plasma nicotine PK parameters AUC₀₋₁₈₀, C_{max} and T_{max}. In addition, geometric mean (Geom Mean) and geometric CV% (Geom CV%) will be calculated for AUC₀₋₁₈₀ and C_{max}. Excluded subjects will be listed in the PK parameter tables, but will be excluded from the summary statistics and noted as such in the tables. The descriptive statistics will be presented for the PK population in both PP and ITT populations.

The level of precision for each concentration and PK parameter statistic will be presented as follows: minimum/maximum in same precision as bioanalytical data/PK parameter, mean/median in one more level of precision than minimum/maximum, SD in one more level of precision than mean/median, n will be presented as an integer and CV% will be presented to the nearest tenth.

9.5 Statistical Analysis of PK Parameters

Paired t-tests (on AUC and Cmax) will be used to compare baseline adjusted nicotine PK parameters at the Week 2 and 6 time points with the baseline (Week -1) values. This analysis will be conducted on subjects in the PK population (from the PP population only). If data are unexpectedly found not to be normally distributed, an appropriate non-parametric test will be performed. Differences will be considered statistically significant at an alpha level of 0.05. Geometric means, geometric mean ratio (GMR), 90% confidence interval for GMR, and p-value will be presented. The analysis is based on the log-transformed data. The same SAS codes used in [Section 7.3](#) for paired t-test will be used for the analysis.

10. SUBJECTIVE EFFECTS

10.1 Measurements and Collection Schedule

The FTCD, QSU-Brief, MNWS-R, perceived health risk scale will be completed at the end of each clinic visit, at the end of Weeks -1 (Baseline), 2, 4 and 6.

10.2 Data Summarization and Presentation of Subjective Effects

10.2.1 Analysis variables

Total score for FTCD will be calculated for each subject at each time point and used as the analysis variable for FTCD questionnaire

The factor scores for QSU-brief: Responses will be used for the QSU-brief questionnaire. There are two factor scores: Factor 1 ('anticipation of pleasure from smoking' calculated as the average of the response scores from Questions 1, 3, 6, 7, and 10) and Factor 2 ('relief of nicotine withdrawal' calculated as the average of the response scores from Questions 2, 4, 5, 8, and 9).

Total score for MNWS-R (calculated as the sum of the responses for each question) will be used as the analysis variable for MNWS-R questionnaire.

Response for perceived health risk scale will be used as the analysis variable.

Questionnaire answers will be listed by subjects for each questionnaire. Change from baseline will be calculated for each post-baseline time point for the analysis variables. All data will be listed by subject and summarized by time point using descriptive statistics. The descriptive statistics will be presented for both PP and ITT populations.

10.3 Statistical Analysis of Subjective Effects

Paired t-tests will be used to compare subjective effects measures at the Week 2 and 6 time points with the baseline (Week -1) values. This analysis will be conducted on the evaluable subjects in the PP population. If data are unexpectedly found not to be

normally distributed, an appropriate non-parametric test will be performed. Differences will be considered statistically significant at an alpha level of 0.05. The same SAS codes used in [Section 7.3](#) for paired t-test will be used for the analysis.

In addition, a linear mixed model analysis of variance will be used to compare the between product group differences in the absolute change from baseline values of each of the urinary and blood BoEs. The same statistical model and SAS codes used in [Section 7.3](#) for product group comparisons will be used for the analysis.

11. SAFETY

All case report form (CRF) data will be listed by subject and chronologically by assessment time points. This will include rechecks, unscheduled assessments, and early termination.

Applicable continuous variables will be summarized using n, arithmetic mean, SD, minimum, median, and maximum.

The level of precision will be presented as follows: minimum/maximum in the same precision as in the database, mean/median in one more precision level than minimum/maximum, SD in one more precision level than mean/median, and n will be presented as an integer.

Where individual data points are missing because of dropouts or other reasons, the data will be summarized based on reduced denominators.

11.1 Subject Discontinuation

Subjects will be summarized by number of subjects enrolled, completed, and discontinued the study with discontinuation reasons by product group and overall.

11.2 Demographics

Descriptive statistics will be calculated for continuous variables (age, weight, height, and body mass index) by product group and overall. Age will be derived from date of birth to date of informed consent.

Frequency counts will be provided for categorical variables (race, ethnicity, and gender) by product group and overall.

11.3 Tobacco Product Use History

Descriptive statistics will be calculated for number of cigarettes smoked per day and number of years used tobacco product based on the self-reported tobacco product use history by product group and overall.

Frequency counts will be provided for categorical variables (Cigarette brand, brand style, flavor, and size) by product group and overall.

11.4 Adverse Events

All adverse events (AEs) occurring during this clinical trial will be coded using the Medical Dictionary for Regulatory Activities (MedDRA[®]) Version 21.0.

All AEs captured in the database will be listed in by-subject data listings including verbatim term, coded term, product, severity, relationship to study medication, and action; however, only product-use-emergent AEs (PUEAEs) will be summarized.

A PUEAE is defined as an AE that is starting or worsening at the time of or after study product administration. Each PUEAE will be attributed to a product based on the onset date and time of the AE. If an AE increases in severity, that AE will be given a resolution date and time and a new record will be initiated with the new severity. If the severity of an AE remains the same or decreases, the AE will be kept open through to resolution.

If the onset time of an AE is missing and the onset date is the same as the product administration date, then the AE will be considered product use emergent in the prior product. If onset time of an AE is missing and the onset date does not fall on an administration date, then the AE will be considered product use emergent for the last product administered. If the onset date of an AE is missing, then the AE will be considered product use emergent and attributed to the product on the study.

PUEAEs will be tabulated by System Organ Class (SOC) and Preferred Term. Summary tables will include number of subjects reporting the AE and as percent of number of subjects used study product. The number of AEs will be tabulated in a similar manner. Tables which tabulate the number of TEAEs by severity and relationship to study product will also be included.

Serious adverse events (SAEs), if present, will also be listed. Applicable narratives will be included in the CSR.

11.5 Clinical Laboratory Tests (Serum Chemistry, Hematology, Urinalysis)

Clinical laboratory tests will be performed at Screening and end-of-study.

Clinical laboratory test results will be summarized overall by time point and listed by subject.

Out-of-range values and corresponding recheck results will be listed.

11.6 Vital Signs

Vital signs (respiratory rate, pulse rate, blood pressure, and oral temperature) will be measured in the sitting position at Screening, at each study visit (weeks -1, 2, 4) and at the end-of-study (Week 6).

Vital signs will be listed by subject and time point of collection and be summarized by product group and time point.

11.7 Electrocardiogram

Electrocardiogram will be performed at Screening and listed by subject.

11.8 Concomitant Medications

All concomitant medications recorded during the study will be coded with the WHO Dictionary Version 01SEP2018 and listed.

11.9 Physical Examination

Physical examinations will be performed at Screening. Symptom-driven physical examination may performed at Week -1, end-of-study (Week 6) and follow-up. All data found in the CRF will be listed. Changes in physical examinations (if any) will be described in the text of the final report.

12. SUMMARY OF CHANGES FROM PROTOCOL-PLANNED ANALYSIS

The analyses described in this SAP are aligned with those analyses described in the protocol.

13. SUMMARY TABLES AND FIGURES

Summary tables and figures are numbered following the International Conference on Harmonization (ICH) structure but may be renumbered as appropriate during the compilation of the tables and figures for the CSR. Note that all summary tables and figures will be generated using SAS[®] Version 9.3.

13.1 In-text Summary Tables and Figures

The following is a list of table and figure titles that will be included in the text of the CSR. Tables and figures will be numbered appropriately during compilation of the CSR.

Section 10:

Table 10-1 Subject Disposition Summary (Safety and PP population)

Section 11:

Table 11-1	Demographic and Smoking History Summary (Safety and PP population)
Table 11-2	Summary of Number of Cigarettes Smoked per Week by Study Product Group and Study Week (PP Population)
Table 11-3	Statistical Comparison of Number of Cigarettes Smoked per Week at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-4	Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)
Table 11-5	Statistical Comparison of Puffing Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-6	Summary of Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Table 11-7	Statistical Comparison of Urinary NNAL Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-8	Summary of Urinary NNN Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Table 11-9	Statistical Comparison of Urinary NNN Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-10	Summary of Urinary 3-HPMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Table 11-11	Statistical Comparison of Urinary 3-HPMA Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-12	Summary of Urinary S-PMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Table 11-13	Statistical Comparison of Urinary S-PMA Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 11-14	Summary of Urinary 1-OHP Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Table 11-15	Statistical Comparison of Urinary 1-OHP Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-16	Summary of Urinary Tneq Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Table 11-17	Statistical Comparison of Urinary Tneq Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-18	Summary of Blood COHb (unit) by Study Product Group and Study Week (PP Population)
Table 11-19	Statistical Comparison of Blood COHb (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-20	Summary of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Prior to and Following Use of VLN Cigarettes (Pharmacokinetic Population from PP)
Table 11-21	Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 Versus Week -1 (Pharmacokinetic Population from PP)
Table 11-22	Summary of FTCD Score by Study Product Group and Study Week (PP Population)
Table 11-23	Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-24	Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)
Table 11-25	Statistical Comparison of QSU-Brief Factor Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-26	Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)
Table 11-27	Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Table 11-28	Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Table 11-29	Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
Figure 11-1	Arithmetic Mean Number of Cigarettes Smoked per Week by Study Product Group and Study Week at Weeks -1, 2, and 6 (PP Population)
Figure 11-2	Arithmetic Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (PP Population)
Figure 11-3	Arithmetic Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (PP Population)
Figure 11-4	Arithmetic Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (PP Population)
Figure 11-5	Arithmetic Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (PP Population)
Figure 11-6	Arithmetic Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (PP Population)
Figure 11-7	Arithmetic Mean Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Figure 11-8	Arithmetic Mean Urinary NNN Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Figure 11-9	Arithmetic Mean Urinary 3-HPMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Figure 11-10	Arithmetic Mean Urinary S-PMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Figure 11-11	Arithmetic Mean Urinary 1-OHP Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Figure 11-12	Arithmetic Mean Urinary Tneq Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
Figure 11-13	Arithmetic Mean Blood COHb (unit) by Study Product Group and Study Week (PP Population)
Figure 11-14	Arithmetic Mean Unadjusted Plasma Nicotine Concentration-Time Profiles Following Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Pharmacokinetic Population from PP)

Figure 11-15 Arithmetic Mean Baseline-Adjusted Plasma Nicotine Concentration-Time Profiles Following Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Pharmacokinetic Population from PP)

Section 12:

Table 12-1 Adverse Event Frequency - Number of Subjects Reporting the Event (% of Subjects Used Product) (Safety Population)

13.2 Section 14 Summary Tables and Figures

The following is a list of table and figure titles that will be included in Section 14 of the report. Table and figure titles may be renumbered as appropriate during the compilation of the report.

14.1 Demographic Data Summary Tables

Table 14.1.1 Summary of Disposition (Safety and PP Populations)

Table 14.1.2 Demographic Summary (Safety and PP Populations)

Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety and PP Populations)

14.2 Pharmacokinetic and Pharmacodynamic Data Summary Tables and Figures

14.2.1 Product Use Tables

Table 14.2.1.1.1 Summary of Number of Cigarettes Smoked per Week by Study Product Group and Study Week (PP Population)

Table 14.2.1.1.2 Summary of Number of Cigarettes Smoked per Week by Study Product Group and Study Week (ITT Population)

Table 14.2.1.1.2 Statistical Comparison of Number of Cigarettes Smoked per Week at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.1.1.3 Statistical Comparison of Number of Cigarettes Smoked per Week Among Study Product Groups at Weeks 2 and 6 (PP Population)

Table 14.2.1.2.1.1 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (PP Population)

Table 14.2.1.2.1.2 Summary of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (ITT Population)

Table 14.2.1.2.2 Statistical Comparison of Number of Cigarette Butts Collected per Week at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.1.2.3 Statistical Comparison of Number of Cigarette Butts Collected per Week Among Study Product Groups at Weeks 2 and 6 (PP Population)

14.2.2 Product Use Figures

Figure 14.2.2.1.1 Mean (\pm SD) of Number of Cigarettes Smoked per Week by Study Product Group and Study Week (PP Population)

Figure 14.2.2.1.2 Mean Number of Cigarettes Smoked per Week by Study Product Group and Study Week at Weeks -1, 2, and 6 (PP Population)

Figure 14.2.2.2.1 Mean (\pm SD) of Number of Cigarette Butts Collected per Week by Study Product Group and Study Week (PP Population)

Figure 14.2.2.2.2 Mean Number of Cigarette Butts Collected per Week by Study Product Group and Study Week at Weeks -1, 2, and 6 (PP Population)

14.2.3 Puff Topography Parameter Tables

Table 14.2.3.1.1 Summary of Puff Topography Parameters by Study Product Group and Study Week (PP Population)

Table 14.2.3.1.2 Summary of Puff Topography Parameters by Study Product Group and Study Week (ITT Population)

Table 14.2.3.2 Statistical Comparison of Puff Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.3.3 Statistical Comparison of Puff Topography Parameters Among Study Product Groups at Weeks 2 and 6 (PP Population)

14.2.4 Puff Topography Parameter Figures

Figure 14.2.4.1 Mean Puffing Topography Parameter (Puff Duration) by Study Product Group and Study Week (PP Population)

Figure 14.2.4.2 Mean Puffing Topography Parameter (Puff Volume) by Study Product Group and Study Week (PP Population)

Figure 14.2.4.3 Mean Puffing Topography Parameter (Peak Puff Flow Rate) by Study Product Group and Study Week (PP Population)

Figure 14.2.4.4 Mean Puffing Topography Parameter (Average Flow Rate) by Study Product Group and Study Week (PP Population)

Figure 14.2.4.5 Mean Puffing Topography Parameter (Inter-puff Interval) by Study Product Group and Study Week (PP Population)

14.2.5 Biomarker Tables

Urine NNAL

- Table 14.2.5.1.1.1.1 Summary of Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.1.1.1.2 Summary of Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.1.1.2.1 Summary of Urinary NNAL Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.1.1.2.2 Summary of Urinary NNAL Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.1.1.3.1 Summary of Urinary NNAL Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.1.1.3.2 Summary of Urinary NNAL Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.1.1.4.1 Summary of Urinary NNAL Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.1.1.4.2 Summary of Urinary NNAL Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.1.1.5.1 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.1.1.5.2 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.1.1.6.1 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.1.1.6.2 Summary of Urinary NNAL Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.1.2 Statistical Comparison of Urinary NNAL Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.1.3 Statistical Comparison of Urinary NNAL Mass Excreted (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Urine NNN

- Table 14.2.5.2.1.1.1 Summary of Urinary NNN Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.1.1.2 Summary of Urinary NNN Mass Excreted (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.2.1.2.1 Summary of Urinary NNN Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.1.2.2 Summary of Urinary NNN Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.2.1.3.1 Summary of Urinary NNN Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.1.3.2 Summary of Urinary NNN Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.2.1.4.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.1.4.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.2.1.5.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.1.5.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.2.1.6.1 Summary of Urinary NNN Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.1.6.2 Summary of Urinary NNN Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.2.2 Statistical Comparison of Urinary NNN Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.2.3 Statistical Comparison of Urinary NNN Mass Excreted (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Urine 3-HPMA

- Table 14.2.5.3.1.1.1 Summary of Urinary 3-HPMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.3.1.1.2 Summary of Urinary 3-HPMA Mass Excreted (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.3.1.2.1 Summary of Urinary 3-HPMA Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.3.1.2.2 Summary of Urinary 3-HPMA Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.3.1.3.1 Summary of Urinary 3-HPMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.3.1.3.2 Summary of Urinary 3-HPMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.3.1.4.1 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.3.1.4.2 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.3.1.5.1 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.3.1.5.2 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.3.1.6.1 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.3.1.6.2 Summary of Urinary 3-HPMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.3.2 Statistical Comparison of Urinary 3-HPMA Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.3.3 Statistical Comparison of Urinary 3-HPMA Mass Excreted (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Urine S-PMA

- Table 14.2.5.4.1.1.1 Summary of Urinary S-PMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.4.1.1.2 Summary of Urinary S-PMA Mass Excreted (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.4.1.2.1 Summary of Urinary S-PMA Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.4.1.2.2 Summary of Urinary S-PMA Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.4.1.3.1 Summary of Urinary S-PMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.4.1.3.2 Summary of Urinary S-PMA Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.4.1.4.1 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.4.1.4.2 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.4.1.5.1 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.4.1.5.2 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.4.1.6.1 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.4.1.6.2 Summary of Urinary S-PMA Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.4.2 Statistical Comparison of Urinary S-PMA Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.4.3 Statistical Comparison of Urinary S-PMA Mass Excreted (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Urine 1-OHP

- Table 14.2.5.5.1.1.1 Summary of Urinary 1-OHP Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.5.1.1.2 Summary of Urinary 1-OHP Mass Excreted (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.5.1.2.1 Summary of Urinary 1-OHP Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.5.1.2.2 Summary of Urinary 1-OHP Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.5.1.3.1 Summary of Urinary 1-OHP Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.5.1.3.2 Summary of Urinary 1-OHP Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.5.1.4.1 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.5.1.4.2 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.5.1.5.1 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.5.1.5.2 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.5.1.6.1 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.5.1.6.2 Summary of Urinary 1-OHP Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.5.2 Statistical Comparison of Urinary 1-OHP Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.5.3 Statistical Comparison of Urinary 1-OHP Mass Excreted (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Urine Tneq

- Table 14.2.5.6.1.1.1 Summary of Urinary Tneq Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.6.1.1.2 Summary of Urinary Tneq Mass Excreted (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.6.1.2.1 Summary of Urinary Tneq Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.6.1.2.2 Summary of Urinary Tneq Mass Excreted Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.6.1.3.1 Summary of Urinary Tneq Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.6.1.3.2 Summary of Urinary Tneq Mass Excreted Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.6.1.4.1 Summary of Urinary Tneq Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.6.1.4.2 Summary of Urinary Tneq Creatinine-Normalized Excretion Level (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.6.1.5.1 Summary of Urinary Tneq Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.6.1.5.2 Summary of Urinary Tneq Creatinine-Normalized Excretion Level Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.6.1.6.1 Summary of Urinary Tneq Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.6.1.6.2 Summary of Urinary Tneq Creatinine-Normalized Excretion Level Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.6.2 Statistical Comparison of Urinary 3-HPMA Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.6.3 Statistical Comparison of Urinary Tneq Mass Excreted (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

Blood COHb

- Table 14.2.5.7.1.1.1 Summary of Blood COHb (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.7.1.1.2 Summary of Blood COHb (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.7.1.2.1 Summary of Blood COHb Change from Baseline (unit) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.7.1.2.2 Summary of Blood COHb Change from Baseline (unit) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.7.1.3.1 Summary of Blood COHb Percent Change from Baseline (%) by Study Product Group and Study Week (PP Population)
- Table 14.2.5.7.1.3.2 Summary of Blood COHb Percent Change from Baseline (%) by Study Product Group and Study Week (ITT Population)
- Table 14.2.5.7.2 Statistical Comparison of Blood COHb (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.5.7.3 Statistical Comparison of Blood COHb (unit) Among Study Product Groups at Weeks 2 and 6 (PP Population)

14.2.6 Biomarker Figures

- Figure 14.2.6.1.1 Mean (\pm SD) of Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.1.2 Mean Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.2.1 Mean (\pm SD) of Urinary NNN Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.2.2 Mean Urinary NNN Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.3.1 Mean (\pm SD) of Urinary 3-HPMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.3.2 Mean Urinary 3-HPMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.4.1 Mean (\pm SD) of Urinary S-PMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.4.2 Mean Urinary S-PMA Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.5.1 Mean (\pm SD) of Urinary 1-OHP Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.5.2 MeanUrinary 1-OHP Mass Excreted (unit) by Study Product Group and Study Week (PP Population)
- Figure 14.2.6.6.1 Mean (\pm SD) of Urinary Tneq Mass Excreted (unit) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.6.2 Mean Urinary Tneq Mass Excreted (unit) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.7.1 Mean (\pm SD) of Blood COHb (unit) by Study Product Group and Study Week (PP Population)

Figure 14.2.6.7.2 Mean Blood COHb (unit) by Study Product Group and Study Week (PP Population)

14.2.7 Plasma Nicotine Tables

Concentrations

Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Table 14.2.7.1.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Table 14.2.7.2.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Table 14.2.7.2.2 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Table 14.2.7.3.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Table 14.2.7.3.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Table 14.2.7.4.1 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Table 14.2.7.4.2 Baseline Adjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Mentholated Filtered Cigarettes and Mentholated VLN Cigarettes (Pharmacokinetic Population from ITT)

Pharmacokinetics

Table 14.2.7.5.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)
Table 14.2.7.5.2	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)
Table 14.2.7.6.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Non-Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from PP)
Table 14.2.7.6.2	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Non-Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from ITT)
Table 14.2.7.7.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Non-mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from PP)
Table 14.2.7.7.2	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Non-mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from ITT)
Table 14.2.7.8.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)
Table 14.2.7.8.2	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from ITT)
Table 14.2.7.9.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Mentholated VLN (Week 2) (Pharmacokinetic Population from PP)
Table 14.2.7.9.2	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Mentholated VLN Cigarettes (Week 2) (Pharmacokinetic Population from ITT)
Table 14.2.7.10.1	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from PP)
Table 14.2.7.10.2	Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of Mentholated VLN Cigarettes (Week 6) (Pharmacokinetic Population from ITT)
Table 14.2.7.11	Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 (VLN Cigarettes) Versus Week -1 (UB Cigarettes) (Pharmacokinetic Population from PP)

14.2.8 Plasma Nicotine Figures

- Figure 14.2.8.1 Mean (SD) Unadjusted Plasma Nicotine Concentration Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.2 Mean Unadjusted Plasma Nicotine Concentration Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.3 Mean Unadjusted Plasma Nicotine Concentration Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.4 Mean (SD) Baseline Adjusted Plasma Nicotine Concentration Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.5 Mean Baseline Adjusted Plasma Nicotine Concentration Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Linear Scale) (Pharmacokinetic Population from PP)
- Figure 14.2.8.6 Mean Baseline Adjusted Plasma Nicotine Concentration Versus Time Profiles Following Use of UB (Week -1) and VLN Cigarettes (Weeks 2 and 6) (Semi-Log Scale) (Pharmacokinetic Population from PP)

Programmer's note: each figure will have 6 profiles: UB Non-Mentholated (Week -1), VLN Non-Mentholated (Week 2), VLN Non-Mentholated (Week 6), UB Mentholated (Week -1), VLN Mentholated (Week 2), and VLN Mentholated (Week 6).

14.2.9 Subjective Effect Tables

FTCD

- Table 14.2.9.1.1.1 Summary of FTCD Score by Study Product Group and Study Week (PP Population)
- Table 14.2.9.1.1.2 Summary of FTCD Score by Study Product Group and Study Week (ITT Population)
- Table 14.2.9.1.2 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)
- Table 14.2.9.1.3 Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

OSU-Brief

Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Table 14.2.9.2.1.2 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (ITT Population)

Table 14.2.9.2.2 Statistical Comparison of QSU-Brief Factor Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.2.3 Statistical Comparison of QSU-Brief Factor Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

MNWS-R

Table 14.2.9.3.1.1 Summary of MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Table 14.2.9.3.1.2 Summary of MNWS-R Total Score by Study Product Group and Study Week (ITT Population)

Table 14.2.9.3.2 Statistical Comparison of MNWS-R Total Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.3.3 Statistical Comparison of MNWS-R Total Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

Perceived Health Risk Scale

Table 14.2.9.4.1.1 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Table 14.2.9.4.1.2 Summary of Perceived Health Risk Scale by Study Product Group and Study Week (ITT Population)

Table 14.2.9.4.2 Statistical Comparison of Perceived Health Risk Scale at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Table 14.2.9.4.3 Statistical Comparison of Perceived Health Risk Scale Among Study Product Groups at Weeks 2 and 6 (PP Population)

14.2.10 Subjective Effect Figures

Figure 14.2.10.1.1 Mean (\pm SD) of FTCD Score by Study Product Group and Study Week (PP Population)

Figure 14.2.10.1.2 Mean FTCD Score by Study Product Group and Study Week (PP Population)

Figure 14.2.10.2.1.1 Mean (\pm SD) of QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)

Figure 14.2.10.2.1.2 Mean QSU-Brief Factor Score (Factor 1) by Study Product Group and Study Week (PP Population)

Figure 14.2.10.2.2.1 Mean (\pm SD) of QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)

Figure 14.2.10.2.2.2 Mean QSU-Brief Factor Score (Factor 2) by Study Product Group and Study Week (PP Population)

Figure 14.2.10.3.1 Mean (\pm SD) of MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Figure 14.2.10.3.2 Mean MNWS-R Total Score by Study Product Group and Study Week (PP Population)

Figure 14.2.10.4.1 Mean (\pm SD) of Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

Figure 14.2.10.4.2 Mean Perceived Health Risk Scale by Study Product Group and Study Week (PP Population)

14.3 Safety Data Summary Tables

14.3.1 Displays of Adverse Events

Table 14.3.1.1 Product-Use-Emergent Adverse Event Frequency – Number of Subjects Reporting the Event (% of Subject Used Study Product) (Safety Population)

Table 14.3.1.2 Product-Use -Emergent Adverse Event Frequency – Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Table 14.3.1.3 Product-Use -Emergent Adverse Event Frequency by Severity, and Relationship to Study Product – Number of Subjects Reporting Adverse Events (Safety Population)

14.3.2 Listings of Deaths, other Serious and Significant Adverse Events

Table 14.3.2.1 Serious Adverse Events (Safety Population) <if no serious adverse event occurred, a statement ‘No serious adverse event is reported’>

14.3.3 Narratives of Deaths, other Serious and Certain other Significant Adverse Events

14.3.4 Abnormal Laboratory Value Listing (each subject)

Table 14.3.4.1 Out-of-Range Values and Recheck Results – Serum Chemistry (Safety Population)

Table 14.3.4.2 Out-of-Range Values and Recheck Results – Hematology (Safety Population)

Table 14.3.4.3 Out-of-Range Values and Recheck Results – Urinalysis (Safety Population)

Table 14.3.4.4 Clinically Significant Values and Recheck Results (Safety Population)

14.3.5 Displays of Other Laboratory, Vital Signs, Electrocardiogram, Physical Examination, and Other Safety Data

Table 14.3.5.1 Clinical Laboratory Summary – Serum Chemistry (Safety Population)

Table 14.3.5.2 Clinical Laboratory Summary – hematology (Safety Population)

Table 14.3.5.3 Clinical Laboratory Summary – Urinalysis (Safety Population)

Table 14.3.5.4 Vital Sign Summary (Safety Population)

13.3 Section 16 Data Listings

Note: Hepatitis and HIV results that are provided by the clinical laboratory will not be presented in subject CRF or data listings and will not be included in any database transfer.

Data listings are numbered following the ICH structure but may be renumbered as appropriate during the compilation of the TFLs for the CSR. The following is a list of appendix numbers and titles that will be included as data listings:

16.1 Study Information

Appendix 16.1.9 Statistical Methods

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

16.2 Subject Data Listings

16.2.1 Subject Discontinuation

Appendix 16.2.1.1 Subject Discontinuation (Safety Population)

Appendix 16.2.1.2 Subject Discontinuation (Screen Failure)

16.2.2 Protocol Deviations

Appendix 16.2.2 Protocol Deviations

16.2.3 Subjects Excluded from Pharmacokinetic, Biomarker, Product Use, or Subjective Effect Analysis

Appendix 16.2.3.1 Subjects Excluded from Product Use Analysis

Appendix 16.2.3.2 Subjects Excluded from Puff Topography Analysis

Appendix 16.2.3.3 Subjects Excluded from Biomarker Analysis

Appendix 16.2.3.4 Subjects Excluded from Pharmacokinetic Analysis

Appendix 16.2.3.5 Subjects Excluded from Subjective Effect Analysis

Note: Appendices 16.2.2 and 16.2.3.1 through 16.2.3.3 are generated in MS Word for inclusion in the study report.

16.2.4 Demographic Data

Appendix 16.2.4.1 Demographics (Safety Population)

- Appendix 16.2.4.2 Physical Examination (Safety Population)
- Appendix 16.2.4.3 Medical History (Safety Population)
- Appendix 16.2.4.4 Tobacco/Nicotine Product Use History (Safety Population)

16.2.5 Compliance and/or Concentration Data

- Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met (Safety Population)
- Appendix 16.2.5.2.1 VLN Product Trial (Safety Population)
 - Appendix 16.2.5.2.2.1 Product Dispensed (Safety Population)
 - Appendix 16.2.5.2.2.2.1 Product Returned (I of II) (Safety Population)
 - Appendix 16.2.5.2.2.2.2 Product Returned (I of II) (Safety Population)
 - Appendix 16.2.5.2.2.3 Puff Topography (Safety Population)
 - Appendix 16.2.5.3.1 Plasma/Blood Sampling (Safety Population)
 - Appendix 16.2.5.3.2 24-Hour Urine Collection (Safety Population)
 - Appendix 16.2.5.4 Prior and Concomitant Medications (Safety Population)

16.2.6 Individual Pharmacokinetic/Pharmacodynamic/Product Use Response Data

- Appendix 16.2.6.1 Number of Cigarettes Smoked and Number of Cigarette Butts Collected per Week (Safety Population)
- Appendix 16.2.6.2 Puff Topography Parameters (Safety Population)
- Appendix 16.2.6.3 Urinary Total NNAL (Safety Population)
- Appendix 16.2.6.4 Urinary Total NNN (Safety Population)
- Appendix 16.2.6.5 Urinary 3-HPMA (Safety Population)
- Appendix 16.2.6.6 Urinary S-PMA (Safety Population)
- Appendix 16.2.6.7 Urinary 1-OHP (Safety Population)
- Appendix 16.2.6.8.1.1 Urinary Nicotine and Metabolites (I of II) (Safety Population)
- Appendix 16.2.6.8.1.2 Urinary Nicotine and Metabolites (II of II) (Safety Population)
- Appendix 16.2.6.8.2 Urinary Tneq (Safety Population)
- Appendix 16.2.6.9 Blood COHb (Safety Population)
- Appendix 16.2.6.10 Plasma Cotinine (Safety Population)
- Appendix 16.2.6.11.1 Unadjusted Plasma Nicotine Concentrations Versus Time (Linear and Semi-Log Scale) for Subject <#>
- Appendix 16.2.6.11.2 Baseline Adjusted Plasma Nicotine Concentrations Versus Time (Linear and Semi-Log Scale) for Subject <#>
- Appendix 16.2.6.12 FTCD Response and Score (Safety Population)
- Appendix 16.2.6.13 QSU-Brief Response and Factor Score (Safety Population)
- Appendix 16.2.6.14 MNWS-R Response and Total Score (Safety Population)
- Appendix 16.2.6.15 Perceived Health Risk Scale (Safety Population)

16.2.7 Adverse Events Listings

Appendix 16.2.7.1 Adverse Events (Safety Population)

16.2.8 Listings of Individual Laboratory Measurements and Other Safety Observations

Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Appendix 16.2.8.1.2 Clinical Laboratory Report - Hematology (Safety Population)

Appendix 16.2.8.1.3 Clinical Laboratory Report - Urinalysis (Safety Population)

Appendix 16.2.8.1.4 Clinical Laboratory Report – Comments (Safety Population)

Appendix 16.2.8.1.5 Urine Drug Screens (Safety Population)

Appendix 16.2.8.1.6 Pregnancy Tests (Safety Population)

Appendix 16.2.8.1.7 Serum FSH (Safety Population)

Appendix 16.2.8.1.8 Urine Cotinine Screens (Safety Population)

Appendix 16.2.8.1.9 Serology Sample Collection (Safety Population)

Appendix 16.2.8.1.10 Exhaled CO Measurement (Safety Population)

Appendix 16.2.8.2 Vital Signs (Safety Population)

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

Appendix 16.2.8.4 Phone Call (Safety Population)

14. TABLE AND FIGURE SHELLS

The following table shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the tables that will be presented and included in the final report. Unless otherwise noted, all tables will be presented in Times New Roman font size 8. These tables will be generated using Celerion ADaM Version 1.0.

14.1 In-text Summary Tables Shells

In-text Table 10-1 will be in the following format:

Table 10-1 Disposition Summary

Population	Disposition	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall
Safety	Enrolled	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)
	Completed	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Discontinued Early	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Reason for Discontinuation	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
ITT	Enrolled	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)
	Completed	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Discontinued Early	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Reason for Discontinuation	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
PP	Enrolled	X (100%)	X (100%)	X (100%)	X (100%)	X (100%)
	Completed	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Discontinued Early	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
	Reason for Discontinuation	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes Source: Table 14.1.1 Program: /CAXXXXX/sas_prg/stsas/intexttest/t_disp.sas DDMMYYYY HH:MM						

In-text Table 11-1 will be in the following format:

Table 11-1 Demographic and Smoking History Summary

Population	Trait	Category/Statistics	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UN Mentholated	Overall
Safety	Gender	Male	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
		Female	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
	Race	Asian	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
		Black or African American	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
		White	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
	Ethnicity	Not Hispanic or Latino	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
		Hispanic or Latino	X(XX%)	X(XX%)	X(XX%)	X(XX%)	X(XX%)
	Age (yrs)	n	X	X	X	X	X
		Mean	XX.X	XX.X	XX.X	XX.X	XX.X
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Minimum	XX	XX	XX	XX	XX
		Median	XX.X	XX.X	XX.X	XX.X	XX.X
		Maximum	XX	XX	XX	XX	XX
	BMI (kg/m ²)	n	X	X	X	X	X
		Mean	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX
		SD	X.XXXX	X.XXXX	X.XXXX	X.XXXX	X.XXXX
		Minimum	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Median	XX.XXX	XX.XXX	XX.XXX	XX.XXX	XX.XXX
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X
	CPD	n	X	X	X	X	X
		Mean	XX.X	XX.X	XX.X	XX.X	XX.X
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Minimum	XX	XX	XX	XX	XX
		Median	XX.X	XX.X	XX.X	XX.X	XX.X
		Maximum	XX	XX	XX	XX	XX
	Duration (Years)	n	X	X	X	X	X
		Mean	XX.X	XX.X	XX.X	XX.X	XX.X
		SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Minimum	XX	XX	XX	XX	XX
		Median	XX.X	XX.X	XX.X	XX.X	XX.X

Population	Trait	Category/Statistics	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UN Mentholated	Overall
		Maximum	XX	XX	XX	XX	XX
BMI = Body mass index, CPD = Cigarettes per day Age is calculated at the date of the informed consent. UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes Source: Tables 14.1.2 and 14.1.3 Program: /CAXXXXX/sas_prg/stsas/intexttest/t_dem.sas DDMMYYYY HH:MM							

Programmer Note: ITT and PP population will also be presented in the table.

In-text Table 11-2 will be in the following format:

Table 11-2 Summary of Number of Cigarettes Smoked per Week by Study Product Group and Study Week (PP Population)

Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated
Week -1 *	n	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX
Week 1	n	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX
<p>*Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes</p> <p>Source: Table 14.2.1.1.1.1 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM</p>					

Programmer Note: All study weeks will be presented in the table.

In-text Table 11-3 will be in the following format:

Table 11-3 Statistical Comparison of Number of Cigarettes Smoked per Week at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week – Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Week 6	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes Paired t-test method is used to perform the analysis.</p> <p>Source: Table 14.2.1.1.2 Program: /CAXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM</p>						

In-text Table 11-4 will be in the following format:

Table 11-4 Summary of Puffing Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter	Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Non-Mentholated	UB Combined
Puff Duration (unit)	Week -1*	n	X	X	X	X	X	X
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
	Week 2	n	X	X	X	X	X	X
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
	Week 6	n	X	X	X	X	X	X
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
*Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes								
Source: Table 14.2.3.1.1 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM								

Programmer Note: All topography parameters will be presented in the table.

In-text Table 11-5 will be in the following format:

Table 11-5 Statistical Comparison of Puffing Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Parameter	Study Week	Product Group	Means		Difference (Test Week – Baseline)	XX% Confidence Interval	p-value
			Test Week	Baseline			
Puff Duration (unit)	Week 2	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	Week 6	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects’ UB non-mentholated filtered cigarettes UB mentholated = Subjects’ UB mentholated filtered cigarettes Paired t-test method is used to perform the analysis.							
Source: Table 14.2.3.2 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM							

Programmer Note: All topography parameters will be presented in the table.

In-text Tables 11-6, 11-8, 11-10, 11-12, 11-14, 11-16, 11-18 will be in the following format:

Table 11-6 Summary of Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week (PP Population)

Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Non-Mentholated	UB Combined
Week -1*	n	X	X	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 2	n	X	X	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 6	n	X	X	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
<p>*Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes</p> <p>Source: Table 14.2.5.1.1.1 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM</p>							

In-text Tables 11-7, 11-9, 11-11, 11-13, 11-15, 11-17, 11-19 will be in the following format:

Table 11-7 Statistical Comparison of Urinary NNAL Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week – Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Week 6	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes Paired t-test method is used to perform the analysis.</p> <p>Source: Table 14.5.1.2 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM</p>						

In-text Table 11-20 will be in the following format:

Table 11-20 Summary of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Prior to and Following Use of VLN Cigarettes (Pharmacokinetic Population)

Study Week	Pharmacokinetic Parameters	Product <Y>	Product <X>
Week -1	Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
	Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
	Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Week 2	Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
	Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
	Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
Week 6	Param1 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
	Param2 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
	Param3 (units)	XXX.X (XX.X) [n=xx]	XXX.X (XX.X) [n=xx]
*Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes AUCs and Cmax values are presented as geometric mean and geometric CV%. Tmax values are presented as median (min, max). Source: Tables 14.2.7.5.1, 14.2.7.6.1, 14.2.7.7.1, 14.2.7.8.1, 14.2.7.9.1, and 14.2.7.10.1			

Notes for Generating the Actual Table:

The following PK parameters will be presented in the following order and with following units: AUC₀₋₁₈₀ (min*ng/mL), C_{max} (ng/mL) and T_{max} (min)
 n will be presented as an integer (with no decimal);
 Please remove footnote 'other parameters are presented...' as this is not applicable.
 Please add column to indicate study week
 Summary statistics will be presented by sex and overall with the same precision as defined in post-text shells
 4 products will be presented in Table 11-20: VLN Non-Mentholated, VLN Non-Mentholated, UB Non-Mentholated, and UB Non-Mentholated.

Program: /CAXXXX/sas_prg/pksas/intext-pk-tables.sas DDMMYYYY HH:MM
 Program: /CAXXXX/sas_prg/pksas/adam_intext_pkparam.sas DDMMYYYY HH:MM

In-text Table 11-21 will be in the following format:

Table 11-21 Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 Versus Week -1 (Pharmacokinetic Population from PP)

Parameter	Study Week	Product Group	LSMeans		GMR (Test Week / Baseline)	XX% Confidence Interval	p-value
			Test Week	Baseline			
AUC0-180	Week 2	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	Week 6	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects’ UB non-mentholated filtered cigarettes UB mentholated = Subjects’ UB mentholated filtered cigarettes Analysis is based on the log-transformed data. Paired t-test method is used to perform the analysis.							
Source: Table 14.2.7.11 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM							

Programmer Note: Cmax will also be presented in the table.

In-text Tables 11-22, 11-26, and 11-28 will be in the following format:

Table 11-22 Summary of FTCD Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	X	X	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 2	n	X	X	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
Week 6	n	X	X	X	X	X	X
	Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
	Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
<p>*Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes</p> <p>Source: Table 14.2.9.1.1 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM</p>							

In-text Tables 11-23, 11-27, and 11-29 will be in the following format:

Table 11-23 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week – Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Week 6	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
<p>Baseline = Week -1 Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes Paired t-test method is used to perform the analysis.</p> <p>Source: Table 14.9.1.2 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM</p>						

In-text Table 11-24 will be in the following format:

Table 11-24 Summary of QSU-brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Factor 1	Week -1*	n	X	X	X	X	X	X
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
	Week 2	n	X	X	X	X	X	X
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
	Week 6	n	X	X	X	X	X	X
		Mean (SD)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)	XX.X (XX.XX)
		Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
		Range	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX	XX, XX
*Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes UB mentholated = Subjects' UB mentholated filtered cigarettes								
Source: Table 14.2.9.2.1 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMYYYY HH:MM								

Programmer Note: Factor 2 will also be presented in the table.

In-text Table 11-25 will be in the following format:

Table 11-25 Statistical Comparison of QSU-brief Factor Score at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Factor	Study Week	Product Group	Means		Difference (Test Week – Baseline)	XX% Confidence Interval	p-value
			Test Week	Baseline			
Factor 1	Week 2	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	Week 6	VLN Non- Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
Baseline = Week -1 *Subjects used their own usual brand cigarettes at Week -1. VLN non-mentholated = Non-mentholated VLN cigarettes VLN mentholated = Mentholated VLN cigarettes UB non-mentholated = Subjects’ UB non-mentholated filtered cigarettes UB mentholated = Subjects’ UB mentholated filtered cigarettes Paired t-test method is used to perform the analysis.							
Source: Table 14.2.9.2.2 Program: /CAXXXXX/sas prg/stsas/intexttest/t dem.sas DDMMMYYYY HH:MM							

Programmer Note: Factor 2 will also be presented in the table.

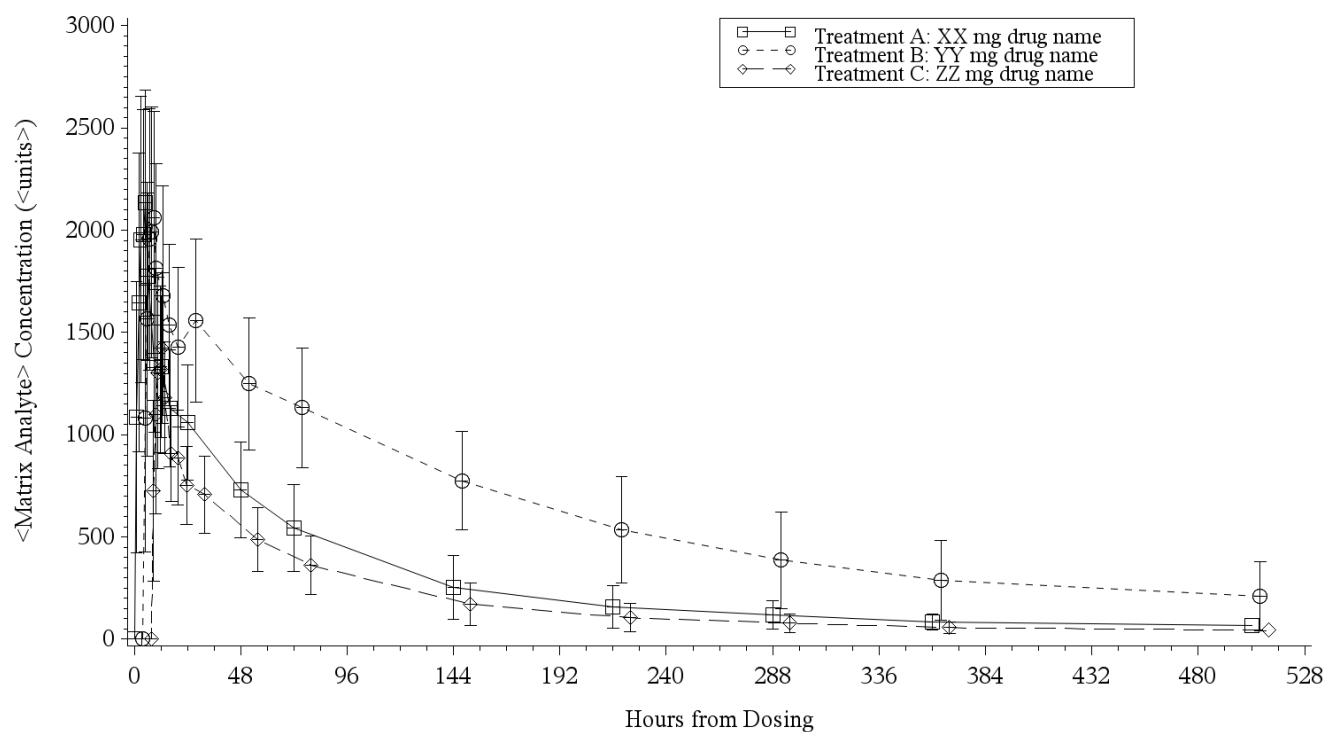
In-text Table 12-1 will be in the following format:

Table 12-1 Adverse Event Frequency - Number of Subjects Reporting the Event (% of Subjects Used Product)

Adverse Events*	Baseline	VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	Overall#
Number of Subjects Used Study Product	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)	XX (100%)
Number of Subjects With Adverse Events	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
General disorders and administration site conditions	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Vessel puncture site pain	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Vessel puncture site reaction	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
<p>*Adverse events are classified according to MedDRA® Version 21.0 Subjects used their own usual brand cigarettes at Week -1. Although a subject may have had 2 or more clinical adverse experiences, the subject is counted only once within a category. The same subject may appear in different categories. # Overall includes AEs after the start of Week1 product use.</p> <p>Source: Table 14.3.1.1 Program: /CAXXXXX/sas_prg/stsas/intexttest/t_ae.sas DDMMMYYYY HH:MM</p>						

14.2 Figures Shells

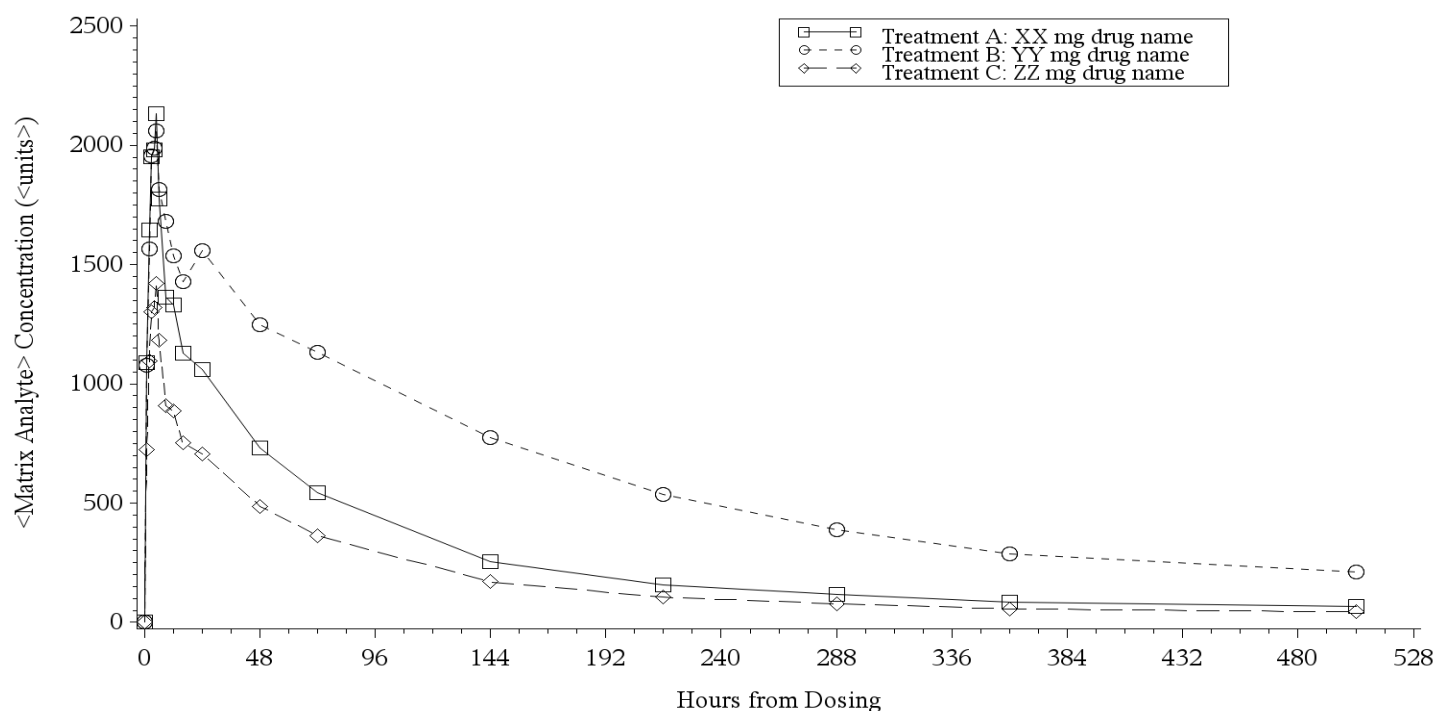
Figures 14.2.2.1.1, 14.2.2.2.1, 14.2.6.1.1, 14.2.6.2.1, 14.2.6.3.1, 14.2.6.4.1, 14.2.6.5.1, 14.2.6.6.1, 14.2.6.7.1, 14.2.8.1, 14.2.8.4, 14.2.10.1.1, 14.2.10.2.1.1, 14.2.10.2.2.1, 14.2.10.3.1, and 14.2.10.4.1 will be in the following format:



Treatments B and C are shifted to the right for ease of reading
 Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMYYYY HH:MM
 Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMYYYY HH:MM

Programmer's note: in the legend and footnotes, "Treatment" will be referred to as "Product" with the appropriate descriptions. The x-axis will be labeled "Time (Minutes)".

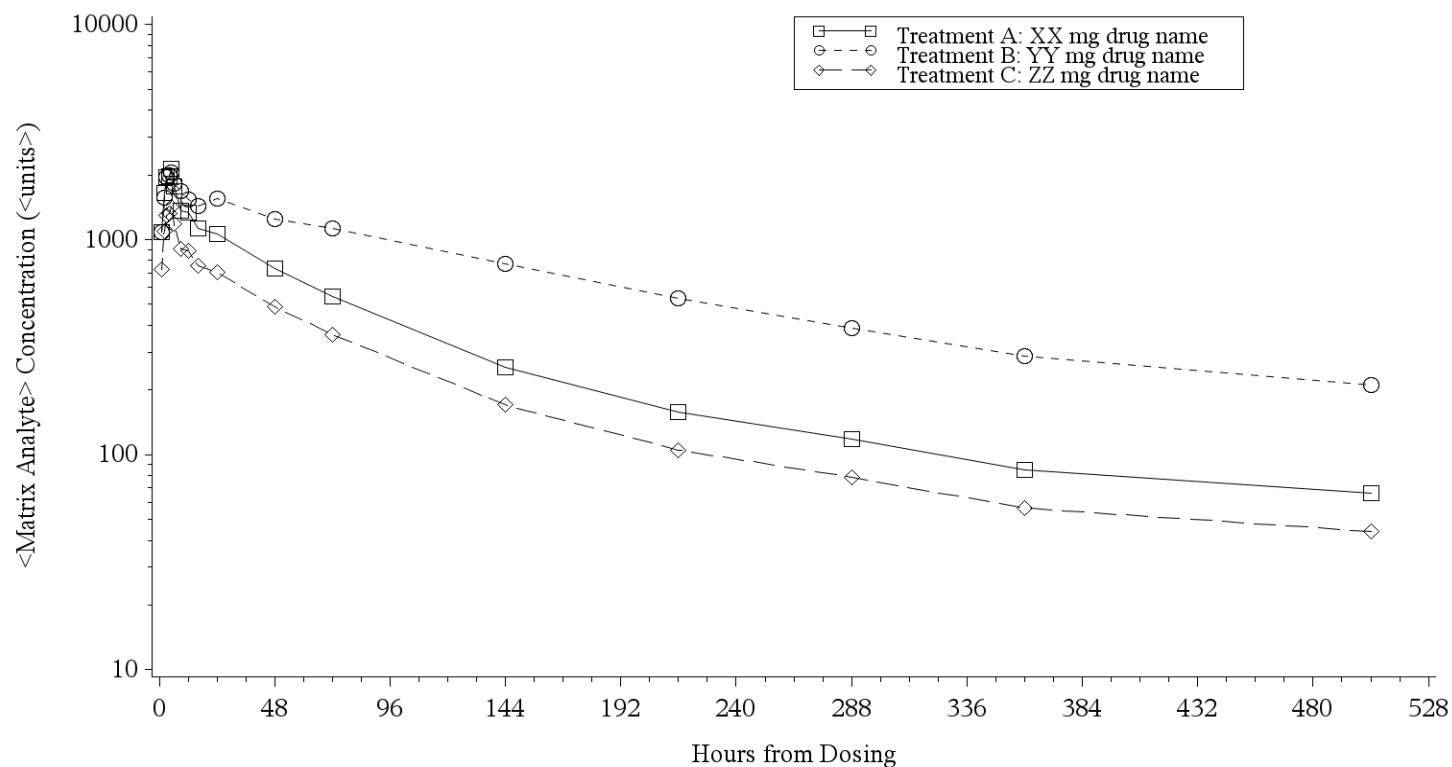
In-text Figures 11-1 through and 11-15 and post-text Figures 14.2.8.2, 14.2.8.5, 14.2.2.1.2, 14.2.2.2.2, 14.2.4.1 through 14.2.4.5, 14.2.6.1.2, 14.2.6.2.2, 14.2.6.3.2, 14.2.6.4.2, 14.2.6.5.2, 14.2.6.6.2, 14.2.6.7.2, 14.2.10.1.2, 14.2.10.2.1.2, 14.2.10.2.2.2, 14.2.10.3.2, and 14.2.10.4.2 will be presented in the following format:



Program: /CAXXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMYYYY HH:MM
 Program: /CAXXXXXX/sas_prg/pksas/meangraph.sas DDMMYYYY HH:MM

Programmer's note: in the legend and footnotes, "Treatment" will be referred to as "Product" with the appropriate descriptions. The x-axis will be labeled "Time (Minutes)".

Figures 14.2.8.3 and 14.2.8.6 will be presented in the following format:



Program: /CAXXXXX/sas_prg/pksas/adam_meangraph.sas DDMMYYYY HH:MM

Program: /CAXXXXX/sas_prg/pksas/meangraph.sas DDMMYYYY HH:MM

Programmer's note: in the legend and footnotes, "Treatment" will be referred to as "Product" with the appropriate descriptions. The x-axis will be labeled "Time (Minutes)".

14.3 Section 14 Summary Tables Shells

Post-text Table 14.1.1 will be in the following format:

Part 1 of X

Table 14.1.1 Summary of Disposition (Safety and PP Populations)

Population	Category	Study Product Group				Overall
		VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
Safety	Enrolled	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
	Completed	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)
	Discontinued Early	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
	<Reason1>	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
	<Reason2>	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
mITT	Enrolled	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
	Completed	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)
	Discontinued Early	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
	<Reason1>	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
	<Reason2>	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
PP	Enrolled	XX(100%)	XX(100%)	XX(100%)	XX(100%)	XX(100%)
	Completed	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)	XX(XX%)
	Discontinued Early	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
	<Reason1>	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)
	<Reason2>	X(X%)	X(X%)	X(X%)	X(X%)	X(X%)

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /XAXXXXX/ECR/sas_prg/stsas/tab prog_name.sas DDMMYYYY HH:MM

Post-text Table 14.1.2 will be in the following format:

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Table 14.1.2 Demographic Summary (Safety and PP Populations)

Population Trait			Study Product Group				Overall
			VLN Non-Mentholated	VLN Mentholated	UB Non-Mentholated	UB Mentholated	
Safety	Gender	Male	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		Female	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Race	American Indian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		Asian	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		Black	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Age* (yrs)	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Weight (kg)	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Height (cm)	n	X	X	X	X	X
		Mean	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		SD	X.XXX	X.XXX	X.XXX	X.XXX	X.XXX
		Minimum	XX.X	XX.X	XX.X	XX.X	XX.X
		Median	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
		Maximum	XX.X	XX.X	XX.X	XX.X	XX.X

Note: * Age is derived from birth date to date of informed consent.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Summary for ITT and PP population will also be presented in the table.

Post-text Table 14.1.3 will be in the following format:

Page 1 of X

Table 14.1.3 Tobacco/Nicotine Product Use History Summary (Safety and PP Populations)

Population Trait			Study Product Group				Overall
			VLN Non-Mentholated	UB Non-Mentholated	VLN Mentholated	UB Mentholated	
Safety	Brand	XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Brand Style	XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Flavor	XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Size	XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
		XXXXXX	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)	X (XX.X%)
	Duration (yrs)	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	CPD	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX

Note: CPD = Cigarettes per day
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Summary for ITT and PP population will also be presented in the table.

Post-text Tables 14.2.1.1.1-2 and 14.2.1.2.1-2 will be in the following format:

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Table 14.2.1.1.1.1 Summary of Number of Cigarettes Smoked per Week by Study Product Group and Study Week
(PP Population)

Study Week	Statistics	Study Product Group					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
Week 1	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX

Note: *Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: All study weeks will be presented in the table.

Post-text Tables 14.2.1.1.2 and 14.2.1.2.2 will be in the following format:

Page 1 of X

Table 14.2.1.1.2 Statistical Comparison of Number of Cigarettes Smoked per Week at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week - Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Week 6	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Tables 14.2.1.1.3 and 14.2.1.2.3 will be in the following format:

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Table 14.2.1.1.3 Statistical Comparison of Number of Cigarettes Smoked per Week Among Study Product Groups
 at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		XX%	p-value
		Test (n)	Reference (n)	(Test - Reference)	Confidence Interval		
Week 2	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX		X.XXXX
	VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX		X.XXXX
	VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX		X.XXXX
Week 6	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX		X.XXXX
	VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX		X.XXXX
	VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX	XX.XX - XXX.XX		X.XXXX

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis

Test = The first product in the comparison
 Reference = The second product in the comparison

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Tables 14.2.3.1.1-2 will be in the following format:

Page 1 of X

Table 14.2.3.1.1 Summary of Puff Topography Parameters by Study Product Group and Study Week (PP Population)

Parameter(unit)	Study Week	Statistics	Study Product Group				
			VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated
Puff Duration (XX)	Week -1*	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Week 2	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX

Note: *Subjects used their own usual brand cigarettes at Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Study Week 6 and other topography parameters will also be presented in the table.

Post-text Table 14.2.3.2 will be in the following format:

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Table 14.2.3.2 Statistical Comparison of Puff Topography Parameters at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

Parameter(unit)	Study Week	Product Group	Means		Difference (Test Week - Baseline)	XX% Confidence Interval	p-value
			Test Week	Baseline			
Puff Duration (XX)	Week 2	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	Week 6	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Paired t-test method is used to perform the analysis.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Other topography parameters will also be presented in the table.

Post-text Table 14.2.3.3 will be in the following format:

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Table 14.2.3.3 Statistical Comparison of Puff Topography Parameters Among Study Product Groups at Weeks 2 and 6
 (PP Population)

Parameter(unit)	Study Week	Comparison	----- LSMeans -----		LSMean Difference		XX% Confidence	
			Test (n)	Reference (n)	(Test - Reference)		Interval	p-value
Puff Duration (XX)	Week 2	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
	Week 6	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis

Test = The first product in the comparison
 Reference = The second product in the comparison

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Other topography parameters will also be presented in the table.

Post-text Tables 14.2.5.1.1.1-2, 14.2.5.1.1.4.1-2, 14.2.5.2.1.1.1-2, 14.2.5.2.1.4.1-2, 14.2.5.3.1.1.1-2, 14.2.5.3.1.4.1-2, 14.2.5.4.1.1.1-2, 14.2.5.4.1.4.1-2, 14.2.5.5.1.1.1-2, 14.2.5.5.1.4.1-2, 14.2.5.6.1.1.1-2, 14.2.5.6.1.4.1-2, and 14.2.5.7.1.1.1-2 will be in the following format:

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Table 14.2.5.1.1.1.1 Summary of Urinary NNAL Mass Excreted (unit) by Study Product Group and Study Week
(PP Population)

Study Week	Statistics	Study Product Group					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
Week 2	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX

Note: *Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Week 6 will also be presented in the table.

Post-text Tables 14.2.5.1.1.2.1-2, 14.2.5.1.1.3.1-2, 14.2.5.1.1.5.1-2, 14.2.5.1.1.6.1-2, 14.2.5.2.1.2.1-2, 14.2.5.2.1.3.1-2, 14.2.5.2.1.5.1-2, 14.2.5.2.1.6.1-2, 14.2.5.3.1.2.1-2, 14.2.5.3.1.3.1-2, 14.2.5.3.1.5.1-2, 14.2.5.3.1.6.1-2, 14.2.5.4.1.2.1-2, 14.2.5.4.1.3.1-2, 14.2.5.4.1.5.1-2, 14.2.5.4.1.6.1-2, 14.2.5.5.1.2.1-2, 14.2.5.5.1.3.1-2, 14.2.5.5.1.5.1-2, 14.2.5.5.1.6.1-2, 14.2.5.6.1.2.1-2, 14.2.5.6.1.3.1-2, 14.2.5.6.1.5.1-2, 14.2.5.6.1.6.1-2, 14.2.5.7.1.2.1-2, and 14.2.5.7.3.1-2 will be in the following format:

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Table 14.2.5.1.1.2.1 Summary of Urinary NNAL Mass Excreted Change from Baseline (unit)
by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week 2	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
Week 6	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Tables 14.2.5.1.2, 14.2.5.2.2, 14.2.5.3.2, 14.2.5.4.2, 14.2.5.5.2, 14.2.5.6.2, and 14.2.5.7.2 will be in the following format:

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Table 14.2.5.1.2 Statistical Comparison of Urinary NNAL Mass Excreted (unit) at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week - Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXXX
Week 6	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXXX

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Tables 14.2.5.1.3, 14.2.5.2.3, 14.2.5.3.3, 14.2.5.4.3, 14.2.5.5.3, 14.2.5.6.3, and 14.2.5.7.3 will be in the following format:

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Table 14.2.5.1.3 Statistical Comparison of Urinary NNAL Mass Excreted (unit) Among Study Product Groups
 at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----			LSMean Difference (Test - Reference)	XX% Confidence Interval	p-value
		Test (n)	Reference (n)				
Week 2	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)		XXX.XX	XX.XX - XXX.XX	X.XXXX
	VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)		XXX.XX	XX.XX - XXX.XX	X.XXXX
	VLN Combined vs UB Combined	X.XX (X)	X.XX (X)		XXX.XX	XX.XX - XXX.XX	X.XXXX
Week 6	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)		XXX.XX	XX.XX - XXX.XX	X.XXXX
	VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)		XXX.XX	XX.XX - XXX.XX	X.XXXX
	VLN Combined vs UB Combined	X.XX (X)	X.XX (X)		XXX.XX	XX.XX - XXX.XX	X.XXXX

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
 n = Number of observation used in the analysis

Test = The first product in the comparison
 Reference = The second product in the comparison

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB Non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Tables 14.2.7.1.1 through 14.2.7.4.2 will be in the following format:

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Table 14.2.7.1.1 Unadjusted Plasma Nicotine Concentrations (ng/mL) Following Use of UB Non-Mentholated Filtered Cigarettes and Non-Mentholated VLN Cigarettes (Pharmacokinetic Population from PP)

Subject	Sample Times (min)								
Number	XX	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
X	BLQ	XX	XX	XX	XX	XX	XX	XX	XX
n	XX	XX	XX	XX	XX	XX	XX	XX	XX
Mean	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	.	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX	XX	XX	XX	XX	XX	XX	XX	XX
Median	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
Maximum	XX	XX	XX	XX	XX	XX	XX	XX	XX

For the calculation of summary statistics, values that are below the limit of quantitation (BLQ) of <XX> are treated as 1/2 limit of quantitation.

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

Concentrations will be presented to same precision as in bio data.

Summary statistics presentation with respect to the precision of the bioanalytical data: n = integer; Mean and Median +1; SD and SEM +2, Min and Max +0, CV% to 1 decimal. Summary statistics will be presented by sex and overall.

Programmer Note:

A row will be added above 'sample time' which will be labelled 'Week' and will have the following numbers: -1, 2, and 6

PK Time points are from Protocol: i.e. preproduct use and 2, 5, 7, 10, 12, 15, 20, 30, 45, 60, 90, 120, 150, and 180 minutes postproduct use

Note that 'sample time' is in 'min' not 'hr'

For Tables 14.2.7.3.1 through 14.2.7.4.2 the following footnote will be added if applicable: 'For the calculation of summary statistics, negative values are assigned a value of zero'

Table follows CPConcl template

Per study design needs, the following changes are made to this table relative to Celerion standard: columns <Product Sequence> and <Study Period> will be removed. Summary statistics will be presented by sex and overall.

```
Program: /CAXXXX/sas_prg/pksas/pk-conc-tables.sas      DDMMYYYY HH:MM  
Program: /CAXXXX/sas_prg/pksas/pk-conc-tables-sig.sas  DDMMYYYY HH:MM  
Program: /CAXXXX/sas_prg/pksas/adam_conc.sas          DDMMYYYY HH:MM
```

Post-text Tables 14.2.7.5.1 through 14.2.7.10.2 will be in the following format:

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Table 14.2.7.5.1 Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters Following Use of UB Non-Mentholated Filtered Cigarettes (Week -1) (Pharmacokinetic Population from PP)

Subject Number	Parameters					
	param1 (units)	param2 (units)	param3 (units)	param4 (units)	param5 (units)	param6 (units)
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
X	X.XX	X.XX	XXX	XXX	XX.X	X.XXX
X	XXX	X.XX	XXX	XXX	XX.X	X.XXX
n	XX	XX	XX	XX	XX	XX
Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
SD	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
SEM	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX	XX.XX
Minimum	XX.X	X.XX	XXX	XXX	XX.X	X.XXX
Median	XX.XX	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Maximum	XXX	X.XX	XXX	XXX	XX.X	X.XXX
Geom Mean	XXX.X	X.XXX	XXX.X	XXX.X	XX.XX	X.XXXX
Geom CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X

. = Value missing or not reportable.

Notes for Generating the Actual Table:

Presentation of Data:

- PK Parameters will be presented in the following order and with following units: AUC0-180 (min*ng/mL), C_{max} (ng/mL), T_{max} (min)

- n will be presented as an integer (with no decimal); Cmax will be presented with precision of the bioanalytical data
- AUC will be presented with, at maximum, the precision of the bioanalytical data, and, at minimum, 3 significant figures (to be determined by the PKist once bioanalytical data are received).
- Summary statistics for parameters will be presented (with respect to the precision of the PK parameter data) as: Mean, Median, and Geom Mean+1; SD and SEM +2, Min and Max +0. Geom Mean and Geom CV% will not be presented for Tmax.
- CV% and Geom CV% for all parameters will be presented with 1 decimal
- Summary statistics will be presented by sex and overall
- Table follows CPPar1 template

Per study design needs, the following changes are made to this table relative to Celerion standard: columns <Product Sequence> and <Study Period> will be removed. Summary statistics will be presented by sex and overall.

Program: /CAXXXX/sas_prg/pksas/pk-tables.sas DDMMYYYY HH:MM
Program: /CAXXXX/sas_prg/pksas/adam_pkparam.sas DDMMYYYY HH:MM

Post-text Table 14.2.7.11 will be in the following format:

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Table 14.2.7.11 Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters at Weeks 2 and 6 (VLN Cigarettes) Versus Week -1 (UB Cigarettes) (Pharmacokinetic Population from PP)

Study Week	Product Group	Geometric Means		GMR (Test Week / Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
Week 6	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Analysis is based on the log-transformed data.
 Paired t-test method is used to perform the analysis.
 Geometric means are calculated by exponentiating the means.
 Geometric Mean Ratios (GMR) are calculated by exponentiating the mean of difference from paired t-test.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Table 14.2.9.1.1.1-2, 14.2.9.3.1.1-2, and 14.2.9.4.1.1-2 will be in the following format:

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Table 14.2.9.1.1.1 Summary of FTCD Score by Study Product Group and Study Week (PP Population)

Study Week	Statistics	Study Product Group					
		VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated	UB Combined
Week -1*	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX
Week 2	n	X	X	X	X	X	X
	Mean	X.X	X.X	X.X	X.X	X.X	X.X
	SD	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	CV%	XX.X	XX.X	XX.X	XX.X	XX.X	XX.X
	SEM	X.XX	X.XX	X.XX	X.XX	X.XX	X.XX
	Minimum	XX	XX	XX	XX	XX	XX
	Median	X.X	X.X	X.X	X.X	X.X	X.X
	Maximum	XX	XX	XX	XX	XX	XX

Note: *Subjects used their own usual brand cigarettes at Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Study Week 6 will also be presented in the table.

Post-text Tables 14.2.9.1.2, 14.2.9.3.2, and 14.2.9.4.2 will be in the following format:

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Table 14.2.9.1.2 Statistical Comparison of FTCD Score at Weeks 2 and 6 Versus Week -1
 by Study Product Group (PP Population)

Study Week	Product Group	Means		Difference (Test Week - Baseline)	XX% Confidence Interval	p-value
		Test Week	Baseline			
Week 2	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
Week 6	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
	UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX

Note: Baseline = Week -1
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 Paired t-test method is used to perform the analysis.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Tables 14.2.9.1.3, 14.2.9.3.3, and 14.2.9.4.3 will be in the following format:

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Table 14.2.9.1.3 Statistical Comparison of FTCD Score Among Study Product Groups at Weeks 2 and 6 (PP Population)

Study Week	Comparison	----- LSMeans -----		LSMean Difference		XX% Confidence Interval	p-value
		Test (n)	Reference (n)	(Test - Reference)			
Week 2	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
	VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
	VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
Week 6	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
	VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
	VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
n = Number of observation used in the analysis

Test = The first product in the comparison
Reference = The second product in the comparison

VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Table 14.2.9.2.1.1-2 will be in the following format:

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Table 14.2.9.2.1.1 Summary of QSU-Brief Factor Score by Study Product Group and Study Week (PP Population)

Factor	Study Week	Statistics	Study Product Group				
			VLN Non-Mentholated	VLN Mentholated	VLN Combined	UB Non-Mentholated	UB Mentholated
Factor 1	Week -1*	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX
	Week 2	n	X	X	X	X	X
		Mean	X.X	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX	X.XX
		CV%	XX.X	XX.X	XX.X	XX.X	XX.X
		SEM	X.XX	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX	XX

Note: *Subjects used their own usual brand cigarettes at Week -1.

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Study Week 6 and Factor 2 will also be presented in the table.

Post-text Table 14.2.9.2.2 will be in the following format:

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Table 14.2.9.2.2 Statistical Comparison of QSU-Brief Factor Score at Weeks 2 and 6 Versus Week -1
by Study Product Group (PP Population)

Factor	Study Week	Product Group	Means		Difference (Test Week - Baseline)	XX% Confidence Interval	p-value
			Test Week	Baseline			
Factor 1	Week 2	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
	Week 6	VLN Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		VLN Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Non-Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Mentholated	XXX	XXX	XXX	XXX - XXX	X.XXXX
		UB Combined	XXX	XXX	XXX	XXX - XXX	X.XXXX

Note: Baseline = Week -1
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Paired t-test method is used to perform the analysis.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Factor 2 will also be presented in the table.

Post-text Table 14.2.9.2.3 will be in the following format:

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Table 14.2.9.2.3 Statistical Comparison of QSU-Brief Factor Score Among Study Product Groups
at Weeks 2 and 6 (PP Population)

Factor	Study Week	Comparison	----- LSMeans -----		LSMean Difference XX% Confidence		Interval	p-value
			Test (n)	Reference (n)	(Test - Reference)			
Factor 1	Week 2	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
	Week 6	VLN Non-mentholated vs UB Non-mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Mentholated vs UB Mentholated	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX
		VLN Combined vs UB Combined	X.XX (X)	X.XX (X)	XXX.XX		XX.XX - XXX.XX	X.XXXX

Note: LSMeans, LSmean difference, CI and p-values are from the ANOVA.
n = Number of observation used in the analysis

Test = The first product in the comparison
Reference = The second product in the comparison

VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Factor 2 will also be presented in the table.

Post-text Table 14.3.1.1 will be in the following format:

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Table 14.3.1.1 Product-Use-Emergent Adverse Event Frequency-
 Number of Subjects Reporting the Event (% of Subjects (% of Subject Used Study Product) (Safety Population)

Adverse Event*	Baseline	VLN Non- Mentholated	VLN Mentholated	UBN non- Mentholated	UB Mentholated	Overall#
Number of Subjects Use Study Product	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)
Number of Subjects With PUEAEs^	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)	X (XX%)
Number of Subjects Without PUEAEs^	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nervous system disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Headache NOS	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Note: *Adverse events are classified according to MedDRA Version 20.0. ^ = Product-use-emergent adverse events
 Subject used their usual brand at Baseline (Week -1).
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes
 # Overall includes AEs after the start of Week1 product use.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab progrname.sas DDMMYYYY HH:MM

Post-text Table 14.3.1.2 will be in the following format:

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Table 14.3.1.2 Product-Use-Emergent Adverse Event Frequency -
Number of Adverse Events (% of Total Adverse Events) (Safety Population)

Adverse Event*	Baseline	VLN Non- Mentholated	VLN Mentholated	UB non- Mentholated	UB Mentholated	Overall#
Number of PUEAEs	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX (XXX%)	XX(XXX%)
Eye disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Vision blurred	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Gastrointestinal disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Dyspepsia	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nausea	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal and connective tissue disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Back pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Muscle cramps	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Musculoskeletal pain	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Nervous system disorders	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)
Headache NOS	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)	X (X%)

Note: *Adverse events are classified according to MedDRA Version 20.0. ^ = Product-use-emergent adverse events
Subject used their usual brand at Baseline (Week -1).
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Overall includes AEs after the start of Week1 product use.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab progrname.sas DDMMYYYY HH:MM

Post-text Table 14.3.1.3 will be in the following format:

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Table 14.3.1.3 Product-Use-Emergent Adverse Event Frequency by Severity and Relationship to Study Product -
Number of Subjects Reporting Adverse Events (Safety Population)

Adverse Event*	Number of Subjects Number With of PUEAEs PUEAEs		Severity			Relationship to Study product				
			Mild	Moderate	Severe	Unrelated	Unlikely	Possibly	Probably	Likely
Abdominal pain	X	X	X	X	X	X	X	X	X	X
Constipation	X	X	X	X	X	X	X	X	X	X
Dry throat	X	X	X	X	X	X	X	X	X	X
Dysmenorrhoea	X	X	X	X	X	X	X	X	X	X
Dyspepsia	X	X	X	X	X	X	X	X	X	X
Baseline	X	X	X	X	X	X	X	X	X	X
UB Non-mentholated	X	X	X	X	X	X	X	X	X	X
UB mentholated	X	X	X	X	X	X	X	X	X	X
VLN Non-mentholated	X	X	X	X	X	X	X	X	X	X
VLN mentholated	X	X	X	X	X	X	X	X	X	X
Overall#	X	X	X	X	X	X	X	X	X	X

Note: * Adverse events are classified according to MedDRA Version 20.0. PUEAEs = Product-use-emergent adverse events
When a subject experienced the same AE at more than one level of severity, only the most severe one was counted.
When a subject experienced the same AE at more than one level of product relationship, only the one most closely
related to study product was counted.
Subject used their usual brand at Baseline (Week -1).
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB Non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes
Overall includes AEs after the start of Week1 product use.
Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Post-text Table 14.3.2 will be in the following format:

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Table 14.3.2 Serious Adverse Events (Safety Population)

Will match 16.2.7

Or contain statement as follows:

"There were no serious adverse events recorded during the study."

Program: /CAXXXXX/ECR/sas_prg/stsas/programname.sas DDMMYYYY HH:MM

Post-text Tables 14.3.4.1, 14.3.4.2, and 14.3.4.3 will be in the following format:

Page 1 of X

Table 14.3.4.1 Out-of-Range Values and Recheck Results - Serum Chemistry (Safety Population)

Subject Number	Age/ Gender	Visit		Product Group	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5	Parameter6
		----- Name	----- Date		<Range1> <Unit1>	<Range2> <Unit2>	<Range3> <Unit3>	<Range4> <Unit4>	<Range5> <Unit5>	<Range6> <Unit6>
XXXXXX	XX/X	Screening	DDMMYYYY	XX	XX HN				XX HN	

Note: F = Female, M = Male
 H = Above Reference Range, L = Below Reference Range
 N = Not Clinically Significant

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Programmer Notes: Replace Parameter1, 2 etc. with actual lab tests in the study. Sort unscheduled assessment and early termination chronologically with other scheduled assessments and rechecks. Recheck should be sorted with the scheduled time point the recheck is for.

Programmer Notes: Clinically significant lab values generally will be captured as AEs, some of which the PI may indicate in Appendix 16.2.8.1.5 lab comments (as per GPG.03.0028 sections 2.9 and 2.10). Derive an additional CS flag for PI flag (+) based on positive comments (i.e. CS/Clinically Significant). Present this derived 4th column in all tables, and list only subjects/tests which are PI-determined clinically significant lab values in Table 14.3.4.4.

Program: /CAXXXXX/sas_prg/stsas/tab_PROGRAMNAME.sas DDMMYYYY HH:MM

Post-text Table 14.3.4.4 will be in the following format:

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Table 14.3.4.4 Clinically Significant Laboratory and Corresponding Results (Safety Population)

Subject Number	Age/ Sex	Visit		Product Group	Date	Time	Department	Test	Result	Reference Range	Unit
		Name	Date								
XXXXXX	XX/X	Screening	DDMMYYYY	XX	02DEC2016	8:34	Serum Chemistry	Cholesterol	XXX	X - X	mg/dL

Programmer Note: All time points for a subject/test with at least one value deemed as CS by the PI will be presented in this table.

Note: F = Female, M = Male
 H = Above Reference Range, L = Below Reference Range
 N = Not Clinically Significant

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

If no event meet this criteria then include a statement as follows:

"There were no clinical laboratory results documented as clinically significant by the PI."

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Post-text Tables 14.3.5.1, 14.3.5.2, and 14.3.5.3 will be in the following format:

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Table 14.3.5.1 Clinical Laboratory Summary - Serum Chemistry (Safety Population)

Laboratory Test (unit)	Reference Range	Statistics	Time Point	
			Screening	End of Study
XXXXXXXXXX	XX -XX	n	X	X
		Mean	X.X	X.X
		SD	X.XX	X.XX
		Minimum	XX	XX
		Median	X.X	X.X
		Maximum	XX	XX
XXXXXXXXXX	XX -XX#	n	X	X
		Mean	X.X	X.X
		SD	X.XX	X.XX
		Minimum	XX	XX
		Median	X.X	X.X
		Maximum	XX	XX

Note: # = Lowest of the lower ranges and highest of the higher ranges are used. Refer to Appendix 16.1.10.1 for the breakdown.

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: All laboratory tests will also be presented in the table.

Post-text Table 14.3.5.4 will be in the following format:

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Table 14.3.5.4 Vital Sign Summary (Safety Population)

Measurement (unit)	Study Week	Statistics	Study Product Group			
			UB Non-Mentholated	UB Mentholated	VLN Non-Mentholated	VLN Mentholated
Systolic BP (mmHg)	Screening	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX
	Week -1	n	X	X	X	X
		Mean	X.X	X.X	X.X	X.X
		SD	X.XX	X.XX	X.XX	X.XX
		Minimum	XX	XX	XX	XX
		Median	X.X	X.X	X.X	X.X
		Maximum	XX	XX	XX	XX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/ECR/sas_prg/stsas/tab programname.sas DDMMYYYY HH:MM

Programmer Note: Study Weeks 2, 4, 6 and other measurements will also be presented in the table.

15. LISTING SHELLS

The following listing shells provide a framework for the display of data from this study. The shells may change due to unforeseen circumstances. These shells may not be reflective of every aspect of this study, but are intended to show the general layout of the listings that will be presented and included in the final report. These listings will be generated from the Celerion SDTM 3.2 All listings will be presented in Courier New size font 9.

Appendix 16.1.10.1 Clinical Laboratory Reference Ranges

Laboratory Group	Test Name	Gender	Age Category	Normal Range	Unit
Serum Chemistry	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
Hematology	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units
	Test Name	<>	<>	XX - XX	units

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Programmer Note: Similar for remaining Laboratory Groups and Test Names.

Appendix 16.2.1.1 Subject Discontinuation (Safety Population)

Site	Subject Number	Randomization Number	Randomization Date	Product	Completion/ Discontinuation Date	Completed Study?	Reason for Discontinuation	Specify
XXX	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	No	Personal Reason	
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		
	XXXXXX	XXX	DDMMYYYY	XX	DDMMYYYY	Yes		

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

<also need site footnotes>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.1.2 Subject Discontinuation (Screen Failures)

Site	Subject Number	Discontinuation Date	Reason for Discontinuation	Specify
XXX	XXXXXX XXXXXX	DDMMYYYY DDMMYYYY	XXXXXXXXXX XXXXXXXXXX	

Note: <also need site footnotes>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.1 Demographics (Safety Population)

Site	Subject Number	Product Group	Age (yrs)	Gender	Race	Ethnicity	Reproductive Status	Height (cm)	Weight (kg)	BMI (kg/m ²)	Informed Consent Date	Informed Re-Consent Date
XXX	XXXXXX	XX	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMYYYY	DDMMYYYY
	XXXXXX	XX	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMYYYY	DDMMYYYY
	XXXXXX	XX	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMYYYY	DDMMYYYY
	XXXXXX	XX	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMYYYY	DDMMYYYY
	XXXXXX	XX	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMYYYY	DDMMYYYY
	XXXXXX	XX	XX	XXXX	XXXXXXXXXX	XXXXXXXXXXXXX	XXXXXXXXXXXXX	XX.X	XXX.X	XX.XX	DDMMYYYY	DDMMYYYY

Note: BMI = Body Mass Index

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

<also need site footnotes>

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.2 Physical Examination (Safety Population)

Subject Number	Visit		Product Group	Was PE Done?	Reason for Not Done	System	Result	Comment	Clinical Significance
	Name	Date							
XXXXXX	Screening	DDMMYYYY	XX	XXX		XXXXXX XXXXXX XXXXXX XXXXXX	XXXXXX XXXXXX XXXXXX XXXXXX	XXXXXX	NCS

Note: NCS = Not clinically significant, CS = Clinically significant

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.3 Medical History (Safety Population)

Subject Number	Any History?	Visit		Product Group	MH Number	Reported Term		Date		Ongoing?
		Name	Date					Start	End	
XXXXXX	XXX	Screening	DDMMYYYY	XX	XX	XXXXXX	XXXXX	MMYYYY		YES
					XX	XXXXXX	XXXXX	MMYYYY	MMYYYY	NO
XXXXXX	XXX	Screening	DDMMYYYY	XX	XX	XXXXXX	XXXXX	MMYYYY	MMYYYY	YES

Note: UNK = Unknown

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.4.4 Tobacco/Nicotine Use History (Safety Population)

Page 1 of X

Subject Number	Visit		Product Group	Not Done?	Reason for Not Done	Duration of Cigarette Use (unit)	Typical Number of CPD	Cigarette			Other Cigarette		
	Name	Date						Brand	Flavor	Size	Brand	Flavor	Size
X	Screening	DDMMYYYY	XX	XX		XX years	XX	XXX	XXX	XX	XXX	XXX	XX

Note: CPD = Cigarette smoked per day
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.1 Inclusion / Exclusion Criteria Not Met (Safety Population)

Subject Number	Visit		Product Group	Met All Eligibility Criteria?	Inclusion/ Exclusion Category	Criterion	
	Name	Date				Identifier	Criterion
X	Screening	DDMMYYYY	XX	No	XX	XXXX	XXXXXXXXXXXXXXXXXXXX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.1 VLN Product Trial (Safety Population)

Subject Number	Visit			Product Group	Number of cigarettes smoked
	Name	Date	Day		
X	XXXX	DDMMYYYY	X	XX	X

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.2.1 Product Dispensed (Safety Population)

Subject Number	Visit			Product Group	Product Dispensed	If Usual Brand, Specify	Date Dispensed	Number of Cigarettes Dispensed
	Name	Date	Day					
X	XXXX	DDMMYYYY	X	XX	XXX		DDMMYYYY	XXX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.2.2.1 Product Returned (I of II) (Safety Population)

Subject Number	Visit			Product Group	Product Name	If Usual Brand, Specify	Date Returned	Number of Cigarettes Returned	Cigarette Butts Returned	Number of Non VLN Butts Returned
	Name	Date	Day							
X	XXXX	DDMMYYYY	X	XX	XXX		DDMMYYYY	XXX	XXX	XX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.2.2.2 Product Returned (II of II) (Safety Population)

Subject Number	Visit			Product Group	Any Tobacco Products Other than e-diary			Additional Information*	
	Name	Date	Day		Answer	When	Amount	Answer	Specify
X	XXXX	DDMMYYYY	X	XX	XX			XX	XXXXXXXX

Note: * any additional information to provide about the difference between reported cigarette use and number of cigarettes and butts returned?

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.2.2.3 Puff Topography (Safety Population)

Subject Number	Visit		Product Group	Date Collection	Did Subject Smoke?	Number of Cigarettes Smoked*	Topography				
	Name	Date					Puff Duration (unit)	Puff Volume (unit)	Puff Flow Rate (unit)	Average Flow Rate (unit)	Inter-Puff Interval (unit)
X	XXXX	DDMMYYYY	XX	DDMMYYYY	XX	XX	XX	XX	XX	XX	XX

Note: * How many cigarettes did the subject smoke during the 1 hour topography session?
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.3.1 Plasma/Blood Sampling (Safety Population)

Page 1 of X

Subject Number	Visit			Product Group	Not Done?	If Not Done, Specify	Assay	Collection Date	Collection Time
	Name	Date	Day						
X	XXXX	DDMMYYYY	X	XX			XXX	DDMMYYYY	HH:MM

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.3.2 24-Hour Urine Collection (Safety Population)

Subject Number	Visit		Product Group	Planned Timepoint	Was the sample Collected?	Reason for Not Done	Start		Stop		Total Weight (g)	Lost or Discard	Comment for Lost/ Discard
	Name	Date					Date	Time	Date	Time			
XXXXXX	XXXXXX	DDMMYYYY	XX	XXXXXXXXXX	YES		DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XXX	XX	
				XXXXXXXXXX	YES		DDMMYYYY	HH:MM	DDMMYYYY	HH:MM	XXX	XX	

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.5.4 Prior and Concomitant Medications (Safety Population)

Subject Number	Study Product	Any Med? (WHO* Term)	Medication (WHO* Term)	Indication	Primary MH Number	Primary AE Number	Dosage	Route	Start Date	Stop Date	Frequency	Ongoing?	Prior to Study?
XXXXXX	X	XXX	ACETAMINOPHEN (XXXXXXXXXX)	Toothache		XX	620 mg	ORAL	DDMMYYYY	DDMMYYYY	Once	No	X

Note: *Concomitant medications are coded with WHO Drug Dictionary Version 01SEP2018.

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Subject Number	Product Group	Study Week	Number of Cigarettes Smoked	Number of Cigarette Butts Collected
X	XX	-1	XXX	XXX

Note: Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.2 Puff Topography Parameters (Safety Population)

Page 1 of X

Subject Number	Product Group	Study Week	Puff Duration (unit)	Puff Volume (unit)	Puff Flow Rate (unit)	Average Flow Rate (unit)	Inter-Puff Interval (unit)
X	XX	-1	XXX	XXX	XXX	XXX	XXX

Note: Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Programmer Note: Replace parameters and units with actual parameter names and units.

Appendices 16.2.6.3, 16.2.6.4, 16.2.6.5, 16.2.6.6, 16.2.6.7, and 16.2.6.8.2 will have following format.

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Appendix 16.2.6.3 Urinary Total NNAL (Safety Population)

Subject Number	Product Group	Study Week	Biomarker Concentration (unit)	Urine Volume (unit)	24-Hour Amount Excreted			Creatinine Concentration (unit)	Creatinine Adjusted Values		
					Amount (unit)	CFB (unit)	PCFB (%)		Amount (unit)	CFB (unit)	PCFB (%)
X	XX	-1	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Note: Baseline = Week -1
 CFB = Change from baseline, PCFB = Percent change from baseline
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.8.1 Urine Nicotine and Metabolites (I of II) (Safety Population)

Subject Number	Product Group	Study Week	Volume (mL)	Nicotine (ng/mL)	Nicotine (mg/24 hours)	Nicotine Glucuronide (ng/mL)	Nicotine Glucuronide (mg/24 hours)	Cotinine (ng/mL)	Cotinine (mg/24 hours)
X	XX	-1	XXX	XXX	XXX	XXXX	XXX	XXX	XXX

Note: Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Programmer Note: 16.2.6.8.2 will present the concentration and amount excreted of 'Cotinine Glucuronide', 'Trans-3-hydroxy Cotinine', and 'Trans-3-hydroxy Cotinine Glucuronide'.

Appendix 16.2.6.9 Blood COHb (Safety Population)

Subject Number	Product Group	Study Week	Biomarker Concentration (unit)	CFB (unit)	PCFB (%)
X	XX	-1	XXX	XXX	XXX

Note: Baseline = Week -1
 CFB = Change from baseline, PCFB = Percent change from baseline
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.10 Plasma Cotinine (Safety Population)

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Subject Number	Product Group	Study Week	Biomarker Concentration (unit)

X	XX	-1	XXX

Note: Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.12 FTCD Response and Score (Safety Population)

Subject Number	Product Group	Study Week	Date	Question*						Total Score
				1	2	3	4	5	6	
X	XX	-1	DDMMYYYY	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Note: *1. How soon after you wake up do you smoke your first cigarette?
 2. Do you find it difficult to refrain from smoking in places where it is forbidden (e.g., in church, at the library, in the cinema, etc.)?
 3. Which cigarette would you hate most to give up?
 4. How many cigarettes per day do you smoke?
 5. Do you smoke more frequently during the first hours after waking than during the rest of the day?
 6. Do you smoke if you are so ill that you are in bed most of the day?
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.13 QSU-Brief Response and Factor Score (Safety Population) (Safety Population)

Subject Number	Product Group	Study Week	Date	Question*										Factor 1 Score	Factor 2 Score
				1	2	3	4	5	6	7	8	9	10		
X	XX	-1	DDMMYYYY	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX

Note: *1. I have a desire to smoke right now. 2. Nothing would be better than smoking right now.
3. If it were possible, I probably would smoke right now. 4. I could control things better right now if I could smoke.
5. All I want right now is a cigarette. 6. I have an urge for a cigarette.
7. A cigarette would taste good now. 8. I would do almost anything for a cigarette now.
9. Smoking would make me less depressed. 10. I am going to smoke as soon as possible.
Factor 1 (anticipation of pleasure from smoking) calculated as the average of the response scores from Questions 1, 3, 6, 7, and 10;
Factor 2 (relief of nicotine withdrawal) calculated as the average of the response scores from Questions 2, 4, 5, 8, and 9).
Scale: 1 = Strongly disagree, 7 = Strongly agree
Subjects used their own usual brand cigarettes at Week -1.
VLN non-mentholated = Non-mentholated VLN cigarettes
VLN mentholated = Mentholated VLN cigarettes
UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.14 MNWS-R Response and Total Score (Safety Population)

Subject Number	Product Group	Study Week	Date	Question*															Total Score
				1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
X	XX	-1	DDMMYYYY	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	XXX	

Note: *1. Angry, irritable, frustrated; 2. Anxious, nervous; 3. Depressed mood, sad; 4. Desire or craving to smoke
 5. Difficulty concentrating; 6. Increased appetite, hungry, weight gain; 7. Insomnia, sleep problems, awakening at night;
 8. Restless; 9. Impatient; 10. Constipation; 11. Dizziness; 12. Coughing; 13. Dreaming or nightmares; 14. Nausea; 15. Sore throat
 Scale: 0 = none, 1 = slight, 2 = mild, 3 = moderate, 4 = severe
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.6.15 Perceived Health Risk Scale (Safety Population)

Subject Number	Product Group	Study Week	Date	Perceived Health Risk Scale*
X	XX	-1	DDMMYYYY	XXX

Note: * Indicate your perception of the risk of becoming addicted to the cigarette you are currently using.
 Scale: 1 = Very low risk, 10 = Very high risk
 Subjects used their own usual brand cigarettes at Week -1.
 VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.7.1 Adverse Events (Safety Population)

Subject Number	Study Product	UE?^	System Organ Class >Preferred Term* >>Adverse Event	Time From Last Product Use ----- (DD:HH:MM)	Onset Date Time/ Resolved Date Time	Frequency	Severity	Serious	Outcome	Relationship to Study Product	Action
XXXXXX	X	XXX	XXXXXXXXXXXXX >XXXXXXXXX >>XXXXXXXXXXXXX	XX:XX:XX	DDMMYYYY HH:MM/ DDMMYYYY HH:MM	XXXXXXX	XXXXX	XXXX	XXXXXX	XXXXXXXX	XXXXX

Note: ^ = Abbreviation for study product use-emergent (UE), UE is assigned to last product used prior to AE start.
 * = Adverse events are classified according to the MedDRA Version 21.0.

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Programmer Note: Other action will also be listed if there is any.

Appendices 16.2.8.1.1 through 16.2.8.1.3 will have the following format.

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Appendix 16.2.8.1.1 Clinical Laboratory Report - Serum Chemistry (Safety Population)

Subject Number	Age/ gender	Visit		Product Group	Parameter1	Parameter2	Parameter3	Parameter4	Parameter5	Parameter6
		Name	Date		<Range1> <Unit1>	<Range2> <Unit2>	<Range3> <Unit3>	<Range4> <Unit4>	<Range5> <Unit5>	<Range6> <Unit6>
XXXXXX	XX/X	Screening	DDMMYYYY	XX	XX HN	XX	XX	XX	XX HN	XX

Note: F = Female, M = Male
 H = Above Reference Range, L = Below Reference Range
 N = Not Clinically Significant

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Programmer Note: Replace Parameter1, 2 etc. with actual lab tests in the study.

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Appendix 16.2.8.1.4 Clinical Laboratory Report - Comments (Safety Population)

Subject Number	Visit		Product Group	Lab Panel	Test	Result	Unit	Comment
	Name	Date						
XXXXXX	Screening	DDMMYYYY	XX	Hematology	XXXXXXXX	XXX	mg/dL	Not significant in the context of this study.

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.5 Urine Drug Screens (Safety Population)

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Subject Number	Visit		Product Group	Was the Urine Sample Collected?	Date of Collection	Test Name	Result
	Name	Date					
XXXXXX	Screening	DDMMYYYY	XX	XXX	DDMMYYYY	XXXXXXXXXXXXXX XXXXXXXXXXXXXX	XXXXXX XXXXXX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.6 Pregnancy Tests (Safety Population)

Page 1 of X

Subject Number	Visit		Product Group	Was the Pregnancy Test Done?	Reason for Not Done	Collection Date	Test Type	Test Result
	Name	Date						
XXXXXX	Screening	DDMMYYYY	XX	XXX		DDMMYYYY	XXXXXX	XXX
	XXXXXXXXX	DDMMYYYY		XXX		DDMMYYYY	XXXXXX	XXX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.7 Serum FSH (Safety Population)

Page 1 of X

Subject Number	Visit		Product Group	Was Serum FSH Collected?	Reason for Not Done	Was Postmenopausal Status Confirmed?	Collection Date
	Name	Date					
XXXXXX	Screening	DDMMYYYY	XX	XXX	XXXX	XXX	DDMMYYYY

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.8 Urine Cotinine Screens (Safety Population)

Page 1 of X

Subject Number	Visit		Product Group	Was the Urine Cotinine Sample Collected?	Date of Collection	Is Result Positive* for Urine Cotinine?
	Name	Date				
XXXXXX	Screening	DDMMYYYY	XX	XXX	DDMMYYYY	XXX

Note: *Positive = greater than or equal to 500 ng/mL

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.9 Serology Sample Collection (Safety Population)

Page 1 of X

Subject Number	Visit		Product Group	Was the Sample Collected?	Collection Date
	Name	Date			
XXXXXX	Screening	DDMMYYYY	XX	XXX	DDMMYYYY

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.1.10 Exhaled CO Measurement (Safety Population)

Page 1 of X

Subject Number	Visit		Product Group	Was Exhaled CO Measurements Performed?	Collection Date	Exhaled CO Measurement (ppm)
	Name	Date				
XXXXXX	Screening	DDMMYYYY	XX	XXX	DDMMYYYY	XX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.2 Vital Signs (Safety Population)

Subject Number	Visit ----- Name	Product Group	Date	Time	Not Done?	Reason for Not Done?	Blood Pressure (mmHg) ----- Systolic/Diastolic	Pulse (bpm)	Respi- ration (rpm)	Temper- ature (°F)
XXXXXX	Screening	XX	DDMMYYYY	HH:MM			XXX/ XX	XX	XX	XX.X
	XXXXXX		DDMMYYYY	HH:MM			XXX/ XX NCS	XX	XX	XX.X
	XXXXXX		DDMMYYYY	HH:MM			XXX/ XX	XX CS	XX	XX.X
	XXXX		DDMMYYYY	HH:MM			XXX/ XX	XX	XX	XX.X

Note: NCS = Not clinically significant, CS = Clinically significant
 mmHg = millimeter of mercury, bpm = beats per minute, rpm = respiration per minute

VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.3 12-Lead Electrocardiogram (Safety Population)

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Subject Number	Visit ----- Name	Product Group	Planned Timepoint?	Date	Time	Was ECG Performed?	Overall Result	Heart Rate (bpm)	PR (msec)	RR (msec)	QRS (msec)	QT (msec)	QTcB* (msec)	QTcF* (msec)	If Abnormal, Specify
XXXXXX	Screening	XX	XXX	DDMMYYYY	HH:MM	Normal	Normal	XX	XXX	XXX	XX	XXX	XXX	XXX	

Note: QTcB* = QTc corrected using Bazett's correction, QTcF* = QTc corrected using Fridericia's correction,
 ANCS = Abnormal, Not Clinically Significant
 bpm = beats per minute, msec = millisecond

VLN non-mentholated = Non-mentholated VLN cigarettes

VLN mentholated = Mentholated VLN cigarettes

UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes

UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

Appendix 16.2.8.4 Phone Call (Safety Population)

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Subject Number	Visit		Product Group	Date of Call	Was Tobacco Cessation Information Provided?	Did Subject Need to Return to the Clinic for a Symptom Driven Physical Exam?
	Name	Date				
X	End of Study	DDMMYYYY	XX	DDMMYYYY	XXX	XXX

Note: VLN non-mentholated = Non-mentholated VLN cigarettes
 VLN mentholated = Mentholated VLN cigarettes
 UB non-mentholated = Subjects' UB non-mentholated filtered cigarettes
 UB mentholated = Subjects' UB mentholated filtered cigarettes

Program: /CAXXXXX/sas_prg/stsas/lis_PROGRAMNAME.sas DDMMYYYY HH:MM

16.1.9.2 Statistical Outputs

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	22	16.5285714	4.2388343	8.8571429	25.2857143
BASE	Baseline Value	22	17.0876623	3.9232417	10.0000000	24.6666667

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	16.0387755	4.2957412	8.8571429	25.2857143
BASE	Baseline Value	42	16.8044218	4.8258240	10.0000000	33.2857143

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	23.6666667	9.5659070	9.4285714	38.4285714
BASE	Baseline Value	11	16.5670996	4.4179958	10.0000000	26.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	26	19.2725275	9.2770839	5.8000000	38.4285714
BASE	Baseline Value	26	15.8653846	5.6054838	7.3333333	29.4285714

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	15.5000000	4.4020550	9.2857143	24.8571429
BASE	Baseline Value	20	16.4928571	5.7486700	10.1428571	33.2857143

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	16.0501587	7.8757921	5.8000000	33.2857143
BASE	Baseline Value	15	15.3507937	6.4418323	7.3333333	29.4285714

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	15.9357143	5.3641758	0	24.0000000
BASE	Baseline Value	20	16.8559524	3.6709482	10.0000000	23.1428571

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	15.3297619	5.0884197	0	24.2857143
BASE	Baseline Value	40	16.6744048	4.7643351	10.0000000	33.2857143

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	21.5686147	8.0126761	11.3333333	35.1428571
BASE	Baseline Value	11	16.5670996	4.4179958	10.0000000	26.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	18.1901361	9.2464225	6.8571429	39.0000000
BASE	Baseline Value	21	16.5578231	5.8002051	7.3333333	29.4285714

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	14.7238095	4.8579192	7.4285714	24.2857143
BASE	Baseline Value	20	16.4928571	5.7486700	10.1428571	33.2857143

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	14.4738095	9.4529870	6.8571429	39.0000000
BASE	Baseline Value	10	16.5476190	7.2851350	7.3333333	29.4285714

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
22	-0.5591	2.8828	0.6146	-8.4667	3.7143		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.5591	-1.8372 0.7191	2.8828	2.2179 4.1196				
DF	t Value	Pr > t					
21	-0.91	0.3733					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
42	-0.7656	4.3528	0.6717	-22.4286	5.1429
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.7656	-2.1221 0.5908	4.3528	3.5815 5.5506		
DF	t Value	Pr > t			
41	-1.14	0.2609			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	7.0996	7.5168	2.2664	-3.0238	22.8095
	Mean	95% CL Mean	Std Dev	95% CL Std Dev	
	7.0996	2.0497 12.1494	7.5168	5.2521 13.1915	
		DF	t Value	Pr > t	
		10	3.13	0.0106	

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
26	3.4071	6.2896	1.2335	-4.3333	22.8095
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
3.4071	0.8667	5.9476	6.2896	4.9326	8.6822
DF	t Value	Pr > t			
25	2.76	0.0106			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.9929	5.6211	1.2569	-22.4286	5.1429
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9929	-3.6236 1.6379	5.6211	4.2748 8.2101		
DF	t Value	Pr > t			
19	-0.79	0.4393			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
15	0.6994	3.4225	0.8837	-4.3333	9.4524		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.6994	-1.1960 2.5947	3.4225	2.5057 5.3976				
DF	t Value	Pr > t					
14	0.79	0.4419					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.9202	3.7577	0.8402	-13.5714	5.8571
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9202	-2.6789	0.8384	3.7577	2.8577	5.4883
DF	t Value	Pr > t			
19	-1.10	0.2871			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-1.3446	4.8648	0.7692	-22.7143	8.1429
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.3446	-2.9005 0.2112	4.8648	3.9850 6.2466		
DF	t Value	Pr > t			
39	-1.75	0.0883			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	5.0015	5.9381	1.7904	-1.6667	19.8095
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
5.0015	1.0123 8.9908	5.9381	4.1490 10.4209		
DF	t Value	Pr > t			
10	2.79	0.0190			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	1.6323	8.0655	1.7600	-18.5952	19.8095
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
1.6323	-2.0391 5.3037	8.0655	6.1706 11.6471		
	DF	t Value	Pr > t		
	20	0.93	0.3648		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-1.7690	5.8377	1.3053	-22.7143	8.1429
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-1.7690	-4.5012	0.9631	5.8377	4.4395	8.5264
	DF	t Value	Pr > t		
	19	-1.36	0.1912		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-2.0738	8.7319	2.7613	-18.5952	15.1667
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.0738	-8.3203	4.1726	8.7319	6.0061	15.9411
DF	t Value	Pr > t			
9	-0.75	0.4718			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttest.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDACPDWCIG
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	68	1007 1010 1011 1015 1016 1017 1018 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2016 2018 2021 2023 2024 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2189 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	68
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	129
Number of Observations Used	129
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	814.83728000	
1	2	753.42038928	0.00000022
2	1	753.42032964	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	39.5150
UN(2,1)	subject	33.5626
UN(2,2)	subject	43.1136

Fit Statistics

-2 Res Log Likelihood	753.4
AIC (smaller is better)	759.4
AICC (smaller is better)	759.6
BIC (smaller is better)	766.1

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	61.42	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	64.1	4.66	0.0052
week	1	57.7	11.14	0.0015
treat*week	3	57.6	1.56	0.2084

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	7.1381	2.3213	64	3.08	0.0031	0.05	2.5008	11.7754
Week 2: VLN Mentholated vs UB Mentholated	0.5502	2.1471	64	0.26	0.7986	0.05	-3.7392	4.8395
Week 2: VLN Combined vs UB Combined	3.8441	1.5810	64	2.43	0.0178	0.05	0.6857	7.0026
Week 2: VLN Combined	19.8584	1.2477	64	15.92	<.0001	0.05	17.3659	22.3509
Week 2: UB Combined	16.0143	0.9711	64	16.49	<.0001	0.05	14.0744	17.9542
Week 6: VLN Non-mentholated vs UB Non-mentholated	5.6693	2.4388	60.4	2.32	0.0235	0.05	0.7917	10.5469
Week 6: VLN Mentholated vs UB Mentholated	-2.2479	2.3525	66.5	-0.96	0.3428	0.05	-6.9441	2.4483
Week 6: VLN Combined vs UB Combined	1.7107	1.6943	63.3	1.01	0.3165	0.05	-1.6746	5.0960
Week 6: VLN Combined	17.0223	1.3507	64.8	12.60	<.0001	0.05	14.3245	19.7200
Week 6: UB Combined	15.3116	1.0228	60.8	14.97	<.0001	0.05	13.2663	17.3568

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	16.5286	1.3402	64	12.33	<.0001	0.05	13.8512	19.2059
treat*week	A	6	15.8993	1.4242	62.1	11.16	<.0001	0.05	13.0524	18.7462
treat*week	B	2	23.6667	1.8953	64	12.49	<.0001	0.05	19.8803	27.4530
treat*week	B	6	21.5686	1.9798	59.6	10.89	<.0001	0.05	17.6080	25.5293
treat*week	C	2	15.5000	1.4056	64	11.03	<.0001	0.05	12.6920	18.3080
treat*week	C	6	14.7238	1.4682	59.6	10.03	<.0001	0.05	11.7865	17.6611
treat*week	D	2	16.0502	1.6231	64	9.89	<.0001	0.05	12.8077	19.2926
treat*week	D	6	12.4759	1.8380	70.9	6.79	<.0001	0.05	8.8108	16.1410

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.6293	0.8795	57.5	0.72	0.4772	0.05	-1.1315	2.3900
treat*week	A	2	B	2	-7.1381	2.3213	64	-3.08	0.0031	0.05	-11.7754	-2.5008
treat*week	A	2	B	6	-5.0400	2.3907	72	-2.11	0.0385	0.05	-9.8059	-0.2742
treat*week	A	2	C	2	1.0286	1.9421	64	0.53	0.5982	0.05	-2.8513	4.9084
treat*week	A	2	C	6	1.8048	1.9879	74.9	0.91	0.3669	0.05	-2.1554	5.7650
treat*week	A	2	D	2	0.4784	2.1049	64	0.23	0.8209	0.05	-3.7265	4.6834
treat*week	A	2	D	6	4.0527	2.2748	84	1.78	0.0784	0.05	-0.4709	8.5762
treat*week	A	6	B	2	-7.7674	2.3708	76.4	-3.28	0.0016	0.05	-12.4888	-3.0459
treat*week	A	6	B	6	-5.6693	2.4388	60.4	-2.32	0.0235	0.05	-10.5469	-0.7917
treat*week	A	6	C	2	0.3993	2.0011	77.3	0.20	0.8424	0.05	-3.5850	4.3836
treat*week	A	6	C	6	1.1755	2.0455	60.8	0.57	0.5676	0.05	-2.9150	5.2660
treat*week	A	6	D	2	-0.1508	2.1593	77.2	-0.07	0.9445	0.05	-4.4504	4.1488
treat*week	A	6	D	6	3.4234	2.3253	67.6	1.47	0.1456	0.05	-1.2171	8.0639

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.3 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	2.0981	1.1872	57	1.77	0.0825	0.05	-0.2793	4.4754
treat*week	B	2	C	2	8.1667	2.3597	64	3.46	0.0010	0.05	3.4527	12.8806
treat*week	B	2	C	6	8.9429	2.3975	75.2	3.73	0.0004	0.05	4.1670	13.7187
treat*week	B	2	D	2	7.6165	2.4953	64	3.05	0.0033	0.05	2.6315	12.6015
treat*week	B	2	D	6	11.1907	2.6402	84.2	4.24	<.0001	0.05	5.9406	16.4409
treat*week	B	6	C	2	6.0686	2.4280	72.6	2.50	0.0147	0.05	1.2292	10.9081
treat*week	B	6	C	6	6.8448	2.4648	59.6	2.78	0.0073	0.05	1.9138	11.7758
treat*week	B	6	D	2	5.5185	2.5600	74.1	2.16	0.0344	0.05	0.4176	10.6193
treat*week	B	6	D	6	9.0927	2.7014	64.8	3.37	0.0013	0.05	3.6972	14.4882
treat*week	C	2	C	6	0.7762	0.8804	57	0.88	0.3817	0.05	-0.9869	2.5393
treat*week	C	2	D	2	-0.5502	2.1471	64	-0.26	0.7986	0.05	-4.8395	3.7392
treat*week	C	2	D	6	3.0241	2.3139	84.3	1.31	0.1948	0.05	-1.5771	7.6253
treat*week	C	6	D	2	-1.3263	2.1886	75.5	-0.61	0.5463	0.05	-5.6858	3.0331
treat*week	C	6	D	6	2.2479	2.3525	66.5	0.96	0.3428	0.05	-2.4483	6.9441
treat*week	D	2	D	6	3.5742	1.2400	58.5	2.88	0.0055	0.05	1.0924	6.0560

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixed.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	22	16.5285714	4.2388343	8.8571429	25.2857143
BASE	Baseline Value	22	17.0876623	3.9232417	10.0000000	24.6666667

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	16.0387755	4.2957412	8.8571429	25.2857143
BASE	Baseline Value	42	16.8044218	4.8258240	10.0000000	33.2857143

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	49	19.7908649	8.7563450	4.4285714	53.8571429
BASE	Baseline Value	49	17.9977648	5.5481931	7.6000000	39.2000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	97	17.4981345	7.9998906	4.4285714	53.8571429
BASE	Baseline Value	97	16.5186549	5.7472397	7.3333333	39.2000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	15.5000000	4.4020550	9.2857143	24.8571429
BASE	Baseline Value	20	16.4928571	5.7486700	10.1428571	33.2857143

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	15.1576389	6.4296289	5.1428571	33.2857143
BASE	Baseline Value	48	15.0087302	5.6053952	7.3333333	32.8333333

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	15.9357143	5.3641758	0	24.0000000
BASE	Baseline Value	20	16.8559524	3.6709482	10.0000000	23.1428571

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	15.3297619	5.0884197	0	24.2857143
BASE	Baseline Value	40	16.6744048	4.7643351	10.0000000	33.2857143

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	16.5109635	7.5707759	5.2000000	35.1428571
BASE	Baseline Value	43	17.9685493	5.3023776	10.0000000	39.2000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	86	14.1389258	7.6772970	2.5000000	39.0000000
BASE	Baseline Value	86	16.6079181	5.6703469	7.3333333	39.2000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	14.7238095	4.8579192	7.4285714	24.2857143
BASE	Baseline Value	20	16.4928571	5.7486700	10.1428571	33.2857143

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	11.7668882	7.1026354	2.5000000	39.0000000
BASE	Baseline Value	43	15.2472868	5.7589245	7.3333333	32.8333333

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
22	-0.5591	2.8828	0.6146	-8.4667	3.7143
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5591	-1.8372 0.7191	2.8828	2.2179 4.1196		
DF	t Value	Pr > t			
21	-0.91	0.3733			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
42	-0.7656	4.3528	0.6717	-22.4286	5.1429
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.7656	-2.1221	0.5908	4.3528	3.5815	5.5506
	DF	t Value	Pr > t		
	41	-1.14	0.2609		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
49	1.7931	7.0125	1.0018	-14.0000	22.8095
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
1.7931	-0.2211 3.8073	7.0125	5.8479 8.7608		
DF	t Value	Pr > t			
48	1.79	0.0798			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
97	0.9795	5.9251	0.6016	-14.0000	22.8095
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.9795	-0.2147 2.1736	5.9251	5.1925 6.9003		
	DF	t Value	Pr > t		
	96	1.63	0.1068		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.9929	5.6211	1.2569	-22.4286	5.1429
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9929	-3.6236 1.6379	5.6211	4.2748 8.2101		
DF	t Value	Pr > t			
19	-0.79	0.4393			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
48	0.1489	4.4822	0.6470	-12.5476	9.4524		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.1489	-1.1526 1.4504	4.4822	3.7313 5.6143				
DF	t Value	Pr > t					
47	0.23	0.8190					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.9202	3.7577	0.8402	-13.5714	5.8571
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9202	-2.6789	0.8384	3.7577	2.8577	5.4883
DF	t Value	Pr > t			
19	-1.10	0.2871			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
40	-1.3446	4.8648	0.7692	-22.7143	8.1429		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-1.3446	-2.9005 0.2112	4.8648	3.9850 6.2466				
DF	t Value	Pr > t					
39	-1.75	0.0883					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-1.4576	7.0779	1.0794	-17.6000	19.8095
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.4576	-3.6358 0.7207	7.0779	5.8360 8.9960		
DF	t Value	Pr > t			
42	-1.35	0.1841			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
86	-2.4690	6.4310	0.6935	-18.5952	19.8095
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-2.4690	-3.8478	-1.0902	6.4310	5.5926	7.5673
	DF	t Value	Pr > t		
	85	-3.56	0.0006		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-1.7690	5.8377	1.3053	-22.7143	8.1429
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-1.7690	-4.5012	0.9631	5.8377	4.4395	8.5264
	DF	t Value	Pr > t		
	19	-1.36	0.1912		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (ACPDW) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.1.1.4 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-3.4804	5.6133	0.8560	-18.5952	15.1667
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.4804	-5.2079	-1.7529	5.6133	4.6284	7.1346
	DF	t Value	Pr > t		
	42	-4.07	0.0002		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsttestITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDACPDWCIG
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	139	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1018 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2016 2017 2018 2020 2021 2023 2024 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2189 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	139
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	265
Number of Observations Used	265
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1742.13328070	
1	2	1632.94171119	0.00000004
2	1	1632.94169024	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	47.1765
UN(2,1)	subject	35.3840
UN(2,2)	subject	45.0392

Fit Statistics

-2 Res Log Likelihood	1632.9
AIC (smaller is better)	1638.9
AICC (smaller is better)	1639.0
BIC (smaller is better)	1647.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	109.19	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	134	4.19	0.0072
week	1	124	25.85	<.0001
treat*week	3	124	4.09	0.0083

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	3.2623	1.7627	135	1.85	0.0664	0.05	-0.2238	6.7484
Week 2: VLN Mentholated vs UB Mentholated	-0.3424	1.8280	135	-0.19	0.8517	0.05	-3.9576	3.2729
Week 2: VLN Combined vs UB Combined	1.4600	1.2697	135	1.15	0.2522	0.05	-1.0512	3.9711
Week 2: VLN Combined	17.4743	0.6974	135	25.06	<.0001	0.05	16.0950	18.8536
Week 2: UB Combined	16.0143	1.0610	135	15.09	<.0001	0.05	13.9159	18.1127
Week 6: VLN Non-mentholated vs UB Non-mentholated	0.03581	1.7622	133	0.02	0.9838	0.05	-3.4497	3.5214
Week 6: VLN Mentholated vs UB Mentholated	-3.2894	1.7988	129	-1.83	0.0698	0.05	-6.8485	0.2697
Week 6: VLN Combined vs UB Combined	-1.6268	1.2591	131	-1.29	0.1986	0.05	-4.1176	0.8640
Week 6: VLN Combined	13.6869	0.6994	134	19.57	<.0001	0.05	12.3036	15.0702
Week 6: UB Combined	15.3137	1.0470	130	14.63	<.0001	0.05	13.2423	17.3851

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	16.5286	1.4644	135	11.29	<.0001	0.05	13.6325	19.4246
treat*week	A	6	15.9036	1.4604	132	10.89	<.0001	0.05	13.0149	18.7922
treat*week	B	2	19.7909	0.9812	135	20.17	<.0001	0.05	17.8503	21.7314
treat*week	B	6	15.9394	0.9863	135	16.16	<.0001	0.05	13.9888	17.8899
treat*week	C	2	15.5000	1.5358	135	10.09	<.0001	0.05	12.4626	18.5374
treat*week	C	6	14.7238	1.5007	127	9.81	<.0001	0.05	11.7542	17.6934
treat*week	D	2	15.1576	0.9914	135	15.29	<.0001	0.05	13.1970	17.1183
treat*week	D	6	11.4344	0.9919	133	11.53	<.0001	0.05	9.4726	13.3963

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.6250	1.0297	125	0.61	0.5450	0.05	-1.4130	2.6630
treat*week	A	2	B	2	-3.2623	1.7627	135	-1.85	0.0664	0.05	-6.7484	0.2238
treat*week	A	2	B	6	0.5892	1.7655	167	0.33	0.7390	0.05	-2.8965	4.0749
treat*week	A	2	C	2	1.0286	2.1221	135	0.48	0.6287	0.05	-3.1682	5.2254
treat*week	A	2	C	6	1.8048	2.0967	166	0.86	0.3906	0.05	-2.3349	5.9444
treat*week	A	2	D	2	1.3709	1.7684	135	0.78	0.4396	0.05	-2.1264	4.8683
treat*week	A	2	D	6	5.0941	1.7687	166	2.88	0.0045	0.05	1.6021	8.5861
treat*week	A	6	B	2	-3.8873	1.7594	164	-2.21	0.0285	0.05	-7.3613	-0.4133
treat*week	A	6	B	6	-0.03581	1.7622	133	-0.02	0.9838	0.05	-3.5214	3.4497
treat*week	A	6	C	2	0.4036	2.1193	171	0.19	0.8492	0.05	-3.7798	4.5869
treat*week	A	6	C	6	1.1798	2.0940	130	0.56	0.5741	0.05	-2.9630	5.3225
treat*week	A	6	D	2	0.7459	1.7651	164	0.42	0.6731	0.05	-2.7392	4.2311
treat*week	A	6	D	6	4.4691	1.7654	133	2.53	0.0125	0.05	0.9772	7.9610

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Number of Cigarettes Smoked per Week (ACPDW)
for Table 14.2.1.1.5 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	3.8515	0.7009	126	5.50	<.0001	0.05	2.4644	5.2386
treat*week	B	2	C	2	4.2909	1.8225	135	2.35	0.0200	0.05	0.6865	7.8953
treat*week	B	2	C	6	5.0671	1.7930	157	2.83	0.0053	0.05	1.5256	8.6085
treat*week	B	2	D	2	4.6332	1.3949	135	3.32	0.0012	0.05	1.8746	7.3918
treat*week	B	2	D	6	8.3564	1.3952	172	5.99	<.0001	0.05	5.6025	11.1104
treat*week	B	6	C	2	0.4394	1.8252	165	0.24	0.8101	0.05	-3.1644	4.0432
treat*week	B	6	C	6	1.2156	1.7957	129	0.68	0.4997	0.05	-2.3373	4.7685
treat*week	B	6	D	2	0.7817	1.3984	173	0.56	0.5769	0.05	-1.9784	3.5419
treat*week	B	6	D	6	4.5049	1.3988	134	3.22	0.0016	0.05	1.7384	7.2715
treat*week	C	2	C	6	0.7762	1.0356	122	0.75	0.4550	0.05	-1.2737	2.8261
treat*week	C	2	D	2	0.3424	1.8280	135	0.19	0.8517	0.05	-3.2729	3.9576
treat*week	C	2	D	6	4.0656	1.8283	165	2.22	0.0275	0.05	0.4556	7.6755
treat*week	C	6	D	2	-0.4338	1.7986	157	-0.24	0.8097	0.05	-3.9863	3.1186
treat*week	C	6	D	6	3.2894	1.7988	129	1.83	0.0698	0.05	-0.2697	6.8485
treat*week	D	2	D	6	3.7232	0.7017	125	5.31	<.0001	0.05	2.3345	5.1119

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_cigstatsmixedITT.sas 13JUN2019 4:37

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	2.6896033	1.9743041	0.9421053	4.8312500
BASE	Baseline Value	3	1.9225529	1.0294601	0.8148810	2.8500000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	2.4178465	1.1715276	0.9421053	4.8312500
BASE	Baseline Value	8	2.1148371	0.6698321	0.8148810	2.8809295

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	2.2547924	0.6035513	1.8464286	3.2837302
BASE	Baseline Value	5	2.2302077	0.4592596	1.6211279	2.8809295

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	2.0654589	1.1200484	0.8630435	3.0791667
BASE	Baseline Value	3	1.9225529	1.0294601	0.8148810	2.8500000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	2.0158826	0.7210438	0.8630435	3.0791667
BASE	Baseline Value	7	2.0053954	0.6416107	0.8148810	2.8500000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	1.9787004	0.4462825	1.3800000	2.3873016
BASE	Baseline Value	4	2.0675272	0.3237175	1.6211279	2.3964286

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	0.7671	1.0520	0.6074	0.1272	1.9813
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.7671	-1.8464	3.3805	1.0520	0.5478	6.6118
	DF	t Value	Pr > t		
	2	1.26	0.3339		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	0.3030	0.7166	0.2534	-0.2836	1.9813
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.3030	-0.2961 0.9021	0.7166	0.4738 1.4585		
DF	t Value	Pr > t			
7	1.20	0.2706			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	0.0246	0.2947	0.1318	-0.2836	0.4028
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.0246	-0.3414 0.3906	0.2947	0.1766 0.8470		
DF	t Value	Pr > t			
4	0.19	0.8611			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	0.1429	0.0908	0.0524	0.0482	0.2292
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.1429	-0.0827	0.3685	0.0908	0.0473	0.5707
	DF	t Value	Pr > t		
	2	2.73	0.1123		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	0.0105	0.2156	0.0815	-0.2411	0.2647
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.0105	-0.1889	0.2099	0.2156	0.1389	0.4748
	DF	t Value	Pr > t		
	6	0.13	0.9018		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-0.0888	0.2383	0.1192	-0.2411	0.2647
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0888	-0.4681	0.2904	0.2383	0.1350	0.8886
	DF	t Value	Pr > t		
	3	-0.75	0.5101		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	26.2666667	7.8232559	17.9000000	33.4000000
BASE	Baseline Value	3	21.2333333	7.7510618	13.0750000	28.5000000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	25.1500000	5.6201646	16.9750000	33.4000000
BASE	Baseline Value	8	25.9843750	8.0908230	13.0750000	35.9500000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	24.4800000	4.8143470	16.9750000	30.0000000
BASE	Baseline Value	5	28.8350000	7.5783326	17.1500000	35.9500000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	23.2750000	3.6127379	19.8500000	27.0500000
BASE	Baseline Value	3	21.2333333	7.7510618	13.0750000	28.5000000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	22.8321429	6.0485314	12.4000000	30.5500000
BASE	Baseline Value	7	24.5607143	7.5798919	13.0750000	33.5500000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	22.5000000	8.0078087	12.4000000	30.5500000
BASE	Baseline Value	4	27.0562500	7.4486121	17.1500000	33.5500000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	5.0333	0.2983	0.1722	4.8250	5.3750
Mean	95% CL Mean		Std Dev	95% CL	Std Dev
5.0333	4.2924	5.7742	0.2983	0.1553	1.8745
	DF	t Value	Pr > t		
	2	29.23	0.0012		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-0.8344	5.6155	1.9854	-9.7750	5.3750
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.8344	-5.5290	3.8603	5.6155	3.7128	11.4291
	DF	t Value	Pr > t		
	7	-0.42	0.6869		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	-4.3550	3.7180	1.6627	-9.7750	-0.1750
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.3550	-8.9715 0.2615	3.7180	2.2276 10.6839		
	DF	t Value	Pr > t		
	4	-2.62	0.0589		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	2.0417	6.6608	3.8456	-5.5750	6.7750
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2.0417	-14.5046	18.5879	6.6608	3.4680	41.8612
	DF	t Value	Pr > t		
	2	0.53	0.6485		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-1.7286	6.9238	2.6170	-13.4500	6.7750
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.7286	-8.1320	4.6749	6.9238	4.4617	15.2467
DF	t Value	Pr > t			
6	-0.66	0.5334			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-4.5562	6.4363	3.2182	-13.4500	1.3750
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.5562	-14.7978	5.6853	6.4363	3.6461	23.9981
DF	t Value	Pr > t			
3	-1.42	0.2518			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	38.9232878	19.3307221	23.3914737	60.5725979
BASE	Baseline Value	3	46.7229965	21.2059652	23.0208492	63.8984596

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	45.7972696	16.2351899	23.3914737	71.5218846
BASE	Baseline Value	8	60.8501379	28.3947736	23.0208492	123.4681329

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	49.9216587	14.7555778	33.1132143	71.5218846
BASE	Baseline Value	5	69.3264228	30.7672345	46.5233333	123.4681329

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	37.3257669	18.5273937	22.7382174	58.1719167
BASE	Baseline Value	3	46.7229965	21.2059652	23.0208492	63.8984596

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	42.3120531	14.1562857	22.7382174	58.1719167
BASE	Baseline Value	7	60.8868069	30.6696563	23.0208492	123.4681329

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	46.0517677	11.3334740	31.8852500	57.5161706
BASE	Baseline Value	4	71.5096647	35.0768678	46.5233333	123.4681329

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-7.7997	20.4696	11.8181	-31.0927	7.3229
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-7.7997	-58.6490	43.0496	20.4696	10.6577	128.6
DF	t Value	Pr > t			
2	-0.66	0.5771			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-15.0529	30.0921	10.6392	-80.7664	14.8046
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-15.0529	-40.2105 10.1048	30.0921	19.8961 61.2457		
	DF	t Value	Pr > t		
	7	-1.41	0.2000		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	-19.4048	36.2223	16.1991	-80.7664	14.8046
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-19.4048	-64.3807 25.5712	36.2223	21.7020 104.1		
	DF	t Value	Pr > t		
	4	-1.20	0.2971		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
3	-9.3972	20.4607	11.8130	-32.8313	4.9222		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-9.3972	-60.2244 41.4299	20.4607	10.6530 128.6				
DF	t Value	Pr > t					
2	-0.80	0.5097					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-18.5748	24.3433	9.2009	-65.9520	4.9222
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-18.5748	-41.0886	3.9391	24.3433	15.6867	53.6056
DF	t Value	Pr > t			
6	-2.02	0.0901			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
4	-25.4579	27.5446	13.7723	-65.9520	-4.3361		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-25.4579	-69.2875 18.3717	27.5446	15.6037 102.7				
DF	t Value	Pr > t					
3	-1.85	0.1617					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	475.7596667	230.8908971	262.1285000	720.7125000
BASE	Baseline Value	3	519.9911667	135.5085370	369.5610000	632.4975000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	523.9178125	207.3368065	262.1285000	929.7845000
BASE	Baseline Value	8	732.9047292	311.9194562	369.5610000	1433.17

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	552.8127000	213.9897502	408.2315000	929.7845000
BASE	Baseline Value	5	860.6528667	326.6254025	621.4143333	1433.17

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	500.0915000	210.3511948	279.2325000	698.0630000
BASE	Baseline Value	3	519.9911667	135.5085370	369.5610000	632.4975000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	500.5904286	142.5366876	279.2325000	698.0630000
BASE	Baseline Value	7	729.4924762	336.7502031	369.5610000	1433.17

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	500.9646250	105.5204351	384.2120000	638.1200000
BASE	Baseline Value	4	886.6184583	371.1479378	621.4143333	1433.17

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-44.2315	285.8	165.0	-370.4	162.8
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-44.2315	-754.3	665.8	285.8	148.8	1796.5
DF	t Value	Pr > t			
2	-0.27	0.8138			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-209.0	354.7	125.4	-920.7	162.8
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-209.0	-505.5	87.5185	354.7	234.5	721.8
DF	t Value	Pr > t			
7	-1.67	0.1395			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	-307.8	383.0	171.3	-920.7	135.7
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-307.8	-783.4	167.7	383.0	229.5	1100.6
DF	t Value	Pr > t			
4	-1.80	0.1467			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-19.8997	288.8	166.7	-353.3	153.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-19.8997	-737.3	697.5	288.8	150.4	1814.9
DF	t Value	Pr > t			
2	-0.12	0.9159			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-228.9	323.8	122.4	-795.0	153.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-228.9	-528.3 70.5240	323.8	208.6 712.9		
DF	t Value	Pr > t			
6	-1.87	0.1106			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-385.7	278.6	139.3	-795.0	-187.7
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-385.7	-828.9	57.6073	278.6	157.8	1038.6
	DF	t Value	Pr > t		
	3	-2.77	0.0696		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	19.4208069	8.6664793	12.1527778	29.0121429
BASE	Baseline Value	3	32.4318411	6.0509891	28.0973982	39.3450000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	26.4803395	11.5994912	12.1527778	49.8843750
BASE	Baseline Value	8	34.7228173	6.1208145	28.0973982	45.8609848

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	30.7160591	11.7516387	20.3318182	49.8843750
BASE	Baseline Value	5	36.0974031	6.3997755	29.3423077	45.8609848

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	19.9878788	7.7492556	11.1068182	25.3750000
BASE	Baseline Value	3	32.4318411	6.0509891	28.0973982	39.3450000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	24.4744443	9.6562099	11.1068182	40.9658730
BASE	Baseline Value	7	34.6426625	6.6066987	28.0973982	45.8609848

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	27.8393685	10.5463065	17.3514423	40.9658730
BASE	Baseline Value	4	36.3007785	7.3711437	29.3423077	45.8609848

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
3	-13.0110	2.8146	1.6250	-15.9446	-10.3329		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-13.0110	-20.0029 -6.0192	2.8146	1.4654 17.6889				
DF	t Value	Pr > t					
2	-8.01	0.0152					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-8.2425	7.3695	2.6055	-17.8144	4.0234
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-8.2425	-14.4035	-2.0814	7.3695	4.8725	14.9989
	DF	t Value	Pr > t		
	7	-3.16	0.0159		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	-5.3813	7.9871	3.5719	-17.8144	4.0234
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.3813	-15.2986	4.5359	7.9871	4.7853	22.9513
DF	t Value	Pr > t			
4	-1.51	0.2064			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-12.4440	5.4716	3.1591	-16.9906	-6.3713
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-12.4440	-26.0363	1.1483	5.4716	2.8489	34.3878
DF	t Value	Pr > t			
2	-3.94	0.0588			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-10.1682	7.8097	2.9518	-20.7948	2.0712
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-10.1682	-17.3910 -2.9454	7.8097	5.0325 17.1975		
	DF	t Value	Pr > t		
	6	-3.44	0.0137		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-8.4614	9.6416	4.8208	-20.7948	2.0712
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-8.4614	-23.8034	6.8806	9.6416	5.4619	35.9493
DF	t Value	Pr > t			
3	-1.76	0.1775			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	43.6665120	27.1678107	16.4724167	70.8079615
BASE	Baseline Value	3	43.4563600	5.7952426	38.3049848	49.7310119

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	39.0301760	17.4959643	16.4724167	70.8079615
BASE	Baseline Value	8	47.8635715	20.6962803	28.8071827	91.4056993

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	36.2483744	11.8680512	24.7269683	53.5968889
BASE	Baseline Value	5	50.5078984	26.6362046	28.8071827	91.4056993

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	37.5340439	12.9832789	22.5902222	46.0438261
BASE	Baseline Value	3	43.4563600	5.7952426	38.3049848	49.7310119

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	37.8644050	11.3791442	22.5902222	54.7654000
BASE	Baseline Value	7	50.5859128	20.7498119	33.9980000	91.4056993

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	38.1121759	12.0996626	26.1599375	54.7654000
BASE	Baseline Value	4	55.9330774	27.3818569	33.9980000	91.4056993

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	0.2102	25.7244	14.8520	-21.8326	28.4749
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.2102	-63.6928 64.1131	25.7244	13.3936 161.7		
	DF	t Value	Pr > t		
	2	0.01	0.9900		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-8.8334	24.3109	8.5952	-56.6824	28.4749
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-8.8334	-29.1578 11.4910	24.3109	16.0737 49.4792		
	DF	t Value	Pr > t		
	7	-1.03	0.3383		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	-14.2595	24.6022	11.0024	-56.6824	7.0782
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-14.2595	-44.8071 16.2881	24.6022	14.7400 70.6957		
	DF	t Value	Pr > t		
	4	-1.30	0.2647		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-5.9223	8.8882	5.1316	-15.7148	1.6350
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.9223	-28.0019 16.1572	8.8882	4.6277 55.8601		
	DF	t Value	Pr > t		
	2	-1.15	0.3677		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-12.7215	18.9264	7.1535	-53.6478	1.6350
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-12.7215	-30.2255	4.7825	18.9264	12.1961	41.6772
DF	t Value	Pr > t			
6	-1.78	0.1257			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-17.8209	24.1423	12.0711	-53.6478	-0.9384
	Mean	95% CL Mean	Std Dev	95% CL Std Dev	
	-17.8209	-56.2367 20.5949	24.1423	13.6764 90.0157	
		DF	t Value	Pr > t	
		3	-1.48	0.2363	

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	21.1807690	11.5236408	7.9749583	29.1976119
BASE	Baseline Value	3	27.0359206	3.8263825	23.4688788	31.0773968

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	23.0150577	8.1374600	7.9749583	32.0552222
BASE	Baseline Value	8	31.4271720	13.6041787	21.1557340	62.1054056

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	24.1156308	6.7414583	17.4706746	32.0552222
BASE	Baseline Value	5	34.0619228	17.1294667	21.1557340	62.1054056

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	22.3820314	9.4824072	11.4408333	28.2182609
BASE	Baseline Value	3	27.0359206	3.8263825	23.4688788	31.0773968

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	23.3600824	6.9467927	11.4408333	30.9562125
BASE	Baseline Value	7	32.8945203	13.9936982	22.4218000	62.1054056

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	24.0936207	5.9074363	16.5238750	30.9562125
BASE	Baseline Value	4	37.2884700	17.9393644	22.4218000	62.1054056

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-5.8552	9.1193	5.2650	-15.4939	2.6361
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-5.8552	-28.5088	16.7985	9.1193	4.7481	57.3126
	DF	t Value	Pr > t		
	2	-1.11	0.3819		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-8.4121	13.9773	4.9417	-39.6610	4.2667
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-8.4121	-20.0974	3.2732	13.9773	9.2414	28.4476
	DF	t Value	Pr > t		
	7	-1.70	0.1325		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
5	-9.9463	17.1015	7.6480	-39.6610	4.2667		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-9.9463	-31.1806 11.2880	17.1015	10.2461 49.1421				
DF	t Value	Pr > t					
4	-1.30	0.2633					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-4.6539	6.6607	3.8455	-12.0280	0.9255
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.6539	-21.1999	11.8921	6.6607	3.4679	41.8605
DF	t Value	Pr > t			
2	-1.21	0.3498			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-9.5344	13.0396	4.9285	-37.5046	0.9255
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-9.5344	-21.5941	2.5252	13.0396	8.4026	28.7141
DF	t Value	Pr > t			
6	-1.93	0.1012			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-13.1948	16.3952	8.1976	-37.5046	-1.7324
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-13.1948	-39.2832 12.8936	16.3952	9.2877 61.1302		
	DF	t Value	Pr > t		
	3	-1.61	0.2059		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	12.6666667	6.0277138	7.0000000	19.0000000
BASE	Baseline Value	3	12.1666667	3.3291641	10.0000000	16.0000000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	8	11.7500000	3.8452197	7.0000000	19.0000000
BASE	Baseline Value	8	12.5833333	2.2218254	10.0000000	16.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	5	11.2000000	2.5884358	8.0000000	14.0000000
BASE	Baseline Value	5	12.8333333	1.6996732	10.6666667	15.0000000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	14.1666667	7.9739158	7.5000000	23.0000000
BASE	Baseline Value	3	12.1666667	3.3291641	10.0000000	16.0000000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	7	12.5714286	5.3729924	7.5000000	23.0000000
BASE	Baseline Value	7	12.5952381	2.3995701	10.0000000	16.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	11.3750000	3.3008837	9.0000000	16.0000000
BASE	Baseline Value	4	12.9166667	1.9507833	10.6666667	15.0000000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

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Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	0.5000	3.1225	1.8028	-3.0000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.5000	-7.2567	8.2567	3.1225	1.6258	19.6241
	DF	t Value	Pr > t		
	2	0.28	0.8075		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
8	-0.8333	2.3821	0.8422	-4.5000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.8333	-2.8249	1.1582	2.3821	1.5750	4.8483
	DF	t Value	Pr > t		
	7	-0.99	0.3554		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
5	-1.6333	1.7095	0.7645	-4.5000	0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.6333	-3.7559	0.4892	1.7095	1.0242	4.9122
DF	t Value	Pr > t			
4	-2.14	0.0995			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	2.0000	4.7697	2.7538	-2.5000	7.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2.0000	-9.8486	13.8486	4.7697	2.4834	29.9763
	DF	t Value	Pr > t		
	2	0.73	0.5432		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

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Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

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----- week=6 treat=BD -----
```

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
7	-0.0238	3.7975	1.4353	-5.0000	7.0000

Mean	95% CL Mean	Std Dev	95% CL Std Dev
-0.0238	-3.5359 3.4882	3.7975	2.4471 8.3622

DF	t Value	Pr > t
6	-0.02	0.9873

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-1.5417	2.5509	1.2754	-5.0000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.5417	-5.6007	2.5173	2.5509	1.4450	9.5110
DF	t Value	Pr > t			
3	-1.21	0.3133			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttest.sas 13JUN2019 5:24

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	2.2123638	0.8812408	0.9421053	4.8312500
BASE	Baseline Value	16	2.1251737	0.5872002	0.8148810	2.9538889

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	2.1899656	0.7779134	0.9421053	4.8312500
BASE	Baseline Value	33	2.2115887	0.6651969	0.8148810	4.5850000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	2.1688849	0.6937404	1.1461538	3.6625000
BASE	Baseline Value	17	2.2929206	0.7397461	1.3215686	4.5850000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	2.0715550	0.7092059	0.8630435	3.7111111
BASE	Baseline Value	17	2.0694603	0.6140615	0.8148810	2.9538889

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	2.0693008	0.6291395	0.8630435	3.7111111
BASE	Baseline Value	32	2.1564521	0.6885121	0.8148810	4.5850000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	2.0667460	0.5491915	1.3223982	3.0250000
BASE	Baseline Value	15	2.2550429	0.7740395	1.3215686	4.5850000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	0.0872	0.6077	0.1519	-0.9700	1.9813
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.0872	-0.2366	0.4110	0.6077	0.4489	0.9405
	DF	t Value	Pr > t		
	15	0.57	0.5745		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-0.0216	0.5436	0.0946	-0.9700	1.9813
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0216	-0.2144 0.1711	0.5436	0.4372 0.7190		
DF	t Value	Pr > t			
32	-0.23	0.8207			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.1240	0.4710	0.1142	-0.9225	0.8137
	Mean	95% CL Mean	Std Dev	95% CL Std Dev	
	-0.1240	-0.3662 0.1181	0.4710	0.3508 0.7169	
		DF	t Value	Pr > t	
		16	-1.09	0.2937	

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	0.00209	0.3698	0.0897	-0.6705	0.9799
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.00209	-0.1880	0.1922	0.3698	0.2754	0.5628
	DF	t Value	Pr > t		
	16	0.02	0.9817		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-0.0872	0.4840	0.0856	-1.8800	0.9799
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.0872	-0.2616	0.0873	0.4840	0.3880	0.6435
	DF	t Value	Pr > t		
	31	-1.02	0.3163		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-0.1883	0.5846	0.1509	-1.8800	0.4458
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.1883	-0.5121	0.1355	0.5846	0.4280	0.9220
	DF	t Value	Pr > t		
	14	-1.25	0.2327		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	23.2820313	8.1070802	11.1500000	37.7000000
BASE	Baseline Value	16	24.5671875	7.7601531	12.8500000	35.6000000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	23.9397727	7.4544905	11.1500000	43.9500000
BASE	Baseline Value	33	26.4780303	7.8056089	12.8500000	45.8500000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	24.5588235	6.9772563	14.9000000	43.9500000
BASE	Baseline Value	17	28.2764706	7.6361623	16.9250000	45.8500000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	21.9661765	7.0242100	7.2500000	33.4000000
BASE	Baseline Value	17	24.0264706	7.8360867	12.8500000	35.6000000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	22.0390625	6.6635925	7.2500000	33.9500000
BASE	Baseline Value	32	25.7390625	7.9432893	12.8500000	45.8500000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	22.1216667	6.4745785	12.1000000	33.9500000
BASE	Baseline Value	15	27.6800000	7.8700790	16.9250000	45.8500000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	-1.2852	5.8282	1.4571	-14.5500	5.3750
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.2852	-4.3908 1.8205	5.8282	4.3053 9.0203		
DF	t Value	Pr > t			
15	-0.88	0.3917			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-2.5383	5.5090	0.9590	-14.5500	9.1500
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-2.5383	-4.4917	-0.5848	5.5090	4.4303	7.2868
	DF	t Value	Pr > t		
	32	-2.65	0.0125		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-3.7176	5.0799	1.2321	-12.7250	9.1500
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.7176	-6.3295 -1.1058	5.0799	3.7834 7.7313		
DF	t Value	Pr > t			
16	-3.02	0.0082			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-2.0603	5.5137	1.3373	-14.7500	6.7750
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.0603	-4.8952 0.7746	5.5137	4.1065 8.3915		
DF	t Value	Pr > t			
16	-1.54	0.1429			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-3.7000	6.0994	1.0782	-18.8000	6.7750
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7000	-5.8991	-1.5009	6.0994	4.8899	8.1090
	DF	t Value	Pr > t		
	31	-3.43	0.0017		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Duration) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-5.5583	6.3772	1.6466	-18.8000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.5583	-9.0899 -2.0268	6.3772	4.6689 10.0574		
	DF	t Value	Pr > t		
	14	-3.38	0.0045		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	44.6595415	13.4855720	20.6866667	73.0970977
BASE	Baseline Value	16	51.0346258	13.4692001	21.4753984	75.0850844

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	47.2751046	13.3661180	20.6866667	82.0725833
BASE	Baseline Value	33	54.3021648	19.7499198	0.6425897	123.4681329

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	49.7368109	13.1731523	33.1132143	82.0725833
BASE	Baseline Value	17	57.3774956	24.2757584	0.6425897	123.4681329

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	47.9732589	13.2547513	22.7382174	79.6780000
BASE	Baseline Value	17	50.2710494	13.1157389	21.4753984	75.0850844

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	47.4004794	12.3353637	22.7382174	79.6780000
BASE	Baseline Value	32	53.0707056	19.8752425	0.6425897	123.4681329

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	46.7513292	11.6314966	26.8003636	65.1991000
BASE	Baseline Value	15	56.2436493	25.6475572	0.6425897	123.4681329

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum	
16	-6.3751	14.3137	3.5784	-41.1831	10.7566	
Mean	95% CL Mean	Std Dev	95% CL Std Dev			
-6.3751	-14.0023	1.2521	14.3137	10.5736	22.1531	
		DF	t Value	Pr > t		
		15	-1.78	0.0951		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-7.0271	19.9649	3.4754	-80.7664	42.1530
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-7.0271	-14.1063	0.0522	19.9649	16.0555	26.4074
DF	t Value	Pr > t			
32	-2.02	0.0516			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-7.6407	24.5823	5.9621	-80.7664	42.1530
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-7.6407	-20.2797	4.9984	24.5823	18.3082	37.4125
DF	t Value	Pr > t			
16	-1.28	0.2183			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-2.2978	11.5269	2.7957	-32.8313	17.8962
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.2978	-8.2244 3.6288	11.5269	8.5849 17.5432		
DF	t Value	Pr > t			
16	-0.82	0.4232			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-5.6702	17.0417	3.0126	-65.9520	42.8729
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.6702	-11.8144 0.4740	17.0417	13.6624 22.6566		
DF	t Value	Pr > t			
31	-1.88	0.0692			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
15	-9.4923	21.4886	5.5483	-65.9520	42.8729		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-9.4923	-21.3923 2.4077	21.4886	15.7324 33.8897				
DF	t Value	Pr > t					
14	-1.71	0.1092					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	473.4289688	145.9870856	249.1145000	783.1855000
BASE	Baseline Value	16	580.8942917	166.1952750	279.6515000	938.6710000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	526.3613333	174.9642579	249.1145000	984.8710000
BASE	Baseline Value	33	646.6355152	235.2609979	7.0590000	1433.17

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	576.1800294	189.2245007	373.1505000	984.8710000
BASE	Baseline Value	17	708.5096078	276.4259796	7.0590000	1433.17

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	508.9263529	119.4607863	279.2325000	717.1020000
BASE	Baseline Value	17	576.8078039	161.9584059	279.6515000	938.6710000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	500.7410156	112.0699802	279.2325000	717.1020000
BASE	Baseline Value	32	630.2626719	233.6203386	7.0590000	1433.17

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	491.4643000	106.4311197	294.8040000	651.9910000
BASE	Baseline Value	15	690.8448556	288.9160447	7.0590000	1433.17

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	-107.5	169.0	42.2407	-430.1	162.8
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-107.5	-197.5 -17.4314	169.0	124.8	261.5	
	DF	t Value	Pr > t		
	15	-2.54	0.0225		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-120.3	230.6	40.1385	-920.7	366.1
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-120.3	-202.0 -38.5148	230.6	185.4	305.0	
		DF	t Value	Pr > t	
		32	-3.00	0.0052	

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
17	-132.3	281.5	68.2770	-920.7	366.1		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-132.3	-277.1 12.4111	281.5	209.7 428.4				
DF	t Value	Pr > t					
16	-1.94	0.0705					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
17	-67.8815	177.9	43.1450	-367.9	271.6		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-67.8815	-159.3 23.5819	177.9	132.5 270.7				
DF	t Value	Pr > t					
16	-1.57	0.1352					

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-129.5	221.5	39.1506	-795.0	471.6
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-129.5	-209.4 -49.6736	221.5	177.6	294.4	
		DF	t Value	Pr > t	
		31	-3.31	0.0024	

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Total Puff Volume) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-199.4	250.2	64.6007	-795.0	471.6
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-199.4	-337.9 -60.8258	250.2	183.2 394.6		
DF	t Value	Pr > t			
14	-3.09	0.0080			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	24.2802314	9.2226844	11.7423077	43.6300000
BASE	Baseline Value	16	29.5049949	10.2204538	16.6892857	52.2985714

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	25.4875371	10.7076077	9.7300000	55.6291667
BASE	Baseline Value	33	29.1887302	9.1818910	14.6955952	52.2985714

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	26.6238249	12.1134019	9.7300000	55.6291667
BASE	Baseline Value	17	28.8910693	8.3958925	14.6955952	45.8609848

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	21.0442468	7.1810355	9.4375000	38.2087302
BASE	Baseline Value	17	29.4560947	9.9001894	16.6892857	52.2985714

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	23.9369640	9.7692746	9.4375000	46.0802083
BASE	Baseline Value	32	29.3875382	8.9660782	14.6955952	52.2985714

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	27.2153768	11.4331957	9.5291667	46.0802083
BASE	Baseline Value	15	29.3098407	8.1227935	14.6955952	45.8609848

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	-5.2248	8.8726	2.2181	-17.9346	12.7864
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.2248	-9.9526 -0.4969	8.8726	6.5542 13.7320		
DF	t Value	Pr > t			
15	-2.36	0.0325			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-3.7012	9.6597	1.6815	-17.9346	30.1383
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7012	-7.1264	-0.2760	9.6597	7.7682	12.7768
	DF	t Value	Pr > t		
	32	-2.20	0.0351		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-2.2672	10.4072	2.5241	-17.8144	30.1383
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.2672	-7.6181 3.0836	10.4072	7.7510 15.8390		
	DF	t Value	Pr > t		
	16	-0.90	0.3824		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-8.4118	8.1809	1.9842	-25.0152	9.4698
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-8.4118	-12.6181 -4.2056	8.1809	6.0929 12.4508		
	DF	t Value	Pr > t		
	16	-4.24	0.0006		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-5.4506	9.7138	1.7172	-25.0152	16.1425
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-5.4506	-8.9528	-1.9484	9.7138	7.7876	12.9143
	DF	t Value	Pr > t		
	31	-3.17	0.0034		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Inter-Puff Interval) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-2.0945	10.4753	2.7047	-20.7948	16.1425
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.0945	-7.8955 3.7066	10.4753	7.6692 16.5206		
DF	t Value	Pr > t			
14	-0.77	0.4516			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	39.7009985	13.7236776	16.4724167	70.8079615
BASE	Baseline Value	16	42.8876348	10.4582383	22.9812610	64.0665202

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	40.5974874	11.7694968	16.4724167	70.8079615
BASE	Baseline Value	33	43.4697379	15.1670397	5.8574444	91.4056993

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	41.4412417	9.9455459	24.7269683	55.2359333
BASE	Baseline Value	17	44.0175996	18.8913103	5.8574444	91.4056993

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	43.4274222	14.7546658	22.5902222	81.1615714
BASE	Baseline Value	17	43.7316689	10.8859686	22.9812610	64.0665202

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	41.8299760	12.3435193	22.0378462	81.1615714
BASE	Baseline Value	32	43.8338917	15.1463525	5.8574444	91.4056993

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	40.0195369	9.0533633	22.0378462	54.7654000
BASE	Baseline Value	15	43.9497443	19.3008583	5.8574444	91.4056993

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	-3.1866	12.8515	3.2129	-24.7884	28.4749
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.1866	-10.0347	3.6615	12.8515	9.4935	19.8902
DF	t Value	Pr > t			
15	-0.99	0.3370			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-2.8723	17.3967	3.0284	-56.6824	44.9169
	Mean	95% CL Mean	Std Dev	95% CL Std Dev	
	-2.8723	-9.0409 3.2964	17.3967	13.9903 23.0105	
		DF	t Value	Pr > t	
		32	-0.95	0.3500	

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-2.5764	21.2193	5.1464	-56.6824	44.9169
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.5764	-13.4863	8.3336	21.2193	15.8035	32.2943
DF	t Value	Pr > t			
16	-0.50	0.6235			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.3042	9.7464	2.3638	-15.7148	19.6325
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.3042	-5.3154	4.7069	9.7464	7.2588	14.8333
	DF	t Value	Pr > t		
	16	-0.13	0.8992		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-2.0039	14.9807	2.6482	-53.6478	37.8476
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.0039	-7.4050 3.3972	14.9807	12.0101 19.9166		
	DF	t Value	Pr > t		
	31	-0.76	0.4549		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Peak Puff Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-3.9302	19.5164	5.0391	-53.6478	37.8476
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.9302	-14.7380	6.8776	19.5164	14.2885	30.7793
DF	t Value	Pr > t			
14	-0.78	0.4484			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	23.6308831	7.8434416	7.9749583	34.6958889
BASE	Baseline Value	16	26.6528116	8.3371390	12.1964396	45.3893939

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	24.5697727	6.7721921	7.9749583	36.4963333
BASE	Baseline Value	33	27.1519154	10.6968942	0.3879829	62.1054056

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	25.4534334	5.6867737	17.4706746	36.4963333
BASE	Baseline Value	17	27.6216601	12.7749713	0.3879829	62.1054056

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	26.7164265	9.7249631	11.4408333	47.8275714
BASE	Baseline Value	17	27.0839568	8.1959915	12.1964396	45.3893939

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	25.5015704	7.9079780	11.4408333	47.8275714
BASE	Baseline Value	32	27.3342423	10.7821675	0.3879829	62.1054056

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	24.1247335	5.1540275	14.9975385	33.1211111
BASE	Baseline Value	15	27.6178992	13.4346273	0.3879829	62.1054056

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	-3.0219	6.7128	1.6782	-15.4939	4.4858
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.0219	-6.5989	0.5551	6.7128	4.9588	10.3893
	DF	t Value	Pr > t		
	15	-1.80	0.0919		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-2.5821	10.6009	1.8454	-39.6610	26.1202
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.5821	-6.3410 1.1768	10.6009	8.5251 14.0217		
	DF	t Value	Pr > t		
	32	-1.40	0.1714		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-2.1682	13.4958	3.2732	-39.6610	26.1202
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.1682	-9.1071 4.7707	13.4958	10.0513 20.5396		
DF	t Value	Pr > t			
16	-0.66	0.5171			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.3675	6.2551	1.5171	-12.0280	11.0268
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3675	-3.5836 2.8486	6.2551	4.6586 9.5199		
	DF	t Value	Pr > t		
	16	-0.24	0.8117		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-1.8327	9.6319	1.7027	-37.5046	19.8181
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.8327	-5.3053 1.6400	9.6319	7.7219 12.8054		
	DF	t Value	Pr > t		
	31	-1.08	0.2901		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Flow Rate) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-3.4932	12.4558	3.2161	-37.5046	19.8181
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.4932	-10.3910 3.4046	12.4558	9.1193 19.6441		
	DF	t Value	Pr > t		
	14	-1.09	0.2958		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	16	11.0781250	3.4274854	6.0000000	19.0000000
BASE	Baseline Value	16	11.6979167	2.4975683	7.0000000	16.0000000

----- week=2 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	33	11.4772727	3.4189063	6.0000000	20.0000000
BASE	Baseline Value	33	12.1616162	2.3893880	7.0000000	19.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	11.8529412	3.4720523	7.0000000	20.0000000
BASE	Baseline Value	17	12.5980392	2.2700181	10.0000000	19.0000000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	11.0588235	3.6779850	7.0000000	23.0000000
BASE	Baseline Value	17	11.7745098	2.4387932	7.0000000	16.0000000

----- week=6 treat=BD -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	32	10.9843750	3.1964809	7.0000000	23.0000000
BASE	Baseline Value	32	12.1510417	2.4268360	7.0000000	19.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	15	10.9000000	2.6739484	8.0000000	16.0000000
BASE	Baseline Value	15	12.5777778	2.4241401	10.0000000	19.0000000

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
16	-0.6198	2.4271	0.6068	-6.0000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.6198	-1.9131	0.6735	2.4271	1.7929	3.7564
DF	t Value	Pr > t			
15	-1.02	0.3232			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
33	-0.6843	2.5485	0.4436	-6.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.6843	-1.5880 0.2193	2.5485	2.0494 3.3708		
	DF	t Value	Pr > t		
	32	-1.54	0.1328		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.7451	2.7311	0.6624	-5.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.7451	-2.1493	0.6591	2.7311	2.0340	4.1565
DF	t Value	Pr > t			
16	-1.12	0.2772			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.7157	3.1274	0.7585	-6.0000	7.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.7157	-2.3236	0.8923	3.1274	2.3292	4.7596
	DF	t Value	Pr > t		
	16	-0.94	0.3594		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
32	-1.1667	2.6650	0.4711	-6.0000	7.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-1.1667	-2.1275	-0.2058	2.6650	2.1365	3.5430
	DF	t Value	Pr > t		
	31	-2.48	0.0189		

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Topography Parameter (Average Number of Puffs) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.3.3 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
15	-1.6778	2.0054	0.5178	-5.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.6778	-2.7883 -0.5672	2.0054	1.4682 3.1627		
DF	t Value	Pr > t			
14	-3.24	0.0059			

Treat B: VLN non-mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_top/adam_topstatsttestITT.sas 13JUN2019 5:25

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	581.0389333	312.7863621	114.9213000	1344.94
BASE	Baseline Value	21	614.0894571	353.9043703	161.2169000	1663.44

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	521.0372585	269.1555816	114.9213000	1344.94
BASE	Baseline Value	41	548.6696263	294.7069372	150.9852800	1663.44

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	194.7383736	63.3150694	97.1989100	280.8500000
BASE	Baseline Value	11	519.0225155	312.4160338	188.2974700	1184.16

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	173.7722204	77.2204616	44.9618400	304.9020000
BASE	Baseline Value	23	433.1636639	245.2693487	172.1750000	1184.16

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	458.0355000	203.4044799	164.9536000	1027.18
BASE	Baseline Value	20	479.9788040	203.2470193	150.9852800	996.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	154.5532467	86.2502756	44.9618400	304.9020000
BASE	Baseline Value	12	354.4597167	132.1144446	172.1750000	602.8540000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	614.7169235	416.6105137	120.5760000	1717.98
BASE	Baseline Value	17	633.4639765	389.8587593	161.2169000	1663.44

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	517.9970361	321.7481164	120.5760000	1717.98
BASE	Baseline Value	36	543.5170467	310.2192407	150.9852800	1663.44

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	159.4458200	45.6912035	89.3200000	235.4300000
BASE	Baseline Value	10	536.9964670	323.2647452	188.2974700	1184.16

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	142.2645311	70.6289879	30.9995000	294.5150000
BASE	Baseline Value	19	450.8653826	264.7532595	172.1750000	1184.16

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	431.4581895	173.9914833	185.8500000	808.7376000
BASE	Baseline Value	19	463.0382147	193.7673163	150.9852800	996.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	123.1742100	89.9799047	30.9995000	294.5150000
BASE	Baseline Value	9	355.1641778	143.4321312	172.1750000	602.8540000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-33.0505	110.5	24.1231	-318.5	186.0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-33.0505	-83.3703 17.2693	110.5	84.5740 159.6		
DF	t Value	Pr > t			
20	-1.37	0.1858			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-27.6324	95.3232	14.8870	-318.5	186.0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-27.6324	-57.7201	2.4553	95.3232	78.2616	122.0
DF	t Value	Pr > t			
40	-1.86	0.0708			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	-324.3	269.6	81.2990	-916.5	24.9910
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-324.3	-505.4 -143.1	269.6	188.4 473.2		
DF	t Value	Pr > t			
10	-3.99	0.0026			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	-259.4	198.8	41.4448	-916.5	24.9910
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-259.4	-345.3 -173.4	198.8	153.7 281.3		
DF	t Value	Pr > t			
22	-6.26	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-21.9433	78.7366	17.6060	-193.4	83.3420
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-21.9433	-58.7931 14.9065	78.7366	59.8784 115.0		
	DF	t Value	Pr > t		
	19	-1.25	0.2278		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-199.9	69.6152	20.0962	-298.0	-63.6055
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-199.9	-244.1	-155.7	69.6152	49.3151	118.2
	DF	t Value	Pr > t		
	11	-9.95	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
17	-18.7471	97.5859	23.6681	-210.4	214.4		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-18.7471	-68.9211 31.4270	97.5859	72.6790 148.5				
DF	t Value	Pr > t					
16	-0.79	0.4399					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-25.5200	93.7620	15.6270	-210.4	214.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-25.5200	-57.2445	6.2045	93.7620	76.0487	122.3
DF	t Value	Pr > t			
35	-1.63	0.1114			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-377.6	303.3	95.9009	-993.3	-45.9358
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-377.6	-594.5 -160.6	303.3	208.6 553.6		
DF	t Value	Pr > t			
9	-3.94	0.0034			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-308.6	234.9	53.8878	-993.3	-45.9358
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-308.6	-421.8 -195.4	234.9	177.5 347.4		
DF	t Value	Pr > t			
18	-5.73	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-31.5800	92.4514	21.2098	-187.3	205.9
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-31.5800	-76.1402	12.9801	92.4514	69.8574	136.7
DF	t Value	Pr > t			
18	-1.49	0.1538			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.1 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-232.0	90.1669	30.0556	-324.4	-78.9404
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-232.0	-301.3	-162.7	90.1669	60.9039	172.7
	DF	t Value	Pr > t		
	8	-7.72	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	581.0389333	312.7863621	114.9213000	1344.94
BASE	Baseline Value	21	614.0894571	353.9043703	161.2169000	1663.44

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	521.0372585	269.1555816	114.9213000	1344.94
BASE	Baseline Value	41	548.6696263	294.7069372	150.9852800	1663.44

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	313.9114850	176.1389569	77.7010000	748.5202000
BASE	Baseline Value	47	588.2075164	291.6921642	67.4706000	1264.49

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	91	266.7660829	163.6123982	11.2960000	748.5202000
BASE	Baseline Value	90	508.9772219	261.1278655	67.4706000	1264.49

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	458.0355000	203.4044799	164.9536000	1027.18
BASE	Baseline Value	20	479.9788040	203.2470193	150.9852800	996.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	214.1386572	131.4077498	11.2960000	656.2600000
BASE	Baseline Value	43	422.3766674	191.3179417	82.0820000	898.6560000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	614.7169235	416.6105137	120.5760000	1717.98
BASE	Baseline Value	17	633.4639765	389.8587593	161.2169000	1663.44

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	517.9970361	321.7481164	120.5760000	1717.98
BASE	Baseline Value	36	543.5170467	310.2192407	150.9852800	1663.44

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	377.0568762	217.6682746	89.3200000	878.5590000
BASE	Baseline Value	41	603.8302846	280.6243628	188.2974700	1264.49

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	83	309.8332854	207.3561721	5.6550000	878.5590000
BASE	Baseline Value	82	521.3684874	253.7534259	82.0820000	1264.49

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	431.4581895	173.9914833	185.8500000	808.7376000
BASE	Baseline Value	19	463.0382147	193.7673163	150.9852800	996.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	240.9700949	173.1282022	5.6550000	691.8512000
BASE	Baseline Value	41	438.9066902	194.1686018	82.0820000	898.6560000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
21	-33.0505	110.5	24.1231	-318.5	186.0		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-33.0505	-83.3703 17.2693	110.5	84.5740 159.6				
DF	t Value	Pr > t					
20	-1.37	0.1858					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-27.6324	95.3232	14.8870	-318.5	186.0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-27.6324	-57.7201	2.4553	95.3232	78.2616	122.0
DF	t Value	Pr > t			
40	-1.86	0.0708			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	-274.1	205.3	29.9529	-916.5	24.9910
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-274.1	-334.4	-213.8	205.3	170.6	257.9
	DF	t Value	Pr > t		
	46	-9.15	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
90	-242.6	168.0	17.7116	-916.5	142.1
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-242.6	-277.8 -207.4	168.0	146.6 196.9		
DF	t Value	Pr > t			
89	-13.70	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-21.9433	78.7366	17.6060	-193.4	83.3420
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-21.9433	-58.7931 14.9065	78.7366	59.8784 115.0		
	DF	t Value	Pr > t		
	19	-1.25	0.2278		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-208.2	106.4	16.2307	-400.0	142.1
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-208.2	-241.0 -175.5	106.4	87.7574	135.3	
	DF	t Value	Pr > t		
	42	-12.83	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
17	-18.7471	97.5859	23.6681	-210.4	214.4		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-18.7471	-68.9211 31.4270	97.5859	72.6790 148.5				
DF	t Value	Pr > t					
16	-0.79	0.4399					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-25.5200	93.7620	15.6270	-210.4	214.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-25.5200	-57.2445	6.2045	93.7620	76.0487	122.3
DF	t Value	Pr > t			
35	-1.63	0.1114			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-227.2	224.3	35.0336	-993.3	64.0281
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-227.2	-298.0 -156.4	224.3	184.2 287.0		
DF	t Value	Pr > t			
40	-6.49	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
82	-212.6	179.7	19.8425	-993.3	175.0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-212.6	-252.1 -173.1	179.7	155.8 212.3		
DF	t Value	Pr > t			
81	-10.71	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-31.5800	92.4514	21.2098	-187.3	205.9
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-31.5800	-76.1402	12.9801	92.4514	69.8574	136.7
DF	t Value	Pr > t			
18	-1.49	0.1538			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNAL Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.1.2.2 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-197.9	120.9	18.8811	-437.3	175.0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-197.9	-236.1 -159.8	120.9	99.2590 154.7		
DF	t Value	Pr > t			
40	-10.48	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDNNAL
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	119
Number of Observations Used	117
Number of Observations Not Used	2

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1417.16430222	
1	2	1354.29675983	0.00085292
2	1	1353.74011528	0.00004727
3	1	1353.71177534	0.00000018
4	1	1353.71166882	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	19196
UN(2,1)	subject	17306
UN(2,2)	subject	22427

Fit Statistics

-2 Res Log Likelihood	1353.7
AIC (smaller is better)	1359.7
AICC (smaller is better)	1359.9
BIC (smaller is better)	1366.2

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	63.45	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	59.9	17.39	<.0001
week	1	50.5	1.87	0.1774
treat*week	3	50.5	1.43	0.2441

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-286.35	52.0080	59	-5.51	<.0001	0.05	-390.42	-182.28
Week 2: VLN Mentholated vs UB Mentholated	-177.96	50.5906	59	-3.52	0.0008	0.05	-279.19	-76.7316
Week 2: VLN Combined vs UB Combined	-232.16	36.2775	59	-6.40	<.0001	0.05	-304.75	-159.57
Week 2: VLN Combined	-262.10	28.9166	59	-9.06	<.0001	0.05	-319.96	-204.23
Week 2: UB Combined	-29.9385	21.9064	59	-1.37	0.1769	0.05	-73.7731	13.8960
Week 6: VLN Non-mentholated vs UB Non-mentholated	-352.69	57.5570	59.6	-6.13	<.0001	0.05	-467.83	-237.54
Week 6: VLN Mentholated vs UB Mentholated	-189.78	56.6152	61.1	-3.35	0.0014	0.05	-302.99	-76.5770
Week 6: VLN Combined vs UB Combined	-271.23	40.3674	60.4	-6.72	<.0001	0.05	-351.97	-190.50
Week 6: VLN Combined	-298.00	32.2816	60.8	-9.23	<.0001	0.05	-362.55	-233.44
Week 6: UB Combined	-26.7654	24.2367	59.6	-1.10	0.2739	0.05	-75.2535	21.7226

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-37.9337	30.9803	59	-1.22	0.2257	0.05	-99.9251	24.0577
treat*week	A	6	-17.4531	34.7812	61.6	-0.50	0.6176	0.05	-86.9898	52.0835
treat*week	B	2	-324.28	41.7738	59	-7.76	<.0001	0.05	-407.87	-240.69
treat*week	B	6	-370.14	45.8593	58.5	-8.07	<.0001	0.05	-461.92	-278.36
treat*week	C	2	-21.9433	30.9803	59	-0.71	0.4815	0.05	-83.9347	40.0481
treat*week	C	6	-36.0777	33.7630	57.5	-1.07	0.2897	0.05	-103.68	31.5201
treat*week	D	2	-199.91	39.9954	59	-5.00	<.0001	0.05	-279.94	-119.88
treat*week	D	6	-225.86	45.4460	63.2	-4.97	<.0001	0.05	-316.67	-135.05

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-20.4806	20.9496	50.6	-0.98	0.3329	0.05	-62.5473	21.5861
treat*week	A	2	B	2	286.35	52.0080	59	5.51	<.0001	0.05	182.28	390.42
treat*week	A	2	B	6	332.21	55.3431	68.3	6.00	<.0001	0.05	221.78	442.63
treat*week	A	2	C	2	-15.9904	43.8127	59	-0.36	0.7164	0.05	-103.66	71.6787
treat*week	A	2	C	6	-1.8560	45.8227	69.3	-0.04	0.9678	0.05	-93.2630	89.5509
treat*week	A	2	D	2	161.97	50.5906	59	3.20	0.0022	0.05	60.7412	263.20
treat*week	A	2	D	6	187.93	55.0011	72.9	3.42	0.0010	0.05	78.3052	297.55
treat*week	A	6	B	2	306.83	54.3579	71.8	5.64	<.0001	0.05	198.46	415.20
treat*week	A	6	B	6	352.69	57.5570	59.6	6.13	<.0001	0.05	237.54	467.83
treat*week	A	6	C	2	4.4902	46.5780	72.6	0.10	0.9235	0.05	-88.3483	97.3287
treat*week	A	6	C	6	18.6246	48.4735	59.6	0.38	0.7022	0.05	-78.3515	115.60
treat*week	A	6	D	2	182.45	53.0034	72	3.44	0.0010	0.05	76.7938	288.11
treat*week	A	6	D	6	208.41	57.2283	62.6	3.64	0.0006	0.05	94.0289	322.78

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.1 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	45.8555	26.4865	50.4	1.73	0.0895	0.05	-7.3334	99.0444
treat*week	B	2	C	2	-302.34	52.0080	59	-5.81	<.0001	0.05	-406.41	-198.27
treat*week	B	2	C	6	-288.21	53.7121	69.1	-5.37	<.0001	0.05	-395.36	-181.06
treat*week	B	2	D	2	-124.38	57.8332	59	-2.15	0.0356	0.05	-240.10	-8.6537
treat*week	B	2	D	6	-98.4251	61.7284	74	-1.59	0.1151	0.05	-221.42	24.5727
treat*week	B	6	C	2	-348.20	55.3431	68.3	-6.29	<.0001	0.05	-458.62	-237.77
treat*week	B	6	C	6	-334.06	56.9475	58.1	-5.87	<.0001	0.05	-448.05	-220.07
treat*week	B	6	D	2	-170.23	60.8499	70	-2.80	0.0066	0.05	-291.60	-48.8704
treat*week	B	6	D	6	-144.28	64.5633	60.8	-2.23	0.0291	0.05	-273.39	-15.1696
treat*week	C	2	C	6	14.1344	19.2118	50.3	0.74	0.4653	0.05	-24.4473	52.7160
treat*week	C	2	D	2	177.96	50.5906	59	3.52	0.0008	0.05	76.7316	279.19
treat*week	C	2	D	6	203.92	55.0011	72.9	3.71	0.0004	0.05	94.2956	313.54
treat*week	C	6	D	2	163.83	52.3409	69.3	3.13	0.0026	0.05	59.4193	268.24
treat*week	C	6	D	6	189.78	56.6152	61.1	3.35	0.0014	0.05	76.5770	302.99
treat*week	D	2	D	6	25.9526	27.9391	50.6	0.93	0.3573	0.05	-30.1473	82.0525

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDNNAL
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	251
Number of Observations Used	247
Number of Observations Not Used	4

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	3112.74547633	
1	2	2996.51940428	0.00017900
2	1	2996.27374742	0.00000262
3	1	2996.27035788	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	21867
UN(2,1)	subject	19741
UN(2,2)	subject	26825

Fit Statistics

-2 Res Log Likelihood	2996.3
AIC (smaller is better)	3002.3
AICC (smaller is better)	3002.4
BIC (smaller is better)	3011.0

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	116.48	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	127	16.45	<.0001
week	1	111	3.54	0.0624
treat*week	3	111	2.14	0.0989

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-233.39	39.3987	128	-5.92	<.0001	0.05	-311.34	-155.43
Week 2: VLN Mentholated vs UB Mentholated	-182.93	39.8378	128	-4.59	<.0001	0.05	-261.75	-104.10
Week 2: VLN Combined vs UB Combined	-208.16	28.0148	128	-7.43	<.0001	0.05	-263.59	-152.73
Week 2: VLN Combined	-238.10	15.4319	130	-15.43	<.0001	0.05	-268.63	-207.57
Week 2: UB Combined	-29.9385	23.3813	128	-1.28	0.2027	0.05	-76.2035	16.3264
Week 6: VLN Non-mentholated vs UB Non-mentholated	-203.03	45.2497	127	-4.49	<.0001	0.05	-292.58	-113.49
Week 6: VLN Mentholated vs UB Mentholated	-152.54	44.5138	119	-3.43	0.0008	0.05	-240.68	-64.3957
Week 6: VLN Combined vs UB Combined	-177.79	31.7372	123	-5.60	<.0001	0.05	-240.61	-114.96
Week 6: VLN Combined	-204.55	17.3756	122	-11.77	<.0001	0.05	-238.95	-170.16
Week 6: UB Combined	-26.7661	26.5583	123	-1.01	0.3155	0.05	-79.3357	25.8035

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-37.9337	33.0661	128	-1.15	0.2534	0.05	-103.36	27.4948
treat*week	A	6	-17.4485	38.1570	128	-0.46	0.6482	0.05	-92.9504	58.0534
treat*week	B	2	-271.32	21.4217	129	-12.67	<.0001	0.05	-313.71	-228.94
treat*week	B	6	-220.48	24.3223	124	-9.07	<.0001	0.05	-268.62	-172.34
treat*week	C	2	-21.9433	33.0661	128	-0.66	0.5081	0.05	-87.3718	43.4852
treat*week	C	6	-36.0837	36.9514	118	-0.98	0.3308	0.05	-109.25	37.0875
treat*week	D	2	-204.87	22.2189	130	-9.22	<.0001	0.05	-248.83	-160.91
treat*week	D	6	-188.62	24.8208	121	-7.60	<.0001	0.05	-237.76	-139.48

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-20.4852	23.9830	111	-0.85	0.3949	0.05	-68.0089	27.0385
treat*week	A	2	B	2	233.39	39.3987	128	5.92	<.0001	0.05	155.43	311.34
treat*week	A	2	B	6	182.55	41.0481	154	4.45	<.0001	0.05	101.46	263.64
treat*week	A	2	C	2	-15.9904	46.7626	128	-0.34	0.7330	0.05	-108.52	76.5394
treat*week	A	2	C	6	-1.8500	49.5860	150	-0.04	0.9703	0.05	-99.8247	96.1246
treat*week	A	2	D	2	166.94	39.8378	128	4.19	<.0001	0.05	88.1137	245.76
treat*week	A	2	D	6	150.69	41.3454	152	3.64	0.0004	0.05	69.0014	232.37
treat*week	A	6	B	2	253.87	43.7590	150	5.80	<.0001	0.05	167.41	340.34
treat*week	A	6	B	6	203.03	45.2497	127	4.49	<.0001	0.05	113.49	292.58
treat*week	A	6	C	2	4.4948	50.4909	158	0.09	0.9292	0.05	-95.2276	104.22
treat*week	A	6	C	6	18.6352	53.1165	123	0.35	0.7263	0.05	-86.5041	123.77
treat*week	A	6	D	2	187.42	44.1547	151	4.24	<.0001	0.05	100.18	274.66
treat*week	A	6	D	6	171.17	45.5195	126	3.76	0.0003	0.05	81.0871	261.26

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNAL Mass Excreted
for Table 14.2.5.1.3.2 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	-50.8396	15.1308	112	-3.36	0.0011	0.05	-80.8197	-20.8594
treat*week	B	2	C	2	-249.38	39.3987	128	-6.33	<.0001	0.05	-327.34	-171.42
treat*week	B	2	C	6	-235.24	42.7118	141	-5.51	<.0001	0.05	-319.68	-150.80
treat*week	B	2	D	2	-66.4511	30.8637	130	-2.15	0.0332	0.05	-127.51	-5.3893
treat*week	B	2	D	6	-82.7013	32.7865	153	-2.52	0.0127	0.05	-147.48	-17.9273
treat*week	B	6	C	2	-198.54	41.0481	154	-4.84	<.0001	0.05	-279.63	-117.45
treat*week	B	6	C	6	-184.40	44.2378	120	-4.17	<.0001	0.05	-271.99	-96.8116
treat*week	B	6	D	2	-15.6116	32.9432	157	-0.47	0.6362	0.05	-80.6793	49.4562
treat*week	B	6	D	6	-31.8617	34.7512	122	-0.92	0.3610	0.05	-100.65	36.9299
treat*week	C	2	C	6	14.1404	22.0144	110	0.64	0.5220	0.05	-29.4853	57.7661
treat*week	C	2	D	2	182.93	39.8378	128	4.59	<.0001	0.05	104.10	261.75
treat*week	C	2	D	6	166.68	41.3454	152	4.03	<.0001	0.05	84.9918	248.36
treat*week	C	6	D	2	168.79	43.1171	142	3.91	0.0001	0.05	83.5534	254.02
treat*week	C	6	D	6	152.54	44.5138	119	3.43	0.0008	0.05	64.3957	240.68
treat*week	D	2	D	6	-16.2501	15.2884	112	-1.06	0.2901	0.05	-46.5409	14.0406

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	20.8089223	21.2300710	2.4263400	96.9871000
BASE	Baseline Value	21	22.0848509	24.6741031	4.3360000	109.5231000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	16.5233809	16.8430268	2.4263400	96.9871000
BASE	Baseline Value	41	17.9657010	19.5248377	1.8553800	109.5231000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	15.5901388	11.9678858	3.0969000	38.7345600
BASE	Baseline Value	11	27.1532302	22.2835363	7.7563200	76.1700400

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	13.5662868	15.1042672	1.1217920	66.7280000
BASE	Baseline Value	23	18.1949132	17.9449352	2.6991600	76.1700400

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	12.0235624	9.0103251	3.3264480	36.8333800
BASE	Baseline Value	20	13.6405937	11.1026261	1.8553800	38.6176000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	11.7110892	17.8386601	1.1217920	66.7280000
BASE	Baseline Value	12	9.9831227	6.2298953	2.6991600	22.8766140

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	22.0946747	25.7769259	2.9296800	93.1848000
BASE	Baseline Value	17	23.3222922	27.2959834	4.3360000	109.5231000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	15.3732764	19.0843629	2.9296800	93.1848000
BASE	Baseline Value	36	17.9316623	20.7651019	1.8553800	109.5231000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	12.6717268	7.3614971	2.0081600	23.9052000
BASE	Baseline Value	10	28.7864190	22.7843910	7.7563200	76.1700400

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	9.1883460	7.0156171	0.6703290	23.9052000
BASE	Baseline Value	19	20.4096859	19.0439290	2.6991600	76.1700400

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	9.3593937	6.0602164	3.2260500	23.8977000
BASE	Baseline Value	19	13.1084671	11.1417570	1.8553800	38.6176000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	5.3179229	4.2138779	0.6703290	11.2750000
BASE	Baseline Value	9	11.1022047	6.8425730	2.6991600	22.8766140

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-1.2759	6.2055	1.3541	-14.8429	9.7711
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.2759	-4.1006	1.5488	6.2055	4.7476	8.9612
DF	t Value	Pr > t			
20	-0.94	0.3573			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-1.4423	5.0443	0.7878	-14.8429	9.7711
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.4423	-3.0345 0.1499	5.0443	4.1415 6.4542		
DF	t Value	Pr > t			
40	-1.83	0.0746			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	-11.5631	16.2454	4.8982	-47.3465	6.1968
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-11.5631	-22.4769 -0.6493	16.2454	11.3510 28.5097		
	DF	t Value	Pr > t		
	10	-2.36	0.0399		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
23	-4.6286	18.3894	3.8345	-47.3465	59.7480		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-4.6286	-12.5808 3.3236	18.3894	14.2223 26.0275				
DF	t Value	Pr > t					
22	-1.21	0.2402					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
20	-1.6170	3.6016	0.8053	-12.7974	2.5511		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-1.6170	-3.3026 0.0686	3.6016	2.7390 5.2604				
DF	t Value	Pr > t					
19	-2.01	0.0591					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
12	1.7280	18.5541	5.3561	-10.3214	59.7480		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
1.7280	-10.0608 13.5167	18.5541	13.1436 31.5026				
DF	t Value	Pr > t					
11	0.32	0.7530					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-1.2276	5.6826	1.3782	-16.3383	9.8871
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.2276	-4.1493 1.6941	5.6826	4.2322 8.6484		
	DF	t Value	Pr > t		
	16	-0.89	0.3863		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-2.5584	5.9565	0.9928	-19.0370	9.8871
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.5584	-4.5738 -0.5430	5.9565	4.8312 7.7699		
DF	t Value	Pr > t			
35	-2.58	0.0143			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-16.1147	18.2281	5.7642	-52.2648	1.6918
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-16.1147	-29.1543 -3.0751	18.2281	12.5379 33.2774		
	DF	t Value	Pr > t		
	9	-2.80	0.0209		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-11.2213	14.4306	3.3106	-52.2648	1.6918
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-11.2213	-18.1767 -4.2660	14.4306	10.9040 21.3404		
DF	t Value	Pr > t			
18	-3.39	0.0033			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-3.7491	6.0923	1.3977	-19.0370	3.8715
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7491	-6.6855	-0.8127	6.0923	4.6034	9.0095
	DF	t Value	Pr > t		
	18	-2.68	0.0152		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.1 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-5.7843	5.6181	1.8727	-14.8478	-1.0752
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.7843	-10.1027	-1.4658	5.6181	3.7948	10.7630
	DF	t Value	Pr > t		
	8	-3.09	0.0149		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	20.8089223	21.2300710	2.4263400	96.9871000
BASE	Baseline Value	21	22.0848509	24.6741031	4.3360000	109.5231000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	16.5233809	16.8430268	2.4263400	96.9871000
BASE	Baseline Value	41	17.9657010	19.5248377	1.8553800	109.5231000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	14.2460379	11.6548104	2.0016000	66.1912000
BASE	Baseline Value	47	20.3976331	14.6934007	1.4295030	76.1700400

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	91	11.7916615	11.2700809	0.1948560	66.7280000
BASE	Baseline Value	90	16.4955025	12.2544244	1.4295030	76.1700400

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	12.0235624	9.0103251	3.3264480	36.8333800
BASE	Baseline Value	20	13.6405937	11.1026261	1.8553800	38.6176000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	9.0518925	10.2761584	0.1948560	66.7280000
BASE	Baseline Value	43	12.2303830	6.7895573	2.4624600	26.4647550

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	22.0946747	25.7769259	2.9296800	93.1848000
BASE	Baseline Value	17	23.3222922	27.2959834	4.3360000	109.5231000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	15.3732764	19.0843629	2.9296800	93.1848000
BASE	Baseline Value	36	17.9316623	20.7651019	1.8553800	109.5231000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	14.8030865	11.4753901	2.0081600	60.6600000
BASE	Baseline Value	41	21.8609118	14.8836862	4.2764030	76.1700400

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	83	10.6432185	9.6903649	0.3890700	60.6600000
BASE	Baseline Value	82	17.6682765	12.6780494	2.4624600	76.1700400

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	9.3593937	6.0602164	3.2260500	23.8977000
BASE	Baseline Value	19	13.1084671	11.1417570	1.8553800	38.6176000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	6.3818903	4.5543594	0.3890700	18.3125000
BASE	Baseline Value	41	13.4756411	8.2416497	2.4624600	43.4490000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-1.2759	6.2055	1.3541	-14.8429	9.7711
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.2759	-4.1006 1.5488	6.2055	4.7476 8.9612		
DF	t Value	Pr > t			
20	-0.94	0.3573			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-1.4423	5.0443	0.7878	-14.8429	9.7711
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.4423	-3.0345 0.1499	5.0443	4.1415 6.4542		
DF	t Value	Pr > t			
40	-1.83	0.0746			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	-6.0009	10.2617	1.4968	-47.3465	11.7934
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-6.0009	-9.0138 -2.9879	10.2617	8.5272 12.8885		
DF	t Value	Pr > t			
46	-4.01	0.0002			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
90	-4.6524	10.5193	1.1088	-47.3465	59.7480
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.6524	-6.8556 -2.4492	10.5193	9.1751 12.3287		
	DF	t Value	Pr > t		
	89	-4.20	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-1.6170	3.6016	0.8053	-12.7974	2.5511
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.6170	-3.3026 0.0686	3.6016	2.7390 5.2604		
DF	t Value	Pr > t			
19	-2.01	0.0591			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-3.1785	10.7189	1.6346	-14.5563	59.7480
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.1785	-6.4773	0.1203	10.7189	8.8381	13.6238
	DF	t Value	Pr > t		
	42	-1.94	0.0586		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-1.2276	5.6826	1.3782	-16.3383	9.8871
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.2276	-4.1493 1.6941	5.6826	4.2322 8.6484		
DF	t Value	Pr > t			
16	-0.89	0.3863			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-2.5584	5.9565	0.9928	-19.0370	9.8871
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.5584	-4.5738 -0.5430	5.9565	4.8312 7.7699		
DF	t Value	Pr > t			
35	-2.58	0.0143			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-6.8664	12.6074	1.9689	-52.2648	16.8564
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-6.8664	-10.8458 -2.8870	12.6074	10.3509 16.1312		
	DF	t Value	Pr > t		
	40	-3.49	0.0012		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
82	-6.9801	10.0153	1.1060	-52.2648	16.8564
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-6.9801	-9.1807 -4.7795	10.0153	8.6822 11.8358		
	DF	t Value	Pr > t		
	81	-6.31	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-3.7491	6.0923	1.3977	-19.0370	3.8715
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.7491	-6.6855 -0.8127	6.0923	4.6034 9.0095		
DF	t Value	Pr > t			
18	-2.68	0.0152			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary NNN Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.2.2.2 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-7.0938	6.6443	1.0377	-27.1011	1.8589
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-7.0938	-9.1909 -4.9966	6.6443	5.4550 8.5014		
DF	t Value	Pr > t			
40	-6.84	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDNNN
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	119
Number of Observations Used	117
Number of Observations Not Used	2

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	841.18787258	
1	2	804.07005492	0.02011768
2	1	796.45426456	0.00649820
3	1	794.10483739	0.00124176
4	1	793.68701968	0.00007159
5	1	793.66489985	0.00000031
6	1	793.66480841	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	125.83
UN(2,1)	subject	109.14
UN(2,2)	subject	129.81

Fit Statistics

-2 Res Log Likelihood	793.7
AIC (smaller is better)	799.7
AICC (smaller is better)	799.9
BIC (smaller is better)	806.1

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	47.52	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	52.4	3.85	0.0146
week	1	47.7	6.77	0.0123
treat*week	3	47.6	0.79	0.5082

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-10.0763	4.2107	59	-2.39	0.0199	0.05	-18.5019	-1.6506
Week 2: VLN Mentholated vs UB Mentholated	3.3450	4.0960	59	0.82	0.4174	0.05	-4.8511	11.5411
Week 2: VLN Combined vs UB Combined	-3.3656	2.9372	59	-1.15	0.2565	0.05	-9.2429	2.5116
Week 2: VLN Combined	-4.9176	2.3412	59	-2.10	0.0400	0.05	-9.6023	-0.2329
Week 2: UB Combined	-1.5519	1.7736	59	-0.88	0.3851	0.05	-5.1009	1.9971
Week 6: VLN Non-mentholated vs UB Non-mentholated	-13.7358	4.3709	43.1	-3.14	0.0030	0.05	-22.5498	-4.9219
Week 6: VLN Mentholated vs UB Mentholated	3.3220	4.2958	44.4	0.77	0.4434	0.05	-5.3335	11.9776
Week 6: VLN Combined vs UB Combined	-5.2069	3.0642	43.7	-1.70	0.0964	0.05	-11.3835	0.9697
Week 6: VLN Combined	-8.1102	2.4499	44.1	-3.31	0.0019	0.05	-13.0472	-3.1731
Week 6: UB Combined	-2.9033	1.8406	43.1	-1.58	0.1220	0.05	-6.6149	0.8084

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-1.4868	2.5083	59	-0.59	0.5556	0.05	-6.5059	3.5322
treat*week	A	6	-1.8131	2.6384	44.7	-0.69	0.4955	0.05	-7.1281	3.5019
treat*week	B	2	-11.5631	3.3822	59	-3.42	0.0011	0.05	-18.3308	-4.7954
treat*week	B	6	-15.5490	3.4847	42.2	-4.46	<.0001	0.05	-22.5802	-8.5177
treat*week	C	2	-1.6170	2.5083	59	-0.64	0.5216	0.05	-6.6361	3.4020
treat*week	C	6	-3.9934	2.5670	41.4	-1.56	0.1274	0.05	-9.1759	1.1891
treat*week	D	2	1.7280	3.2382	59	0.53	0.5956	0.05	-4.7516	8.2075
treat*week	D	6	-0.6714	3.4444	46.1	-0.19	0.8463	0.05	-7.6043	6.2616

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.3263	1.5295	48.1	0.21	0.8320	0.05	-2.7488	3.4014
treat*week	A	2	B	2	10.0763	4.2107	59	2.39	0.0199	0.05	1.6506	18.5019
treat*week	A	2	B	6	14.0621	4.2936	56.7	3.28	0.0018	0.05	5.4633	22.6610
treat*week	A	2	C	2	0.1302	3.5472	59	0.04	0.9708	0.05	-6.9678	7.2282
treat*week	A	2	C	6	2.5066	3.5890	60.8	0.70	0.4876	0.05	-4.6706	9.6837
treat*week	A	2	D	2	-3.2148	4.0960	59	-0.78	0.4357	0.05	-11.4109	4.9813
treat*week	A	2	D	6	-0.8155	4.2609	60.9	-0.19	0.8489	0.05	-9.3360	7.7051
treat*week	A	6	B	2	9.7500	4.2896	65.8	2.27	0.0263	0.05	1.1851	18.3148
treat*week	A	6	B	6	13.7358	4.3709	43.1	3.14	0.0030	0.05	4.9219	22.5498
treat*week	A	6	C	2	-0.1961	3.6404	63.5	-0.05	0.9572	0.05	-7.4699	7.0777
treat*week	A	6	C	6	2.1803	3.6812	43.1	0.59	0.5568	0.05	-5.2430	9.6035
treat*week	A	6	D	2	-3.5411	4.1770	65.7	-0.85	0.3996	0.05	-11.8815	4.7993
treat*week	A	6	D	6	-1.1418	4.3388	45.6	-0.26	0.7936	0.05	-9.8776	7.5941

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.1 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	3.9859	1.9338	47	2.06	0.0448	0.05	0.09557	7.8762
treat*week	B	2	C	2	-9.9461	4.2107	59	-2.36	0.0215	0.05	-18.3717	-1.5204
treat*week	B	2	C	6	-7.5697	4.2460	63.7	-1.78	0.0794	0.05	-16.0528	0.9134
treat*week	B	2	D	2	-13.2911	4.6824	59	-2.84	0.0062	0.05	-22.6605	-3.9216
treat*week	B	2	D	6	-10.8917	4.8273	65.1	-2.26	0.0274	0.05	-20.5324	-1.2511
treat*week	B	6	C	2	-13.9319	4.2936	56.7	-3.24	0.0020	0.05	-22.5308	-5.3331
treat*week	B	6	C	6	-11.5556	4.3282	42	-2.67	0.0107	0.05	-20.2904	-2.8208
treat*week	B	6	D	2	-17.2769	4.7570	60.8	-3.63	0.0006	0.05	-26.7897	-7.7642
treat*week	B	6	D	6	-14.8776	4.8997	44.1	-3.04	0.0040	0.05	-24.7517	-5.0035
treat*week	C	2	C	6	2.3764	1.4027	46.5	1.69	0.0969	0.05	-0.4462	5.1990
treat*week	C	2	D	2	-3.3450	4.0960	59	-0.82	0.4174	0.05	-11.5411	4.8511
treat*week	C	2	D	6	-0.9457	4.2609	60.9	-0.22	0.8251	0.05	-9.4662	7.5749
treat*week	C	6	D	2	-5.7214	4.1322	63.5	-1.38	0.1710	0.05	-13.9778	2.5351
treat*week	C	6	D	6	-3.3220	4.2958	44.4	-0.77	0.4434	0.05	-11.9776	5.3335
treat*week	D	2	D	6	2.3993	2.0397	48.6	1.18	0.2452	0.05	-1.7006	6.4993

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDNNN
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	251
Number of Observations Used	247
Number of Observations Not Used	4

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1762.35683763	
1	3	1671.12845875	0.00327480
2	1	1668.78391547	0.00030635
3	1	1668.58309005	0.00000361
4	1	1668.58085175	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	85.4989
UN(2,1)	subject	77.9176
UN(2,2)	subject	105.38

Fit Statistics

-2 Res Log Likelihood	1668.6
AIC (smaller is better)	1674.6
AICC (smaller is better)	1674.7
BIC (smaller is better)	1683.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	93.78	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	117	1.39	0.2485
week	1	109	4.88	0.0293
treat*week	3	109	0.79	0.5002

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-4.5186	2.4635	127	-1.83	0.0690	0.05	-9.3934	0.3563
Week 2: VLN Mentholated vs UB Mentholated	-1.8274	2.4909	127	-0.73	0.4645	0.05	-6.7563	3.1014
Week 2: VLN Combined vs UB Combined	-3.1730	1.7517	127	-1.81	0.0724	0.05	-6.6392	0.2932
Week 2: VLN Combined	-4.7249	0.9648	128	-4.90	<.0001	0.05	-6.6339	-2.8160
Week 2: UB Combined	-1.5519	1.4620	127	-1.06	0.2905	0.05	-4.4451	1.3412
Week 6: VLN Non-mentholated vs UB Non-mentholated	-4.7139	2.8340	107	-1.66	0.0992	0.05	-10.3318	0.9040
Week 6: VLN Mentholated vs UB Mentholated	-1.4973	2.7893	100	-0.54	0.5926	0.05	-7.0310	4.0365
Week 6: VLN Combined vs UB Combined	-3.1056	1.9882	104	-1.56	0.1213	0.05	-7.0484	0.8372
Week 6: VLN Combined	-6.0209	1.0886	103	-5.53	<.0001	0.05	-8.1797	-3.8621
Week 6: UB Combined	-2.9153	1.6637	104	-1.75	0.0827	0.05	-6.2145	0.3839

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-1.4868	2.0676	127	-0.72	0.4734	0.05	-5.5784	2.6047
treat*week	A	6	-1.8248	2.3896	108	-0.76	0.4468	0.05	-6.5612	2.9117
treat*week	B	2	-6.0054	1.3393	128	-4.48	<.0001	0.05	-8.6556	-3.3552
treat*week	B	6	-6.5387	1.5236	105	-4.29	<.0001	0.05	-9.5597	-3.5177
treat*week	C	2	-1.6170	2.0676	127	-0.78	0.4356	0.05	-5.7086	2.4745
treat*week	C	6	-4.0058	2.3156	99.7	-1.73	0.0867	0.05	-8.6000	0.5884
treat*week	D	2	-3.4445	1.3890	129	-2.48	0.0144	0.05	-6.1927	-0.6962
treat*week	D	6	-5.5031	1.5552	102	-3.54	0.0006	0.05	-8.5878	-2.4183

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.3379	1.4810	109	0.23	0.8199	0.05	-2.5975	3.2733
treat*week	A	2	B	2	4.5186	2.4635	127	1.83	0.0690	0.05	-0.3563	9.3934
treat*week	A	2	B	6	5.0518	2.5683	148	1.97	0.0510	0.05	-0.02333	10.1270
treat*week	A	2	C	2	0.1302	2.9240	127	0.04	0.9646	0.05	-5.6561	5.9165
treat*week	A	2	C	6	2.5190	3.1043	139	0.81	0.4185	0.05	-3.6187	8.6566
treat*week	A	2	D	2	1.9576	2.4909	127	0.79	0.4334	0.05	-2.9712	6.8865
treat*week	A	2	D	6	4.0162	2.5872	147	1.55	0.1227	0.05	-1.0967	9.1292
treat*week	A	6	B	2	4.1806	2.7394	133	1.53	0.1293	0.05	-1.2377	9.5990
treat*week	A	6	B	6	4.7139	2.8340	107	1.66	0.0992	0.05	-0.9040	10.3318
treat*week	A	6	C	2	-0.2077	3.1599	147	-0.07	0.9477	0.05	-6.4525	6.0371
treat*week	A	6	C	6	2.1810	3.3275	104	0.66	0.5136	0.05	-4.4174	8.7795
treat*week	A	6	D	2	1.6197	2.7640	135	0.59	0.5589	0.05	-3.8467	7.0861
treat*week	A	6	D	6	3.6783	2.8511	106	1.29	0.1998	0.05	-1.9741	9.3307

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary NNN Mass Excreted
for Table 14.2.5.2.3.2 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.5333	0.9341	109	0.57	0.5693	0.05	-1.3180	2.3846
treat*week	B	2	C	2	-4.3884	2.4635	127	-1.78	0.0772	0.05	-9.2632	0.4865
treat*week	B	2	C	6	-1.9996	2.6750	125	-0.75	0.4562	0.05	-7.2939	3.2947
treat*week	B	2	D	2	-2.5609	1.9296	128	-1.33	0.1868	0.05	-6.3788	1.2569
treat*week	B	2	D	6	-0.5023	2.0524	141	-0.24	0.8070	0.05	-4.5598	3.5551
treat*week	B	6	C	2	-4.9216	2.5683	148	-1.92	0.0572	0.05	-9.9968	0.1535
treat*week	B	6	C	6	-2.5329	2.7718	101	-0.91	0.3630	0.05	-8.0313	2.9655
treat*week	B	6	D	2	-3.0942	2.0617	147	-1.50	0.1356	0.05	-7.1687	0.9803
treat*week	B	6	D	6	-1.0356	2.1771	103	-0.48	0.6353	0.05	-5.3532	3.2820
treat*week	C	2	C	6	2.3888	1.3583	108	1.76	0.0815	0.05	-0.3037	5.0813
treat*week	C	2	D	2	1.8274	2.4909	127	0.73	0.4645	0.05	-3.1014	6.7563
treat*week	C	2	D	6	3.8860	2.5872	147	1.50	0.1352	0.05	-1.2269	8.9990
treat*week	C	6	D	2	-0.5613	2.7002	127	-0.21	0.8357	0.05	-5.9048	4.7822
treat*week	C	6	D	6	1.4973	2.7893	100	0.54	0.5926	0.05	-4.0365	7.0310
treat*week	D	2	D	6	2.0586	0.9435	110	2.18	0.0313	0.05	0.1886	3.9286

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	1710.75	732.7758743	388.3670000	3886.81
BASE	Baseline Value	21	1888.02	799.0914311	791.9040000	3933.29

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	1524.94	595.1579932	388.3670000	3886.81
BASE	Baseline Value	41	1708.95	726.4914908	791.9040000	3933.29

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	1519.91	722.7629877	461.0940000	2770.25
BASE	Baseline Value	11	1551.99	676.0674177	710.7050000	2678.55

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	1377.92	630.1955700	461.0940000	2770.25
BASE	Baseline Value	23	1576.35	569.3934288	710.7050000	2678.55

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	1329.84	319.7909019	775.9780000	1913.32
BASE	Baseline Value	20	1520.92	605.2479810	851.2920000	3056.94

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	1247.75	529.8594510	575.0900000	2230.04
BASE	Baseline Value	12	1598.68	481.4194530	782.2500000	2226.96

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	1815.38	828.3605906	555.8880000	3482.05
BASE	Baseline Value	17	1914.53	867.7257879	791.9040000	3933.29

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	1562.43	673.6060019	555.8880000	3482.05
BASE	Baseline Value	36	1679.68	751.7823328	791.9040000	3933.29

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	1194.70	462.4303132	555.0160000	1861.20
BASE	Baseline Value	10	1439.33	593.9149954	710.7050000	2544.75

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	1131.23	456.8387424	512.2000000	1993.42
BASE	Baseline Value	19	1534.90	562.9869618	710.7050000	2544.75

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	1336.10	397.2952534	690.1680000	2185.87
BASE	Baseline Value	19	1469.55	575.3022910	851.2920000	3056.94

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	1060.72	467.3087509	512.2000000	1993.42
BASE	Baseline Value	9	1641.09	540.5709613	782.2500000	2226.96

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-177.3	296.7	64.7492	-749.1	300.8
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-177.3	-312.3 -42.2078	296.7	227.0	428.5	
		DF	t Value	Pr > t	
		20	-2.74	0.0127	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-184.0	335.5	52.3893	-1190.1	332.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-184.0	-289.9 -78.1235	335.5	275.4 429.2		
DF	t Value	Pr > t			
40	-3.51	0.0011			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	-32.0750	390.1	117.6	-873.4	519.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-32.0750	-294.2 230.0	390.1	272.6 684.7		
DF	t Value	Pr > t			
10	-0.27	0.7906			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	-198.4	361.0	75.2692	-873.4	519.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-198.4	-354.5 -42.3328	361.0	279.2	510.9	
		DF	t Value	Pr > t	
		22	-2.64	0.0151	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-191.1	379.6	84.8904	-1190.1	332.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-191.1	-368.8 -13.3993	379.6	288.7 554.5		
DF	t Value	Pr > t			
19	-2.25	0.0364			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-350.9	263.1	75.9407	-647.3	149.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-350.9	-518.1 -183.8	263.1	186.4 446.7		
DF	t Value	Pr > t			
11	-4.62	0.0007			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-99.1444	530.1	128.6	-1094.9	998.7
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-99.1444	-371.7	173.4	530.1	394.8	806.8
DF	t Value	Pr > t			
16	-0.77	0.4519			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
36	-117.3	471.6	78.6018	-1553.6	998.7		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-117.3	-276.8 42.3198	471.6	382.5 615.2				
DF	t Value	Pr > t					
35	-1.49	0.1447					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-244.6	459.8	145.4	-1364.3	176.0
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-244.6	-573.6	84.3103	459.8	316.3	839.5
	DF	t Value	Pr > t		
	9	-1.68	0.1268		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-403.7	451.2	103.5	-1364.3	176.0
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-403.7	-621.2 -186.2	451.2	341.0 667.3		
DF	t Value	Pr > t			
18	-3.90	0.0011			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
19	-133.5	426.7	97.8914	-1553.6	663.3		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-133.5	-339.1 72.2115	426.7	322.4 631.0				
DF	t Value	Pr > t					
18	-1.36	0.1896					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.1 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-580.4	391.8	130.6	-1142.0	69.4200
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-580.4	-881.6 -279.2	391.8	264.7 750.7		
DF	t Value	Pr > t			
8	-4.44	0.0022			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	1710.75	732.7758743	388.3670000	3886.81
BASE	Baseline Value	21	1888.02	799.0914311	791.9040000	3933.29

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	1524.94	595.1579932	388.3670000	3886.81
BASE	Baseline Value	41	1708.95	726.4914908	791.9040000	3933.29

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	1706.86	901.3990175	461.0940000	5931.54
BASE	Baseline Value	47	1787.78	711.2474411	570.3450000	4443.63

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	91	1469.50	790.9739141	71.3060000	5931.54
BASE	Baseline Value	90	1714.76	619.9814060	570.3450000	4443.63

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	1329.84	319.7909019	775.9780000	1913.32
BASE	Baseline Value	20	1520.92	605.2479810	851.2920000	3056.94

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	1204.53	543.2654752	71.3060000	2230.04
BASE	Baseline Value	43	1634.96	497.9713171	658.6580000	2592.74

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	1815.38	828.3605906	555.8880000	3482.05
BASE	Baseline Value	17	1914.53	867.7257879	791.9040000	3933.29

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	1562.43	673.6060019	555.8880000	3482.05
BASE	Baseline Value	36	1679.68	751.7823328	791.9040000	3933.29

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	1481.69	694.6764611	555.0160000	3870.45
BASE	Baseline Value	41	1806.47	712.6515808	710.7050000	4443.63

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	83	1261.07	634.0203089	132.1650000	3870.45
BASE	Baseline Value	82	1726.11	627.4850324	658.6580000	4443.63

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	1336.10	397.2952534	690.1680000	2185.87
BASE	Baseline Value	19	1469.55	575.3022910	851.2920000	3056.94

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	1035.06	475.3511807	132.1650000	1993.42
BASE	Baseline Value	41	1645.75	525.5550931	658.6580000	2592.74

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-177.3	296.7	64.7492	-749.1	300.8
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-177.3	-312.3 -42.2078	296.7	227.0	428.5	
	DF	t Value	Pr > t		
	20	-2.74	0.0127		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	-184.0	335.5	52.3893	-1190.1	332.4		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-184.0	-289.9 -78.1235	335.5	275.4 429.2				
DF	t Value	Pr > t					
40	-3.51	0.0011					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
47	-83.5784	542.2	79.0903	-1411.6	1487.9		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-83.5784	-242.8 75.6222	542.2	450.6 681.0				
DF	t Value	Pr > t					
46	-1.06	0.2961					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
90	-249.3	497.3	52.4161	-1411.6	1487.9
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-249.3	-353.4 -145.1	497.3	433.7 582.8		
DF	t Value	Pr > t			
89	-4.76	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-191.1	379.6	84.8904	-1190.1	332.4
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-191.1	-368.8 -13.3993	379.6	288.7	554.5	
	DF	t Value	Pr > t		
	19	-2.25	0.0364		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-430.4	371.0	56.5803	-1376.1	266.9
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-430.4	-544.6 -316.2	371.0	305.9 471.6		
DF	t Value	Pr > t			
42	-7.61	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-99.1444	530.1	128.6	-1094.9	998.7
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-99.1444	-371.7	173.4	530.1	394.8	806.8
DF	t Value	Pr > t			
16	-0.77	0.4519			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
36	-117.3	471.6	78.6018	-1553.6	998.7		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-117.3	-276.8 42.3198	471.6	382.5 615.2				
DF	t Value	Pr > t					
35	-1.49	0.1447					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-316.3	502.8	78.5272	-1512.2	1031.7
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-316.3	-475.0	-157.6	502.8	412.8	643.4
	DF	t Value	Pr > t		
	40	-4.03	0.0002		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
82	-463.5	493.1	54.4569	-1674.4	1031.7
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-463.5	-571.9 -355.2	493.1	427.5 582.8		
DF	t Value	Pr > t			
81	-8.51	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
19	-133.5	426.7	97.8914	-1553.6	663.3		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-133.5	-339.1 72.2115	426.7	322.4 631.0				
DF	t Value	Pr > t					
18	-1.36	0.1896					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 3-HPMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.3.2.2 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-610.7	441.8	68.9995	-1674.4	231.3
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-610.7	-750.1 -471.2	441.8	362.7 565.3		
DF	t Value	Pr > t			
40	-8.85	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDHPMA3
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	119
Number of Observations Used	117
Number of Observations Not Used	2

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1637.03343946	
1	2	1588.08035036	0.00001731
2	1	1588.06802015	0.00000003
3	1	1588.06799963	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	112881
UN(2,1)	subject	115866
UN(2,2)	subject	210488

Fit Statistics

-2 Res Log Likelihood	1588.1
AIC (smaller is better)	1594.1
AICC (smaller is better)	1594.3
BIC (smaller is better)	1600.5

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	48.97	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	59.6	2.46	0.0713
week	1	50	3.38	0.0719
treat*week	3	50	4.21	0.0098

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	162.28	126.12	59	1.29	0.2032	0.05	-90.0876	414.64
Week 2: VLN Mentholated vs UB Mentholated	-159.85	122.68	59	-1.30	0.1977	0.05	-405.33	85.6379
Week 2: VLN Combined vs UB Combined	1.2140	87.9728	59	0.01	0.9890	0.05	-174.82	177.25
Week 2: VLN Combined	-191.50	70.1226	59	-2.73	0.0083	0.05	-331.82	-51.1850
Week 2: UB Combined	-192.71	53.1228	59	-3.63	0.0006	0.05	-299.01	-86.4155
Week 6: VLN Non-mentholated vs UB Non-mentholated	-154.53	178.08	57.6	-0.87	0.3891	0.05	-511.05	201.98
Week 6: VLN Mentholated vs UB Mentholated	-444.95	175.94	59.1	-2.53	0.0141	0.05	-796.99	-92.9120
Week 6: VLN Combined vs UB Combined	-299.74	125.17	58.4	-2.39	0.0199	0.05	-550.26	-49.2277
Week 6: VLN Combined	-421.70	100.22	58.8	-4.21	<.0001	0.05	-622.26	-221.14
Week 6: UB Combined	-121.96	74.9779	57.6	-1.63	0.1093	0.05	-272.07	28.1499

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-194.35	75.1270	59	-2.59	0.0122	0.05	-344.68	-44.0222
treat*week	A	6	-77.3922	108.22	59.6	-0.72	0.4773	0.05	-293.90	139.12
treat*week	B	2	-32.0750	101.30	59	-0.32	0.7526	0.05	-234.78	170.63
treat*week	B	6	-231.93	141.42	56.4	-1.64	0.1066	0.05	-515.18	51.3222
treat*week	C	2	-191.08	75.1270	59	-2.54	0.0136	0.05	-341.41	-40.7482
treat*week	C	6	-166.53	103.80	55.3	-1.60	0.1143	0.05	-374.52	41.4666
treat*week	D	2	-350.93	96.9886	59	-3.62	0.0006	0.05	-545.00	-156.85
treat*week	D	6	-611.48	142.06	61.1	-4.30	<.0001	0.05	-895.53	-327.43

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-116.96	75.9587	50	-1.54	0.1299	0.05	-269.53	35.6073
treat*week	A	2	B	2	-162.28	126.12	59	-1.29	0.2032	0.05	-414.64	90.0876
treat*week	A	2	B	6	37.5759	160.14	67.8	0.23	0.8152	0.05	-281.99	357.14
treat*week	A	2	C	2	-3.2740	106.25	59	-0.03	0.9755	0.05	-215.87	209.32
treat*week	A	2	C	6	-27.8240	128.13	71.4	-0.22	0.8287	0.05	-283.29	227.65
treat*week	A	2	D	2	156.57	122.68	59	1.28	0.2069	0.05	-88.9119	402.06
treat*week	A	2	D	6	417.12	160.70	73.3	2.60	0.0114	0.05	96.8698	737.38
treat*week	A	6	B	2	-45.3172	148.24	78.3	-0.31	0.7606	0.05	-340.41	249.78
treat*week	A	6	B	6	154.53	178.08	57.6	0.87	0.3891	0.05	-201.98	511.05
treat*week	A	6	C	2	113.68	131.74	75.6	0.86	0.3909	0.05	-148.73	376.10
treat*week	A	6	C	6	89.1348	149.96	57.6	0.59	0.5546	0.05	-211.08	389.35
treat*week	A	6	D	2	273.53	145.32	78.2	1.88	0.0635	0.05	-15.7743	562.84
treat*week	A	6	D	6	534.08	178.58	60.6	2.99	0.0040	0.05	176.93	891.24

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.1 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	199.85	95.8883	50	2.08	0.0423	0.05	7.2557	392.45
treat*week	B	2	C	2	159.00	126.12	59	1.26	0.2124	0.05	-93.3616	411.37
treat*week	B	2	C	6	134.45	145.04	74.3	0.93	0.3569	0.05	-154.52	423.43
treat*week	B	2	D	2	318.85	140.25	59	2.27	0.0266	0.05	38.2200	599.48
treat*week	B	2	D	6	579.40	174.48	77.8	3.32	0.0014	0.05	232.03	926.77
treat*week	B	6	C	2	-40.8499	160.14	67.8	-0.26	0.7994	0.05	-360.41	278.71
treat*week	B	6	C	6	-65.4000	175.42	56	-0.37	0.7107	0.05	-416.81	286.01
treat*week	B	6	D	2	119.00	171.48	71.8	0.69	0.4900	0.05	-222.86	460.86
treat*week	B	6	D	6	379.55	200.45	58.8	1.89	0.0632	0.05	-21.5740	780.67
treat*week	C	2	C	6	-24.5500	69.5122	50	-0.35	0.7254	0.05	-164.17	115.07
treat*week	C	2	D	2	159.85	122.68	59	1.30	0.1977	0.05	-85.6379	405.33
treat*week	C	2	D	6	420.40	160.70	73.3	2.62	0.0108	0.05	100.14	740.65
treat*week	C	6	D	2	184.40	142.06	74.1	1.30	0.1983	0.05	-98.6576	467.45
treat*week	C	6	D	6	444.95	175.94	59.1	2.53	0.0141	0.05	92.9120	796.99
treat*week	D	2	D	6	260.55	101.37	50	2.57	0.0132	0.05	56.9429	464.16

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDHPMA3
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	251
Number of Observations Used	247
Number of Observations Not Used	4

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	3629.77192690	
1	2	3577.60457739	0.00000236
2	1	3577.60083340	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	188975
UN(2,1)	subject	122463
UN(2,2)	subject	221174

Fit Statistics

-2 Res Log Likelihood	3577.6
AIC (smaller is better)	3583.6
AICC (smaller is better)	3583.7
BIC (smaller is better)	3592.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	52.17	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	130	6.71	0.0003
week	1	115	3.17	0.0776
treat*week	3	115	4.28	0.0067

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	115.92	115.93	126	1.00	0.3193	0.05	-113.51	345.35
Week 2: VLN Mentholated vs UB Mentholated	-233.97	117.37	126	-1.99	0.0484	0.05	-466.23	-1.6982
Week 2: VLN Combined vs UB Combined	-59.0215	82.4867	126	-0.72	0.4756	0.05	-222.26	104.22
Week 2: VLN Combined	-251.74	45.6036	127	-5.52	<.0001	0.05	-341.97	-161.50
Week 2: UB Combined	-192.71	68.7341	125	-2.80	0.0059	0.05	-328.74	-56.6860
Week 6: VLN Non-mentholated vs UB Non-mentholated	-235.82	134.10	128	-1.76	0.0811	0.05	-501.16	29.5250
Week 6: VLN Mentholated vs UB Mentholated	-455.44	129.10	122	-3.53	0.0006	0.05	-711.01	-199.87
Week 6: VLN Combined vs UB Combined	-345.63	93.0706	125	-3.71	0.0003	0.05	-529.83	-161.43
Week 6: VLN Combined	-467.98	50.8660	124	-9.20	<.0001	0.05	-568.66	-367.31
Week 6: UB Combined	-122.35	77.9409	125	-1.57	0.1190	0.05	-276.61	31.9016

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-194.35	97.2047	125	-2.00	0.0477	0.05	-386.72	-1.9783
treat*week	A	6	-90.3708	113.41	128	-0.80	0.4270	0.05	-314.76	134.02
treat*week	B	2	-78.4290	63.1798	127	-1.24	0.2168	0.05	-203.45	46.5952
treat*week	B	6	-326.19	71.5634	126	-4.56	<.0001	0.05	-467.81	-184.56
treat*week	C	2	-191.08	97.2047	125	-1.97	0.0515	0.05	-383.45	1.2957
treat*week	C	6	-154.33	106.95	121	-1.44	0.1516	0.05	-366.07	57.3995
treat*week	D	2	-425.04	65.7804	128	-6.46	<.0001	0.05	-555.20	-294.89
treat*week	D	6	-609.78	72.3055	123	-8.43	<.0001	0.05	-752.90	-466.65

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-103.98	100.32	116	-1.04	0.3021	0.05	-302.67	94.7121
treat*week	A	2	B	2	-115.92	115.93	126	-1.00	0.3193	0.05	-345.35	113.51
treat*week	A	2	B	6	131.84	120.71	183	1.09	0.2762	0.05	-106.32	369.99
treat*week	A	2	C	2	-3.2740	137.47	125	-0.02	0.9810	0.05	-275.33	268.78
treat*week	A	2	C	6	-40.0177	144.52	184	-0.28	0.7822	0.05	-325.15	245.12
treat*week	A	2	D	2	230.69	117.37	126	1.97	0.0516	0.05	-1.5758	462.96
treat*week	A	2	D	6	415.43	121.15	181	3.43	0.0008	0.05	176.38	654.47
treat*week	A	6	B	2	-11.9418	129.82	172	-0.09	0.9268	0.05	-268.19	244.30
treat*week	A	6	B	6	235.82	134.10	128	1.76	0.0811	0.05	-29.5250	501.16
treat*week	A	6	C	2	100.71	149.36	193	0.67	0.5010	0.05	-193.89	395.30
treat*week	A	6	C	6	63.9625	155.88	125	0.41	0.6823	0.05	-244.54	372.47
treat*week	A	6	D	2	334.67	131.10	175	2.55	0.0115	0.05	75.9198	593.42
treat*week	A	6	D	6	519.41	134.50	127	3.86	0.0002	0.05	253.26	785.55

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 3-HPMA Mass Excreted
for Table 14.2.5.3.3.2 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	247.76	63.4251	116	3.91	0.0002	0.05	122.14	373.38
treat*week	B	2	C	2	112.65	115.93	126	0.97	0.3331	0.05	-116.78	342.08
treat*week	B	2	C	6	75.9043	124.22	164	0.61	0.5420	0.05	-169.36	321.17
treat*week	B	2	D	2	346.61	91.2072	127	3.80	0.0002	0.05	166.14	527.09
treat*week	B	2	D	6	531.35	96.0197	187	5.53	<.0001	0.05	341.92	720.77
treat*week	B	6	C	2	-135.11	120.71	183	-1.12	0.2645	0.05	-373.27	103.04
treat*week	B	6	C	6	-171.86	128.68	123	-1.34	0.1842	0.05	-426.59	82.8741
treat*week	B	6	D	2	98.8531	97.2028	193	1.02	0.3104	0.05	-92.8621	290.57
treat*week	B	6	D	6	283.59	101.73	124	2.79	0.0061	0.05	82.2371	484.94
treat*week	C	2	C	6	-36.7438	92.9545	113	-0.40	0.6934	0.05	-220.91	147.42
treat*week	C	2	D	2	233.97	117.37	126	1.99	0.0484	0.05	1.6982	466.23
treat*week	C	2	D	6	418.70	121.15	181	3.46	0.0007	0.05	179.65	657.74
treat*week	C	6	D	2	270.71	125.56	167	2.16	0.0325	0.05	22.8249	518.59
treat*week	C	6	D	6	455.44	129.10	122	3.53	0.0006	0.05	199.87	711.01
treat*week	D	2	D	6	184.73	64.2558	116	2.87	0.0048	0.05	57.4728	312.00

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	7.5608248	3.7582009	1.2544322	15.4648000
BASE	Baseline Value	21	7.9057814	3.8185124	1.2295800	15.6002400

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	7.6436375	4.8712832	1.1871690	21.2464800
BASE	Baseline Value	41	8.0682315	5.7300141	1.2295800	30.4500000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	8.7667244	7.0465663	0.8442000	20.9076850
BASE	Baseline Value	11	6.3987941	5.2563966	1.2765400	18.1525500

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	7.4783812	5.8861993	0.7834320	20.9076850
BASE	Baseline Value	23	6.3688737	4.4279208	0.7079950	18.1525500

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	7.7305909	5.9223009	1.1871690	21.2464800
BASE	Baseline Value	20	8.2388041	7.3289823	1.2639240	30.4500000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	6.2973999	4.5796572	0.7834320	15.7250800
BASE	Baseline Value	12	6.3414466	3.7541091	0.7079950	13.8071400

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	7.2610719	4.4329259	1.1053980	18.3432800
BASE	Baseline Value	17	7.8118106	4.2600608	1.2295800	15.6002400

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	7.0417274	4.8353475	1.1053980	22.3197600
BASE	Baseline Value	36	7.4201906	4.7706639	1.2295800	21.0122640

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	7.2706234	5.6919933	0.4626160	17.7746400
BASE	Baseline Value	10	6.4726066	5.5347161	1.2765400	18.1525500

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.5770622	4.6444472	0.4626160	17.7746400
BASE	Baseline Value	19	6.8899774	4.6318296	1.2765400	18.1525500

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.8454719	5.2828731	1.2159000	22.3197600
BASE	Baseline Value	19	7.0697938	5.2771167	1.2639240	21.0122640

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	5.8064386	3.2888429	1.3086900	11.2091000
BASE	Baseline Value	9	7.3537227	3.6536618	2.1314400	13.8071400

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
21	-0.3450	1.1993	0.2617	-3.3980	1.5968		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.3450	-0.8909 0.2010	1.1993	0.9175 1.7319				
DF	t Value	Pr > t					
20	-1.32	0.2024					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-0.4246	2.0530	0.3206	-9.2035	3.3785
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4246	-1.0726 0.2234	2.0530	1.6855 2.6268		
DF	t Value	Pr > t			
40	-1.32	0.1929			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	2.3679	2.6370	0.7951	-0.4323	8.2821
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2.3679	0.5964	4.1395	2.6370	1.8425	4.6278
	DF	t Value	Pr > t		
	10	2.98	0.0139		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	1.1095	2.5697	0.5358	-2.2056	8.2821
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
1.1095	-0.00172	2.2207	2.5697	1.9874	3.6370
DF	t Value	Pr > t			
22	2.07	0.0503			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.5082	2.7101	0.6060	-9.2035	3.3785
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5082	-1.7766 0.7602	2.7101	2.0610 3.9583		
DF	t Value	Pr > t			
19	-0.84	0.4121			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
12	-0.0440	1.9621	0.5664	-2.2056	4.7989		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.0440	-1.2907 1.2026	1.9621	1.3899 3.3314				
DF	t Value	Pr > t					
11	-0.08	0.9394					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.5507	1.4095	0.3419	-2.8717	2.7430
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5507	-1.2755 0.1740	1.4095	1.0498 2.1452		
DF	t Value	Pr > t			
16	-1.61	0.1267			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-0.3785	1.7186	0.2864	-4.5303	4.0021
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.3785	-0.9600	0.2030	1.7186	1.3939	2.2418
	DF	t Value	Pr > t		
	35	-1.32	0.1950		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
10	0.7980	3.4846	1.1019	-7.1903	5.6231		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.7980	-1.6947 3.2907	3.4846	2.3968 6.3614				
DF	t Value	Pr > t					
9	0.72	0.4873					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.3129	3.2898	0.7547	-7.1903	5.6231
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.3129	-1.8986	1.2727	3.2898	2.4858	4.8651
	DF	t Value	Pr > t		
	18	-0.41	0.6833		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.2243	1.9809	0.4545	-4.5303	4.0021
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.2243	-1.1791	0.7305	1.9809	1.4968	2.9294
	DF	t Value	Pr > t		
	18	-0.49	0.6276		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.1 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-1.5473	2.7267	0.9089	-6.4610	2.5285
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.5473	-3.6432 0.5487	2.7267	1.8418 5.2238		
DF	t Value	Pr > t			
8	-1.70	0.1271			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	7.5608248	3.7582009	1.2544322	15.4648000
BASE	Baseline Value	21	7.9057814	3.8185124	1.2295800	15.6002400

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	7.6436375	4.8712832	1.1871690	21.2464800
BASE	Baseline Value	41	8.0682315	5.7300141	1.2295800	30.4500000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	8.1598954	7.8142281	0.5976320	47.5335900
BASE	Baseline Value	47	7.0613970	6.0275461	0.7340124	34.5034800

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	91	7.4861337	6.5560195	0.1069590	47.5335900
BASE	Baseline Value	90	6.9911938	5.1281225	0.7079950	34.5034800

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	7.7305909	5.9223009	1.1871690	21.2464800
BASE	Baseline Value	20	8.2388041	7.3289823	1.2639240	30.4500000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	6.7340277	4.7616780	0.1069590	21.0279200
BASE	Baseline Value	43	6.9144602	3.9903597	0.7079950	17.2235800

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	7.2610719	4.4329259	1.1053980	18.3432800
BASE	Baseline Value	17	7.8118106	4.2600608	1.2295800	15.6002400

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	7.0417274	4.8353475	1.1053980	22.3197600
BASE	Baseline Value	36	7.4201906	4.7706639	1.2295800	21.0122640

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	7.2822358	6.4349850	0.4619520	38.5893200
BASE	Baseline Value	41	7.4848663	6.3440240	0.7340124	34.5034800

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	83	6.4457372	5.2791872	0.4619520	38.5893200
BASE	Baseline Value	82	7.2453628	5.2656586	0.7340124	34.5034800

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.8454719	5.2828731	1.2159000	22.3197600
BASE	Baseline Value	19	7.0697938	5.2771167	1.2639240	21.0122640

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	5.5888362	3.6333889	0.4774250	12.4364800
BASE	Baseline Value	41	7.0058593	3.9728159	1.2630240	17.2235800

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.3450	1.1993	0.2617	-3.3980	1.5968
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3450	-0.8909 0.2010	1.1993	0.9175 1.7319		
DF	t Value	Pr > t			
20	-1.32	0.2024			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	-0.4246	2.0530	0.3206	-9.2035	3.3785		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.4246	-1.0726 0.2234	2.0530	1.6855 2.6268				
DF	t Value	Pr > t					
40	-1.32	0.1929					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	1.2139	2.9212	0.4261	-4.8697	13.0301
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1.2139	0.3562	2.0716	2.9212	2.4275	3.6690
	DF	t Value	Pr > t		
	46	2.85	0.0065		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
90	0.5477	3.1223	0.3291	-9.0243	13.0301
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.5477	-0.1062	1.2017	3.1223	2.7233	3.6594
	DF	t Value	Pr > t		
	89	1.66	0.0996		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.5082	2.7101	0.6060	-9.2035	3.3785
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5082	-1.7766 0.7602	2.7101	2.0610 3.9583		
DF	t Value	Pr > t			
19	-0.84	0.4121			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-0.1804	3.2051	0.4888	-9.0243	11.1513
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1804	-1.1668 0.8060	3.2051	2.6428 4.0737		
DF	t Value	Pr > t			
42	-0.37	0.7139			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-0.5507	1.4095	0.3419	-2.8717	2.7430
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5507	-1.2755 0.1740	1.4095	1.0498 2.1452		
DF	t Value	Pr > t			
16	-1.61	0.1267			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-0.3785	1.7186	0.2864	-4.5303	4.0021
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3785	-0.9600 0.2030	1.7186	1.3939 2.2418		
DF	t Value	Pr > t			
35	-1.32	0.1950			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	-0.0963	2.6479	0.4135	-7.1903	5.6231		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.0963	-0.9321 0.7394	2.6479	2.1740 3.3880				
DF	t Value	Pr > t					
40	-0.23	0.8170					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted ($\mu\text{g}/24$ hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
82	-0.7567	2.8117	0.3105	-11.3281	5.6231
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.7567	-1.3745	-0.1389	2.8117	2.4375	3.3228
	DF	t Value	Pr > t		
	81	-2.44	0.0170		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.2243	1.9809	0.4545	-4.5303	4.0021
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.2243	-1.1791	0.7305	1.9809	1.4968	2.9294
	DF	t Value	Pr > t		
	18	-0.49	0.6276		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary S-PMA Mass Excreted (µg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.4.2.2 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-1.4170	2.8467	0.4446	-11.3281	4.7433
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.4170	-2.3156 -0.5185	2.8467	2.3372 3.6424		
DF	t Value	Pr > t			
40	-3.19	0.0028			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDSPMA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	119
Number of Observations Used	117
Number of Observations Not Used	2

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	506.96004951	
1	2	488.43805207	0.00176352
2	1	488.15743486	0.00005892
3	1	488.14874994	0.00000008
4	1	488.14873795	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	4.7360
UN(2,1)	subject	3.1473
UN(2,2)	subject	5.8329

Fit Statistics

-2 Res Log Likelihood	488.1
AIC (smaller is better)	494.1
AICC (smaller is better)	494.4
BIC (smaller is better)	500.6

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	18.81	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	53.5	3.27	0.0280
week	1	49.7	8.17	0.0062
treat*week	3	49.5	2.39	0.0802

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	2.7560	0.8169	59	3.37	0.0013	0.05	1.1213	4.3906
Week 2: VLN Mentholated vs UB Mentholated	0.4642	0.7946	59	0.58	0.5614	0.05	-1.1259	2.0542
Week 2: VLN Combined vs UB Combined	1.6101	0.5698	59	2.83	0.0064	0.05	0.4698	2.7503
Week 2: VLN Combined	1.1619	0.4542	59	2.56	0.0131	0.05	0.2531	2.0708
Week 2: UB Combined	-0.4481	0.3441	59	-1.30	0.1979	0.05	-1.1366	0.2404
Week 6: VLN Non-mentholated vs UB Non-mentholated	1.2438	0.9522	49.1	1.31	0.1976	0.05	-0.6696	3.1572
Week 6: VLN Mentholated vs UB Mentholated	-1.1503	0.9472	50.5	-1.21	0.2302	0.05	-3.0523	0.7518
Week 6: VLN Combined vs UB Combined	0.04677	0.6715	49.8	0.07	0.9448	0.05	-1.3022	1.3957
Week 6: VLN Combined	-0.4581	0.5388	50.2	-0.85	0.3992	0.05	-1.5402	0.6240
Week 6: UB Combined	-0.5049	0.4009	49.1	-1.26	0.2138	0.05	-1.3104	0.3006

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-0.3880	0.4866	59	-0.80	0.4284	0.05	-1.3618	0.5857
treat*week	A	6	-0.4813	0.5837	50.9	-0.82	0.4135	0.05	-1.6533	0.6907
treat*week	B	2	2.3679	0.6562	59	3.61	0.0006	0.05	1.0550	3.6809
treat*week	B	6	0.7625	0.7523	48	1.01	0.3159	0.05	-0.7501	2.2751
treat*week	C	2	-0.5082	0.4866	59	-1.04	0.3006	0.05	-1.4819	0.4655
treat*week	C	6	-0.5285	0.5495	47	-0.96	0.3411	0.05	-1.6340	0.5771
treat*week	D	2	-0.04405	0.6282	59	-0.07	0.9443	0.05	-1.3011	1.2130
treat*week	D	6	-1.6787	0.7715	52.2	-2.18	0.0341	0.05	-3.2267	-0.1307

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.09327	0.5127	50.1	0.18	0.8564	0.05	-0.9364	1.1229
treat*week	A	2	B	2	-2.7560	0.8169	59	-3.37	0.0013	0.05	-4.3906	-1.1213
treat*week	A	2	B	6	-1.1505	0.8960	70.5	-1.28	0.2033	0.05	-2.9373	0.6362
treat*week	A	2	C	2	0.1202	0.6882	59	0.17	0.8620	0.05	-1.2569	1.4972
treat*week	A	2	C	6	0.1404	0.7340	77.8	0.19	0.8488	0.05	-1.3210	1.6018
treat*week	A	2	D	2	-0.3440	0.7946	59	-0.43	0.6667	0.05	-1.9341	1.2461
treat*week	A	2	D	6	1.2907	0.9121	75.8	1.42	0.1612	0.05	-0.5261	3.1074
treat*week	A	6	B	2	-2.8492	0.8782	85.4	-3.24	0.0017	0.05	-4.5953	-1.1032
treat*week	A	6	B	6	-1.2438	0.9522	49.1	-1.31	0.1976	0.05	-3.1572	0.6696
treat*week	A	6	C	2	0.02691	0.7600	81.9	0.04	0.9718	0.05	-1.4849	1.5387
treat*week	A	6	C	6	0.04715	0.8017	49.1	0.06	0.9533	0.05	-1.5639	1.6582
treat*week	A	6	D	2	-0.4373	0.8576	85.4	-0.51	0.6114	0.05	-2.1422	1.2677
treat*week	A	6	D	6	1.1974	0.9674	51.7	1.24	0.2214	0.05	-0.7442	3.1390

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.1 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	1.6054	0.6514	48.8	2.46	0.0173	0.05	0.2963	2.9145
treat*week	B	2	C	2	2.8761	0.8169	59	3.52	0.0008	0.05	1.2415	4.5108
treat*week	B	2	C	6	2.8964	0.8559	81.2	3.38	0.0011	0.05	1.1935	4.5993
treat*week	B	2	D	2	2.4120	0.9084	59	2.66	0.0102	0.05	0.5943	4.2297
treat*week	B	2	D	6	4.0466	1.0128	84.3	4.00	0.0001	0.05	2.0327	6.0606
treat*week	B	6	C	2	1.2707	0.8960	70.5	1.42	0.1605	0.05	-0.5160	3.0575
treat*week	B	6	C	6	1.2909	0.9316	47.7	1.39	0.1723	0.05	-0.5826	3.1645
treat*week	B	6	D	2	0.8065	0.9801	77.8	0.82	0.4131	0.05	-1.1448	2.7579
treat*week	B	6	D	6	2.4412	1.0776	50.2	2.27	0.0278	0.05	0.2771	4.6054
treat*week	C	2	C	6	0.02024	0.4733	48.3	0.04	0.9661	0.05	-0.9313	0.9718
treat*week	C	2	D	2	-0.4642	0.7946	59	-0.58	0.5614	0.05	-2.0542	1.1259
treat*week	C	2	D	6	1.1705	0.9121	75.8	1.28	0.2033	0.05	-0.6462	2.9873
treat*week	C	6	D	2	-0.4844	0.8347	81.1	-0.58	0.5633	0.05	-2.1451	1.1762
treat*week	C	6	D	6	1.1503	0.9472	50.5	1.21	0.2302	0.05	-0.7518	3.0523
treat*week	D	2	D	6	1.6347	0.6821	50.7	2.40	0.0203	0.05	0.2650	3.0043

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDSPMA
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	251
Number of Observations Used	247
Number of Observations Not Used	4

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1173.69468000	
1	2	1135.68843949	0.00000081
2	1	1135.68815755	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	7.8375
UN(2,1)	subject	3.6545
UN(2,2)	subject	6.2178

Fit Statistics

-2 Res Log Likelihood	1135.7
AIC (smaller is better)	1141.7
AICC (smaller is better)	1141.8
BIC (smaller is better)	1150.4

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	38.01	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	129	2.63	0.0529
week	1	120	6.57	0.0116
treat*week	3	120	2.08	0.1060

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	1.5786	0.7468	127	2.11	0.0365	0.05	0.1008	3.0563
Week 2: VLN Mentholated vs UB Mentholated	0.3561	0.7563	128	0.47	0.6386	0.05	-1.1404	1.8527
Week 2: VLN Combined vs UB Combined	0.9673	0.5314	127	1.82	0.0711	0.05	-0.08427	2.0189
Week 2: VLN Combined	0.5192	0.2941	129	1.77	0.0799	0.05	-0.06271	1.1011
Week 2: UB Combined	-0.4481	0.4426	127	-1.01	0.3133	0.05	-1.3240	0.4278
Week 6: VLN Non-mentholated vs UB Non-mentholated	0.3674	0.7171	123	0.51	0.6093	0.05	-1.0520	1.7868
Week 6: VLN Mentholated vs UB Mentholated	-0.9923	0.6864	118	-1.45	0.1509	0.05	-2.3515	0.3669
Week 6: VLN Combined vs UB Combined	-0.3124	0.4963	120	-0.63	0.5302	0.05	-1.2951	0.6702
Week 6: VLN Combined	-0.7835	0.2711	120	-2.89	0.0046	0.05	-1.3203	-0.2467
Week 6: UB Combined	-0.4710	0.4157	121	-1.13	0.2595	0.05	-1.2941	0.3520

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-0.3880	0.6260	127	-0.62	0.5365	0.05	-1.6268	0.8507
treat*week	A	6	-0.5043	0.6069	123	-0.83	0.4076	0.05	-1.7055	0.6969
treat*week	B	2	1.1905	0.4072	128	2.92	0.0041	0.05	0.3847	1.9963
treat*week	B	6	-0.1369	0.3820	121	-0.36	0.7207	0.05	-0.8931	0.6193
treat*week	C	2	-0.5082	0.6260	127	-0.81	0.4184	0.05	-1.7470	0.7305
treat*week	C	6	-0.4377	0.5683	117	-0.77	0.4427	0.05	-1.5632	0.6878
treat*week	D	2	-0.1521	0.4244	129	-0.36	0.7207	0.05	-0.9919	0.6877
treat*week	D	6	-1.4300	0.3849	119	-3.72	0.0003	0.05	-2.1921	-0.6679

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.1163	0.6283	123	0.19	0.8535	0.05	-1.1273	1.3599
treat*week	A	2	B	2	-1.5786	0.7468	127	-2.11	0.0365	0.05	-3.0563	-0.1008
treat*week	A	2	B	6	-0.2511	0.7333	181	-0.34	0.7324	0.05	-1.6981	1.1959
treat*week	A	2	C	2	0.1202	0.8853	127	0.14	0.8922	0.05	-1.6317	1.8720
treat*week	A	2	C	6	0.04968	0.8455	195	0.06	0.9532	0.05	-1.6178	1.7171
treat*week	A	2	D	2	-0.2359	0.7563	128	-0.31	0.7556	0.05	-1.7325	1.2606
treat*week	A	2	D	6	1.0420	0.7349	180	1.42	0.1579	0.05	-0.4081	2.4921
treat*week	A	6	B	2	-1.6948	0.7309	186	-2.32	0.0215	0.05	-3.1366	-0.2530
treat*week	A	6	B	6	-0.3674	0.7171	123	-0.51	0.6093	0.05	-1.7868	1.0520
treat*week	A	6	C	2	0.003904	0.8719	204	0.00	0.9964	0.05	-1.7151	1.7229
treat*week	A	6	C	6	-0.06659	0.8314	121	-0.08	0.9363	0.05	-1.7127	1.5795
treat*week	A	6	D	2	-0.3522	0.7406	190	-0.48	0.6349	0.05	-1.8130	1.1086
treat*week	A	6	D	6	0.9257	0.7186	122	1.29	0.2001	0.05	-0.4969	2.3483

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary S-PMA Mass Excreted
for Table 14.2.5.4.3.2 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	1.3274	0.3999	122	3.32	0.0012	0.05	0.5358	2.1190
treat*week	B	2	C	2	1.6987	0.7468	127	2.27	0.0246	0.05	0.2210	3.1765
treat*week	B	2	C	6	1.6282	0.6992	181	2.33	0.0210	0.05	0.2487	3.0078
treat*week	B	2	D	2	1.3426	0.5882	129	2.28	0.0241	0.05	0.1788	2.5065
treat*week	B	2	D	6	2.6205	0.5603	199	4.68	<.0001	0.05	1.5156	3.7255
treat*week	B	6	C	2	0.3713	0.7333	181	0.51	0.6132	0.05	-1.0757	1.8183
treat*week	B	6	C	6	0.3008	0.6847	119	0.44	0.6612	0.05	-1.0551	1.6567
treat*week	B	6	D	2	0.01520	0.5710	203	0.03	0.9788	0.05	-1.1106	1.1411
treat*week	B	6	D	6	1.2931	0.5422	120	2.38	0.0187	0.05	0.2195	2.3667
treat*week	C	2	C	6	-0.07050	0.5911	116	-0.12	0.9053	0.05	-1.2413	1.1003
treat*week	C	2	D	2	-0.3561	0.7563	128	-0.47	0.6386	0.05	-1.8527	1.1404
treat*week	C	2	D	6	0.9218	0.7349	180	1.25	0.2113	0.05	-0.5283	2.3719
treat*week	C	6	D	2	-0.2856	0.7093	185	-0.40	0.6877	0.05	-1.6850	1.1138
treat*week	C	6	D	6	0.9923	0.6864	118	1.45	0.1509	0.05	-0.3669	2.3515
treat*week	D	2	D	6	1.2779	0.4080	120	3.13	0.0022	0.05	0.4702	2.0857

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	289.0714267	97.7693825	117.5020000	426.5300000
BASE	Baseline Value	21	309.5860905	92.4202639	138.4000000	462.9015000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	276.5024771	99.4242266	67.6725000	456.9600000
BASE	Baseline Value	41	312.9910395	116.9084271	105.7336000	658.1896000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	241.0562464	91.3472239	69.2788000	395.0800000
BASE	Baseline Value	11	331.7767491	121.5615327	105.0335000	496.9440000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	232.0304787	118.3813520	53.3352000	563.5980000
BASE	Baseline Value	23	315.3928504	120.8089850	95.3172000	503.3070000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	263.3050800	101.9362692	67.6725000	456.9600000
BASE	Baseline Value	20	316.5662360	140.5579113	105.7336000	658.1896000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	223.7568583	142.4303603	53.3352000	563.5980000
BASE	Baseline Value	12	300.3742767	123.4556720	95.3172000	503.3070000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	299.3122000	118.7805353	128.6430000	544.0270000
BASE	Baseline Value	17	304.6421706	99.0767181	138.4000000	462.9015000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	286.0430500	122.9241398	83.4918000	544.0270000
BASE	Baseline Value	36	307.0978228	121.0119667	105.7336000	658.1896000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	228.4390900	76.7788798	85.1885000	338.3940000
BASE	Baseline Value	10	327.9904340	127.4515517	105.0335000	496.9440000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	202.8898684	90.0884613	59.3406000	397.0860000
BASE	Baseline Value	19	307.3343505	128.3072450	95.3172000	503.3070000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	274.1706526	128.5495317	83.4918000	488.2700000
BASE	Baseline Value	19	309.2949853	140.4917928	105.7336000	658.1896000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	174.5018444	99.5309259	59.3406000	397.0860000
BASE	Baseline Value	9	284.3831467	132.8188824	95.3172000	503.3070000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-20.5147	55.5882	12.1303	-124.6	89.3030
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-20.5147	-45.8181	4.7888	55.5882	42.5283	80.2732
DF	t Value	Pr > t			
20	-1.69	0.1063			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-36.4886	80.0512	12.5019	-382.0	89.3030
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-36.4886	-61.7558 -11.2213	80.0512	65.7231 102.4		
	DF	t Value	Pr > t		
	40	-2.92	0.0057		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	-90.7205	44.7283	13.4861	-167.7	-17.1390
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-90.7205	-120.8 -60.6716	44.7283	31.2524 78.4952		
DF	t Value	Pr > t			
10	-6.73	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	-83.3624	68.2620	14.2336	-181.0	142.5
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-83.3624	-112.9 -53.8437	68.2620	52.7935 96.6147		
DF	t Value	Pr > t			
22	-5.86	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-53.2612	98.2858	21.9774	-382.0	54.2820
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-53.2612	-99.2603 -7.2620	98.2858	74.7454 143.6		
DF	t Value	Pr > t			
19	-2.42	0.0255			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-76.6174	86.0051	24.8275	-181.0	142.5
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-76.6174	-131.3 -21.9724	86.0051	60.9256	146.0	
DF	t Value	Pr > t			
11	-3.09	0.0104			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-5.3300	81.0547	19.6586	-124.4	119.5
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.3300	-47.0044 36.3445	81.0547	60.3671 123.4		
	DF	t Value	Pr > t		
	16	-0.27	0.7898		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-21.0548	86.7640	14.4607	-333.7	121.3
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-21.0548	-50.4115	8.3019	86.7640	70.3726	113.2
DF	t Value	Pr > t			
35	-1.46	0.1543			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-99.5513	65.8860	20.8350	-181.5	6.8382
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-99.5513	-146.7 -52.4193	65.8860	45.3187 120.3		
DF	t Value	Pr > t			
9	-4.78	0.0010			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
19	-104.4	61.0800	14.0127	-226.7	6.8382		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-104.4	-133.9 -75.0049	61.0800	46.1528 90.3266				
DF	t Value	Pr > t					
18	-7.45	<.0001					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-35.1243	91.4078	20.9704	-333.7	121.3
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-35.1243	-79.1815	8.9328	91.4078	69.0689	135.2
DF	t Value	Pr > t			
18	-1.67	0.1112			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.1 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-109.9	58.7150	19.5717	-226.7	-35.9766
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-109.9	-155.0 -64.7490	58.7150	39.6594	112.5	
	DF	t Value	Pr > t		
	8	-5.61	0.0005		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	289.0714267	97.7693825	117.5020000	426.5300000
BASE	Baseline Value	21	309.5860905	92.4202639	138.4000000	462.9015000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	276.5024771	99.4242266	67.6725000	456.9600000
BASE	Baseline Value	41	312.9910395	116.9084271	105.7336000	658.1896000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	262.7555550	157.8691820	69.2788000	905.9821000
BASE	Baseline Value	47	329.5284279	164.4942665	68.9220000	945.3605000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	91	239.7217113	141.4376515	47.3020000	905.9821000
BASE	Baseline Value	90	317.0800468	156.3272305	68.9220000	945.3605000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	263.3050800	101.9362692	67.6725000	456.9600000
BASE	Baseline Value	20	316.5662360	140.5579113	105.7336000	658.1896000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	214.0095137	117.0219882	47.3020000	563.5980000
BASE	Baseline Value	43	303.4736767	147.6056022	95.1230000	791.1560000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	299.3122000	118.7805353	128.6430000	544.0270000
BASE	Baseline Value	17	304.6421706	99.0767181	138.4000000	462.9015000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	286.0430500	122.9241398	83.4918000	544.0270000
BASE	Baseline Value	36	307.0978228	121.0119667	105.7336000	658.1896000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	278.9976548	178.6065426	81.4086000	1077.05
BASE	Baseline Value	41	340.2954807	170.3914337	68.9220000	945.3605000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	83	241.6523386	157.0509340	27.1161000	1077.05
BASE	Baseline Value	82	321.8587270	160.5433589	68.9220000	945.3605000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	274.1706526	128.5495317	83.4918000	488.2700000
BASE	Baseline Value	19	309.2949853	140.4917928	105.7336000	658.1896000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	203.3961610	122.0692724	27.1161000	593.4024000
BASE	Baseline Value	41	303.4219732	149.8753826	95.1230000	791.1560000

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-20.5147	55.5882	12.1303	-124.6	89.3030
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-20.5147	-45.8181	4.7888	55.5882	42.5283	80.2732
DF	t Value	Pr > t			
20	-1.69	0.1063			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-36.4886	80.0512	12.5019	-382.0	89.3030
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-36.4886	-61.7558 -11.2213	80.0512	65.7231 102.4		
	DF	t Value	Pr > t		
	40	-2.92	0.0057		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	-67.8681	65.4207	9.5426	-238.1	73.1276
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-67.8681	-87.0764 -48.6599	65.4207	54.3629 82.1674		
	DF	t Value	Pr > t		
	46	-7.11	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
90	-78.1862	80.4045	8.4754	-471.5	142.5
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-78.1862	-95.0266 -61.3458	80.4045	70.1298 94.2345		
	DF	t Value	Pr > t		
	89	-9.23	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-53.2612	98.2858	21.9774	-382.0	54.2820
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-53.2612	-99.2603 -7.2620	98.2858	74.7454 143.6		
DF	t Value	Pr > t			
19	-2.42	0.0255			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-89.4642	93.6086	14.2752	-471.5	142.5
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-89.4642	-118.3 -60.6557	93.6086	77.1841 119.0		
	DF	t Value	Pr > t		
	42	-6.27	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	-5.3300	81.0547	19.6586	-124.4	119.5
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.3300	-47.0044 36.3445	81.0547	60.3671 123.4		
DF	t Value	Pr > t			
16	-0.27	0.7898			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-21.0548	86.7640	14.4607	-333.7	121.3
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-21.0548	-50.4115	8.3019	86.7640	70.3726	113.2
DF	t Value	Pr > t			
35	-1.46	0.1543			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-63.3419	82.1715	12.8330	-271.5	131.7
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-63.3419	-89.2784 -37.4054	82.1715	67.4638 105.1		
	DF	t Value	Pr > t		
	40	-4.94	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
82	-81.6839	96.1443	10.6174	-475.3	179.6
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-81.6839	-102.8 -60.5586	96.1443	83.3470 113.6		
DF	t Value	Pr > t			
81	-7.69	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-35.1243	91.4078	20.9704	-333.7	121.3
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-35.1243	-79.1815	8.9328	91.4078	69.0689	135.2
DF	t Value	Pr > t			
18	-1.67	0.1112			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary 1-OHP Mass Excreted (ng/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.5.2.2 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-100.0	106.2	16.5844	-475.3	179.6
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-100.0	-133.5 -66.5075	106.2	87.1849	135.9	
	DF	t Value	Pr > t		
	40	-6.03	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDOHP1
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	119
Number of Observations Used	117
Number of Observations Not Used	2

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1281.01762987	
1	2	1247.32492122	0.00000123
2	1	1247.32427358	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	5873.01
UN(2,1)	subject	4229.20
UN(2,2)	subject	6332.88

Fit Statistics

-2 Res Log Likelihood	1247.3
AIC (smaller is better)	1253.3
AICC (smaller is better)	1253.6
BIC (smaller is better)	1259.8

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	33.69	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	59.3	5.27	0.0027
week	1	51.9	0.18	0.6711
treat*week	3	51.8	2.89	0.0442

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-69.5109	28.7674	59	-2.42	0.0188	0.05	-127.07	-11.9476
Week 2: VLN Mentholated vs UB Mentholated	-23.3563	27.9834	59	-0.83	0.4073	0.05	-79.3508	32.6383
Week 2: VLN Combined vs UB Combined	-46.4336	20.0663	59	-2.31	0.0242	0.05	-86.5862	-6.2810
Week 2: VLN Combined	-83.6690	15.9947	59	-5.23	<.0001	0.05	-115.67	-51.6636
Week 2: UB Combined	-37.2354	12.1171	59	-3.07	0.0032	0.05	-61.4817	-12.9890
Week 6: VLN Non-mentholated vs UB Non-mentholated	-103.05	31.0819	56.2	-3.32	0.0016	0.05	-165.31	-40.7896
Week 6: VLN Mentholated vs UB Mentholated	-82.1470	30.7932	57.6	-2.67	0.0099	0.05	-143.80	-20.4990
Week 6: VLN Combined vs UB Combined	-92.5985	21.8764	56.9	-4.23	<.0001	0.05	-136.41	-48.7900
Week 6: VLN Combined	-110.46	17.5310	57.3	-6.30	<.0001	0.05	-145.56	-75.3566
Week 6: UB Combined	-17.8592	13.0858	56.1	-1.36	0.1778	0.05	-44.0720	8.3535

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-21.2096	17.1362	59	-1.24	0.2207	0.05	-55.4991	13.0800
treat*week	A	6	3.5929	18.9559	58	0.19	0.8503	0.05	-34.3513	41.5371
treat*week	B	2	-90.7205	23.1065	59	-3.93	0.0002	0.05	-136.96	-44.4845
treat*week	B	6	-99.4571	24.6325	55	-4.04	0.0002	0.05	-148.82	-50.0935
treat*week	C	2	-53.2612	17.1362	59	-3.11	0.0029	0.05	-87.5507	-18.9716
treat*week	C	6	-39.3114	18.0452	54	-2.18	0.0338	0.05	-75.4902	-3.1325
treat*week	D	2	-76.6174	22.1228	59	-3.46	0.0010	0.05	-120.88	-32.3499
treat*week	D	6	-121.46	24.9518	59.4	-4.87	<.0001	0.05	-171.38	-71.5371

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-24.8025	15.1677	52.2	-1.64	0.1080	0.05	-55.2355	5.6306
treat*week	A	2	B	2	69.5109	28.7674	59	2.42	0.0188	0.05	11.9476	127.07
treat*week	A	2	B	6	78.2476	30.0068	74.3	2.61	0.0110	0.05	18.4620	138.03
treat*week	A	2	C	2	32.0516	24.2343	59	1.32	0.1911	0.05	-16.4411	80.5443
treat*week	A	2	C	6	18.1018	24.8853	77.6	0.73	0.4692	0.05	-31.4453	67.6489
treat*week	A	2	D	2	55.4079	27.9834	59	1.98	0.0524	0.05	-0.5867	111.40
treat*week	A	2	D	6	100.25	30.2695	79.8	3.31	0.0014	0.05	40.0083	160.49
treat*week	A	6	B	2	94.3134	29.8871	81.2	3.16	0.0022	0.05	34.8495	153.78
treat*week	A	6	B	6	103.05	31.0819	56.2	3.32	0.0016	0.05	40.7896	165.31
treat*week	A	6	C	2	56.8541	25.5534	81.9	2.22	0.0288	0.05	6.0189	107.69
treat*week	A	6	C	6	42.9043	26.1717	56.1	1.64	0.1067	0.05	-9.5213	95.3298
treat*week	A	6	D	2	80.2103	29.1332	81.6	2.75	0.0073	0.05	22.2511	138.17
treat*week	A	6	D	6	125.05	31.3356	58.9	3.99	0.0002	0.05	62.3468	187.76

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.1 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	8.7366	19.2802	51.3	0.45	0.6524	0.05	-29.9636	47.4369
treat*week	B	2	C	2	-37.4593	28.7674	59	-1.30	0.1979	0.05	-95.0227	20.1040
treat*week	B	2	C	6	-51.4091	29.3179	77.3	-1.75	0.0835	0.05	-109.78	6.9664
treat*week	B	2	D	2	-14.1031	31.9895	59	-0.44	0.6609	0.05	-78.1139	49.9077
treat*week	B	2	D	6	30.7378	34.0074	83.7	0.90	0.3687	0.05	-36.8927	98.3684
treat*week	B	6	C	2	-46.1960	30.0068	74.3	-1.54	0.1279	0.05	-105.98	13.5896
treat*week	B	6	C	6	-60.1458	30.5350	54.7	-1.97	0.0539	0.05	-121.35	1.0560
treat*week	B	6	D	2	-22.8397	33.1086	78.3	-0.69	0.4923	0.05	-88.7500	43.0705
treat*week	B	6	D	6	22.0012	35.0621	57.3	0.63	0.5328	0.05	-48.2012	92.2036
treat*week	C	2	C	6	-13.9498	14.0129	51	-1.00	0.3242	0.05	-42.0823	14.1827
treat*week	C	2	D	2	23.3563	27.9834	59	0.83	0.4073	0.05	-32.6383	79.3508
treat*week	C	2	D	6	68.1972	30.2695	79.8	2.25	0.0270	0.05	7.9567	128.44
treat*week	C	6	D	2	37.3061	28.5490	77.7	1.31	0.1952	0.05	-19.5346	94.1467
treat*week	C	6	D	6	82.1470	30.7932	57.6	2.67	0.0099	0.05	20.4990	143.80
treat*week	D	2	D	6	44.8409	20.1778	52.6	2.22	0.0306	0.05	4.3614	85.3204

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDOHP1
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	251
Number of Observations Used	247
Number of Observations Not Used	4

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	2836.68613122	
1	2	2780.53205089	0.00000030
2	1	2780.53170468	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	6564.02
UN(2,1)	subject	4610.50
UN(2,2)	subject	8426.65

Fit Statistics

-2 Res Log Likelihood	2780.5
AIC (smaller is better)	2786.5
AICC (smaller is better)	2786.6
BIC (smaller is better)	2795.2

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	56.15	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	129	5.63	0.0012
week	1	111	0.83	0.3640
treat*week	3	112	1.42	0.2414

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-46.4052	21.6050	123	-2.15	0.0337	0.05	-89.1694	-3.6410
Week 2: VLN Mentholated vs UB Mentholated	-32.3648	21.8707	124	-1.48	0.1415	0.05	-75.6532	10.9236
Week 2: VLN Combined vs UB Combined	-39.3850	15.3713	124	-2.56	0.0116	0.05	-69.8098	-8.9603
Week 2: VLN Combined	-76.6204	8.4956	125	-9.02	<.0001	0.05	-93.4342	-59.8066
Week 2: UB Combined	-37.2354	12.8102	123	-2.91	0.0043	0.05	-62.5921	-11.8786
Week 6: VLN Non-mentholated vs UB Non-mentholated	-65.6649	26.1080	128	-2.52	0.0131	0.05	-117.32	-14.0060
Week 6: VLN Mentholated vs UB Mentholated	-62.4517	25.1780	122	-2.48	0.0145	0.05	-112.29	-12.6085
Week 6: VLN Combined vs UB Combined	-64.0583	18.1353	125	-3.53	0.0006	0.05	-99.9499	-28.1667
Week 6: VLN Combined	-81.9606	9.9129	125	-8.27	<.0001	0.05	-101.58	-62.3411
Week 6: UB Combined	-17.9023	15.1863	125	-1.18	0.2407	0.05	-47.9570	12.1525

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-21.2096	18.1163	123	-1.17	0.2440	0.05	-57.0694	14.6503
treat*week	A	6	3.4038	22.0745	129	0.15	0.8777	0.05	-40.2715	47.0792
treat*week	B	2	-67.6148	11.7719	124	-5.74	<.0001	0.05	-90.9139	-44.3156
treat*week	B	6	-62.2611	13.9409	126	-4.47	<.0001	0.05	-89.8494	-34.6727
treat*week	C	2	-53.2612	18.1163	123	-2.94	0.0039	0.05	-89.1210	-17.4013
treat*week	C	6	-39.2083	20.8618	121	-1.88	0.0626	0.05	-80.5092	2.0925
treat*week	D	2	-85.6260	12.2526	126	-6.99	<.0001	0.05	-109.87	-61.3780
treat*week	D	6	-101.66	14.0967	123	-7.21	<.0001	0.05	-129.56	-73.7569

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-24.6134	18.8264	112	-1.31	0.1938	0.05	-61.9170	12.6902
treat*week	A	2	B	2	46.4052	21.6050	123	2.15	0.0337	0.05	3.6410	89.1694
treat*week	A	2	B	6	41.0515	22.8593	180	1.80	0.0742	0.05	-4.0544	86.1574
treat*week	A	2	C	2	32.0516	25.6203	123	1.25	0.2133	0.05	-18.6619	82.7651
treat*week	A	2	C	6	17.9988	27.6300	179	0.65	0.5156	0.05	-36.5235	72.5210
treat*week	A	2	D	2	64.4164	21.8707	124	2.95	0.0039	0.05	21.1280	107.70
treat*week	A	2	D	6	80.4505	22.9547	178	3.50	0.0006	0.05	35.1525	125.75
treat*week	A	6	B	2	71.0186	25.0172	168	2.84	0.0051	0.05	21.6297	120.41
treat*week	A	6	B	6	65.6649	26.1080	128	2.52	0.0131	0.05	14.0060	117.32
treat*week	A	6	C	2	56.6650	28.5567	189	1.98	0.0487	0.05	0.3336	113.00
treat*week	A	6	C	6	42.6122	30.3726	125	1.40	0.1631	0.05	-17.4972	102.72
treat*week	A	6	D	2	89.0298	25.2470	171	3.53	0.0005	0.05	39.1930	138.87
treat*week	A	6	D	6	105.06	26.1916	127	4.01	0.0001	0.05	53.2366	156.89

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary 1-OHP Mass Excreted
for Table 14.2.5.5.3.2 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	-5.3537	11.8856	112	-0.45	0.6533	0.05	-28.9026	18.1951
treat*week	B	2	C	2	-14.3536	21.6050	123	-0.66	0.5077	0.05	-57.1178	28.4106
treat*week	B	2	C	6	-28.4064	23.9540	160	-1.19	0.2374	0.05	-75.7132	18.9003
treat*week	B	2	D	2	18.0112	16.9913	125	1.06	0.2912	0.05	-15.6163	51.6388
treat*week	B	2	D	6	34.0453	18.3656	182	1.85	0.0654	0.05	-2.1919	70.2824
treat*week	B	6	C	2	-8.9999	22.8593	180	-0.39	0.6943	0.05	-54.1058	36.1060
treat*week	B	6	C	6	-23.0527	25.0911	123	-0.92	0.3600	0.05	-72.7200	26.6146
treat*week	B	6	D	2	23.3649	18.5600	189	1.26	0.2096	0.05	-13.2471	59.9770
treat*week	B	6	D	6	39.3990	19.8259	125	1.99	0.0491	0.05	0.1601	78.6379
treat*week	C	2	C	6	-14.0528	17.3887	109	-0.81	0.4208	0.05	-48.5150	20.4093
treat*week	C	2	D	2	32.3648	21.8707	124	1.48	0.1415	0.05	-10.9236	75.6532
treat*week	C	2	D	6	48.3989	22.9547	178	2.11	0.0364	0.05	3.1009	93.6969
treat*week	C	6	D	2	46.4176	24.1939	163	1.92	0.0568	0.05	-1.3568	94.1921
treat*week	C	6	D	6	62.4517	25.1780	122	2.48	0.0145	0.05	12.6085	112.29
treat*week	D	2	D	6	16.0341	12.0220	113	1.33	0.1850	0.05	-7.7839	39.8520

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	16.9624166	6.2674811	4.0841465	27.7768758
BASE	Baseline Value	21	17.4998417	6.5256968	4.7082686	28.9108660

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	16.1412295	5.5593607	4.0841465	27.7768758
BASE	Baseline Value	41	16.7328805	6.2293164	4.7082686	28.9108660

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	1.1368162	0.6371723	0.2546295	2.3383110
BASE	Baseline Value	11	16.1443570	6.4418334	8.4087475	26.5926911

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	1.0819857	0.5680378	0.2546295	2.3383110
BASE	Baseline Value	23	15.8602502	6.2377315	8.1300119	27.8122248

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	15.2789831	4.7105848	8.1347227	23.4948930
BASE	Baseline Value	20	15.9275712	5.9610917	8.3189218	27.3436930

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	1.0317243	0.5200875	0.3329202	2.0296135
BASE	Baseline Value	12	15.5998190	6.3197420	8.1300119	27.8122248

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	17.5300894	7.3994091	5.3681134	30.6533939
BASE	Baseline Value	17	17.1784343	6.6069764	4.7082686	28.1094030

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	15.8876314	6.5702981	5.3681134	30.6533939
BASE	Baseline Value	36	16.2011421	6.0170447	4.7082686	28.1094030

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	0.9788694	0.6589446	0.3869885	2.5289679
BASE	Baseline Value	10	15.4626952	6.3583652	8.4087475	26.5926911

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	1.1437584	0.9235398	0.2283505	3.9567146
BASE	Baseline Value	19	16.0989885	6.3704856	8.1300119	27.8122248

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	14.4180638	5.5176244	6.3438720	26.4635555
BASE	Baseline Value	19	15.3267227	5.4669231	8.3189218	26.6652743

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	1.3269684	1.1656979	0.2283505	3.9567146
BASE	Baseline Value	9	16.8059812	6.6903760	8.1300119	27.8122248

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.5374	2.3092	0.5039	-6.0261	3.4680
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5374	-1.5885 0.5137	2.3092	1.7666 3.3346		
DF	t Value	Pr > t			
20	-1.07	0.2989			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-0.5917	3.0573	0.4775	-8.5907	4.6024
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5917	-1.5566 0.3733	3.0573	2.5100 3.9118		
DF	t Value	Pr > t			
40	-1.24	0.2225			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	-15.0075	6.3466	1.9136	-25.6133	-6.3875
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-15.0075	-19.2713 -10.7438	6.3466	4.4345 11.1379		
	DF	t Value	Pr > t		
	10	-7.84	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	-14.7783	6.2205	1.2971	-27.0620	-6.3875
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-14.7783	-17.4682 -12.0883	6.2205	4.8109 8.8042		
DF	t Value	Pr > t			
22	-11.39	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
20	-0.6486	3.7494	0.8384	-8.5907	4.6024		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.6486	-2.4034 1.1062	3.7494	2.8514 5.4763				
DF	t Value	Pr > t					
19	-0.77	0.4487					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-14.5681	6.3774	1.8410	-27.0620	-6.9291
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-14.5681	-18.6201 -10.5161	6.3774	4.5177 10.8280		
	DF	t Value	Pr > t		
	11	-7.91	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	0.3517	3.2613	0.7910	-6.0141	7.7842
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.3517	-1.3251 2.0285	3.2613	2.4289 4.9634		
DF	t Value	Pr > t			
16	0.44	0.6626			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
36	-0.3135	3.5447	0.5908	-9.4224	8.1393		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.3135	-1.5129 0.8858	3.5447	2.8750 4.6238				
DF	t Value	Pr > t					
35	-0.53	0.5990					

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-14.4838	6.1794	1.9541	-25.8557	-7.2455
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-14.4838	-18.9043 -10.0634	6.1794	4.2504 11.2811		
	DF	t Value	Pr > t		
	9	-7.41	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-14.9552	6.1280	1.4058	-27.2631	-6.6406
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-14.9552	-17.9088 -12.0017	6.1280	4.6304 9.0622		
	DF	t Value	Pr > t		
	18	-10.64	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.9087	3.7664	0.8641	-9.4224	8.1393
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.9087	-2.7240	0.9067	3.7664	2.8459	5.5699
	DF	t Value	Pr > t		
	18	-1.05	0.3069		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.1 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-15.4790	6.3990	2.1330	-27.2631	-6.6406
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-15.4790	-20.3977 -10.5603	6.3990	4.3223 12.2591		
	DF	t Value	Pr > t		
	8	-7.26	<.0001		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	16.9624166	6.2674811	4.0841465	27.7768758
BASE	Baseline Value	21	17.4998417	6.5256968	4.7082686	28.9108660

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	16.1412295	5.5593607	4.0841465	27.7768758
BASE	Baseline Value	41	16.7328805	6.2293164	4.7082686	28.9108660

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	48	5.4037645	4.5528439	0.2546295	20.5567653
BASE	Baseline Value	47	17.2336533	6.0404309	8.3513447	40.3679535

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	91	4.5591679	4.1858265	0.2546295	20.5567653
BASE	Baseline Value	90	16.6539022	5.8257961	6.0128492	40.3679535

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	15.2789831	4.7105848	8.1347227	23.4948930
BASE	Baseline Value	20	15.9275712	5.9610917	8.3189218	27.3436930

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	3.6163623	3.5530211	0.3329202	12.5608496
BASE	Baseline Value	43	16.0202209	5.5831252	6.0128492	27.8122248

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	17	17.5300894	7.3994091	5.3681134	30.6533939
BASE	Baseline Value	17	17.1784343	6.6069764	4.7082686	28.1094030

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	36	15.8876314	6.5702981	5.3681134	30.6533939
BASE	Baseline Value	36	16.2011421	6.0170447	4.7082686	28.1094030

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	9.1498014	6.1240240	0.3869885	23.1470394
BASE	Baseline Value	41	17.5588890	6.2655616	8.3513447	40.3679535

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	83	7.9892609	5.7791681	0.2283505	23.1470394
BASE	Baseline Value	82	16.8482776	5.9197480	6.0128492	40.3679535

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	14.4180638	5.5176244	6.3438720	26.4635555
BASE	Baseline Value	19	15.3267227	5.4669231	8.3189218	26.6652743

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	6.8004146	5.2118478	0.2283505	18.6052288
BASE	Baseline Value	41	16.1376663	5.5380928	6.0128492	27.8122248

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.5374	2.3092	0.5039	-6.0261	3.4680
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.5374	-1.5885	0.5137	2.3092	1.7666	3.3346
	DF	t Value	Pr > t		
	20	-1.07	0.2989		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-0.5917	3.0573	0.4775	-8.5907	4.6024
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5917	-1.5566 0.3733	3.0573	2.5100 3.9118		
DF	t Value	Pr > t			
40	-1.24	0.2225			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	-11.8117	6.0548	0.8832	-25.6133	-1.7992
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-11.8117	-13.5895 -10.0339	6.0548	5.0314 7.6048		
DF	t Value	Pr > t			
46	-13.37	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
90	-12.0946	5.6304	0.5935	-27.0620	-1.7992
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-12.0946	-13.2739 -10.9154	5.6304	4.9109 6.5988		
DF	t Value	Pr > t			
89	-20.38	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.6486	3.7494	0.8384	-8.5907	4.6024
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.6486	-2.4034	1.1062	3.7494	2.8514	5.4763
	DF	t Value	Pr > t		
	19	-0.77	0.4487		

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-12.4039	5.1803	0.7900	-27.0620	-3.2979
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-12.4039	-13.9981 -10.8096	5.1803	4.2714 6.5843		
DF	t Value	Pr > t			
42	-15.70	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
17	0.3517	3.2613	0.7910	-6.0141	7.7842
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.3517	-1.3251 2.0285	3.2613	2.4289 4.9634		
DF	t Value	Pr > t			
16	0.44	0.6626			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
36	-0.3135	3.5447	0.5908	-9.4224	8.1393
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3135	-1.5129 0.8858	3.5447	2.8750 4.6238		
DF	t Value	Pr > t			
35	-0.53	0.5990			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-8.3944	6.5925	1.0296	-25.8557	1.2862
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-8.3944	-10.4752 -6.3136	6.5925	5.4125 8.4351		
DF	t Value	Pr > t			
40	-8.15	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
82	-8.8658	6.2150	0.6863	-27.2631	4.7158
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-8.8658	-10.2314 -7.5002	6.2150	5.3878 7.3447		
DF	t Value	Pr > t			
81	-12.92	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.9087	3.7664	0.8641	-9.4224	8.1393
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9087	-2.7240 0.9067	3.7664	2.8459 5.5699		
DF	t Value	Pr > t			
18	-1.05	0.3069			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Summary of Urinary Theq Mass Excreted (mg/24 hour) at Weeks 2 and 6 Versus Week -1 by Study Product Group
for Table 14.2.5.6.2.2 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-9.3373	5.8568	0.9147	-27.2631	4.7158
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-9.3373	-11.1859 -7.4886	5.8568	4.8085 7.4938		
DF	t Value	Pr > t			
40	-10.21	<.0001			

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsttest.sas 12JUN2019 10:39

Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDTNEQ
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	119
Number of Observations Used	117
Number of Observations Not Used	2

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	663.62149564	
1	2	584.25475802	0.00035303
2	1	584.18286102	0.00000345
3	1	584.18219535	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	20.7077
UN(2,1)	subject	19.3015
UN(2,2)	subject	22.4690

Fit Statistics

-2 Res Log Likelihood	584.2
AIC (smaller is better)	590.2
AICC (smaller is better)	590.4
BIC (smaller is better)	596.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	79.44	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	58.8	47.31	<.0001
week	1	50.2	0.23	0.6313
treat*week	3	50.2	1.45	0.2391

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-14.3984	1.7082	59	-8.43	<.0001	0.05	-17.8165	-10.9803
Week 2: VLN Mentholated vs UB Mentholated	-13.9195	1.6616	59	-8.38	<.0001	0.05	-17.2444	-10.5946
Week 2: VLN Combined vs UB Combined	-14.1589	1.1915	59	-11.88	<.0001	0.05	-16.5432	-11.7747
Week 2: VLN Combined	-14.7878	0.9498	59	-15.57	<.0001	0.05	-16.6883	-12.8874
Week 2: UB Combined	-0.6289	0.7195	59	-0.87	0.3856	0.05	-2.0686	0.8109
Week 6: VLN Non-mentholated vs UB Non-mentholated	-15.3936	1.8074	57.4	-8.52	<.0001	0.05	-19.0124	-11.7749
Week 6: VLN Mentholated vs UB Mentholated	-12.9630	1.7713	58.6	-7.32	<.0001	0.05	-16.5080	-9.4181
Week 6: VLN Combined vs UB Combined	-14.1783	1.2653	58	-11.21	<.0001	0.05	-16.7112	-11.6454
Week 6: VLN Combined	-14.6498	1.0108	58.3	-14.49	<.0001	0.05	-16.6730	-12.6267
Week 6: UB Combined	-0.4715	0.7612	57.3	-0.62	0.5381	0.05	-1.9955	1.0525

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-0.6092	1.0175	59	-0.60	0.5517	0.05	-2.6452	1.4269
treat*week	A	6	0.2852	1.0871	59	0.26	0.7940	0.05	-1.8901	2.4605
treat*week	B	2	-15.0075	1.3720	59	-10.94	<.0001	0.05	-17.7530	-12.2621
treat*week	B	6	-15.1084	1.4440	56.5	-10.46	<.0001	0.05	-18.0005	-12.2164
treat*week	C	2	-0.6486	1.0175	59	-0.64	0.5263	0.05	-2.6847	1.3875
treat*week	C	6	-1.2282	1.0657	55.7	-1.15	0.2540	0.05	-3.3633	0.9069
treat*week	D	2	-14.5681	1.3136	59	-11.09	<.0001	0.05	-17.1967	-11.9395
treat*week	D	6	-14.1912	1.4149	60.3	-10.03	<.0001	0.05	-17.0212	-11.3613

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-0.8943	0.5357	50.3	-1.67	0.1012	0.05	-1.9702	0.1815
treat*week	A	2	B	2	14.3984	1.7082	59	8.43	<.0001	0.05	10.9803	17.8165
treat*week	A	2	B	6	14.4993	1.7665	63.8	8.21	<.0001	0.05	10.9702	18.0284
treat*week	A	2	C	2	0.03943	1.4390	59	0.03	0.9782	0.05	-2.8400	2.9189
treat*week	A	2	C	6	0.6190	1.4735	64.6	0.42	0.6758	0.05	-2.3240	3.5621
treat*week	A	2	D	2	13.9589	1.6616	59	8.40	<.0001	0.05	10.6340	17.2839
treat*week	A	2	D	6	13.5821	1.7428	67.1	7.79	<.0001	0.05	10.1036	17.0606
treat*week	A	6	B	2	15.2927	1.7505	66.5	8.74	<.0001	0.05	11.7982	18.7873
treat*week	A	6	B	6	15.3936	1.8074	57.4	8.52	<.0001	0.05	11.7749	19.0124
treat*week	A	6	C	2	0.9338	1.4890	66.9	0.63	0.5327	0.05	-2.0384	3.9059
treat*week	A	6	C	6	1.5134	1.5223	57.3	0.99	0.3243	0.05	-1.5346	4.5614
treat*week	A	6	D	2	14.8533	1.7051	66.6	8.71	<.0001	0.05	11.4495	18.2570
treat*week	A	6	D	6	14.4764	1.7843	59.8	8.11	<.0001	0.05	10.9071	18.0458

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.1 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.1009	0.6769	50.1	0.15	0.8821	0.05	-1.2586	1.4604
treat*week	B	2	C	2	-14.3590	1.7082	59	-8.41	<.0001	0.05	-17.7770	-10.9409
treat*week	B	2	C	6	-13.7793	1.7373	64.8	-7.93	<.0001	0.05	-17.2492	-10.3095
treat*week	B	2	D	2	-0.4394	1.8995	59	-0.23	0.8178	0.05	-4.2404	3.3615
treat*week	B	2	D	6	-0.8163	1.9709	67.8	-0.41	0.6800	0.05	-4.7494	3.1167
treat*week	B	6	C	2	-14.4599	1.7665	63.8	-8.19	<.0001	0.05	-17.9890	-10.9307
treat*week	B	6	C	6	-13.8802	1.7946	56.2	-7.73	<.0001	0.05	-17.4751	-10.2854
treat*week	B	6	D	2	-0.5404	1.9521	65.1	-0.28	0.7828	0.05	-4.4389	3.3582
treat*week	B	6	D	6	-0.9172	2.0216	58.3	-0.45	0.6517	0.05	-4.9634	3.1290
treat*week	C	2	C	6	0.5796	0.4909	50	1.18	0.2433	0.05	-0.4063	1.5655
treat*week	C	2	D	2	13.9195	1.6616	59	8.38	<.0001	0.05	10.5946	17.2444
treat*week	C	2	D	6	13.5426	1.7428	67.1	7.77	<.0001	0.05	10.0642	17.0211
treat*week	C	6	D	2	13.3399	1.6916	64.8	7.89	<.0001	0.05	9.9615	16.7183
treat*week	C	6	D	6	12.9630	1.7713	58.6	7.32	<.0001	0.05	9.4181	16.5080
treat*week	D	2	D	6	-0.3769	0.7146	50.4	-0.53	0.6003	0.05	-1.8119	1.0582

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDTNEQ
Dependent Variable	CHG
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	251
Number of Observations Used	247
Number of Observations Not Used	4

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1502.39805170	
1	2	1404.65838769	0.00002159
2	1	1404.64778645	0.00000002
3	1	1404.64777902	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	25.0109
UN(2,1)	subject	21.0609
UN(2,2)	subject	30.9229

Fit Statistics

-2 Res Log Likelihood	1404.6
AIC (smaller is better)	1410.6
AICC (smaller is better)	1410.7
BIC (smaller is better)	1419.4

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	97.75	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	129	36.45	<.0001
week	1	113	22.30	<.0001
treat*week	3	113	6.96	0.0002

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-11.2513	1.3328	129	-8.44	<.0001	0.05	-13.8884	-8.6142
Week 2: VLN Mentholated vs UB Mentholated	-11.7042	1.3482	129	-8.68	<.0001	0.05	-14.3716	-9.0368
Week 2: VLN Combined vs UB Combined	-11.4777	0.9479	129	-12.11	<.0001	0.05	-13.3532	-9.6023
Week 2: VLN Combined	-12.1066	0.5227	130	-23.16	<.0001	0.05	-13.1407	-11.0725
Week 2: UB Combined	-0.6289	0.7907	128	-0.80	0.4279	0.05	-2.1935	0.9357
Week 6: VLN Non-mentholated vs UB Non-mentholated	-8.4462	1.5511	131	-5.45	<.0001	0.05	-11.5148	-5.3776
Week 6: VLN Mentholated vs UB Mentholated	-8.0781	1.5159	123	-5.33	<.0001	0.05	-11.0787	-5.0775
Week 6: VLN Combined vs UB Combined	-8.2622	1.0844	127	-7.62	<.0001	0.05	-10.4081	-6.1163
Week 6: VLN Combined	-8.7180	0.5934	126	-14.69	<.0001	0.05	-9.8923	-7.5437
Week 6: UB Combined	-0.4558	0.9077	127	-0.50	0.6164	0.05	-2.2519	1.3403

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	-0.6092	1.1183	128	-0.54	0.5869	0.05	-2.8218	1.6035
treat*week	A	6	0.2857	1.3092	132	0.22	0.8276	0.05	-2.3040	2.8754
treat*week	B	2	-11.8605	0.7252	129	-16.36	<.0001	0.05	-13.2952	-10.4257
treat*week	B	6	-8.1605	0.8319	128	-9.81	<.0001	0.05	-9.8066	-6.5145
treat*week	C	2	-0.6486	1.1183	128	-0.58	0.5629	0.05	-2.8613	1.5641
treat*week	C	6	-1.1973	1.2576	122	-0.95	0.3429	0.05	-3.6868	1.2922
treat*week	D	2	-12.3528	0.7530	131	-16.40	<.0001	0.05	-13.8424	-10.8631
treat*week	D	6	-9.2754	0.8464	124	-10.96	<.0001	0.05	-10.9506	-7.6002

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-0.8948	0.9265	113	-0.97	0.3362	0.05	-2.7304	0.9407
treat*week	A	2	B	2	11.2513	1.3328	129	8.44	<.0001	0.05	8.6142	13.8884
treat*week	A	2	B	6	7.5514	1.3938	163	5.42	<.0001	0.05	4.7992	10.3035
treat*week	A	2	C	2	0.03943	1.5815	128	0.02	0.9801	0.05	-3.0898	3.1686
treat*week	A	2	C	6	0.5882	1.6829	161	0.35	0.7272	0.05	-2.7352	3.9116
treat*week	A	2	D	2	11.7436	1.3482	129	8.71	<.0001	0.05	9.0762	14.4110
treat*week	A	2	D	6	8.6663	1.4025	161	6.18	<.0001	0.05	5.8967	11.4358
treat*week	A	6	B	2	12.1462	1.4966	159	8.12	<.0001	0.05	9.1903	15.1020
treat*week	A	6	B	6	8.4462	1.5511	131	5.45	<.0001	0.05	5.3776	11.5148
treat*week	A	6	C	2	0.9343	1.7218	170	0.54	0.5881	0.05	-2.4645	4.3331
treat*week	A	6	C	6	1.4830	1.8153	127	0.82	0.4155	0.05	-2.1092	5.0752
treat*week	A	6	D	2	12.6385	1.5103	160	8.37	<.0001	0.05	9.6559	15.6211
treat*week	A	6	D	6	9.5611	1.5589	129	6.13	<.0001	0.05	6.4768	12.6454

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Urinary Theq Mass Excreted
for Table 14.2.5.6.3.2 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	-3.6999	0.5846	114	-6.33	<.0001	0.05	-4.8582	-2.5417
treat*week	B	2	C	2	-11.2119	1.3328	129	-8.41	<.0001	0.05	-13.8490	-8.5748
treat*week	B	2	C	6	-10.6631	1.4517	149	-7.35	<.0001	0.05	-13.5317	-7.7946
treat*week	B	2	D	2	0.4923	1.0454	130	0.47	0.6385	0.05	-1.5759	2.5605
treat*week	B	2	D	6	-2.5851	1.1146	163	-2.32	0.0216	0.05	-4.7859	-0.3843
treat*week	B	6	C	2	-7.5119	1.3938	163	-5.39	<.0001	0.05	-10.2641	-4.7598
treat*week	B	6	C	6	-6.9632	1.5078	124	-4.62	<.0001	0.05	-9.9477	-3.9787
treat*week	B	6	D	2	4.1922	1.1221	169	3.74	0.0003	0.05	1.9771	6.4074
treat*week	B	6	D	6	1.1149	1.1868	126	0.94	0.3493	0.05	-1.2337	3.4634
treat*week	C	2	C	6	0.5487	0.8520	112	0.64	0.5209	0.05	-1.1394	2.2369
treat*week	C	2	D	2	11.7042	1.3482	129	8.68	<.0001	0.05	9.0368	14.3716
treat*week	C	2	D	6	8.6268	1.4025	161	6.15	<.0001	0.05	5.8573	11.3964
treat*week	C	6	D	2	11.1554	1.4658	151	7.61	<.0001	0.05	8.2593	14.0515
treat*week	C	6	D	6	8.0781	1.5159	123	5.33	<.0001	0.05	5.0775	11.0787
treat*week	D	2	D	6	-3.0773	0.5909	114	-5.21	<.0001	0.05	-4.2480	-1.9067

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pdurine/adam_urinestatsmixed.sas 12JUN2019 10:39

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	1	-0.6067934	.	-0.6067934	-0.6067934
base	Analysis Value	1	2.1225589	.	2.1225589	2.1225589

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	-1.3997323	0.6595798	-2.0387424	-0.7213469
base	Analysis Value	3	2.2997074	0.6052733	1.9391633	2.9984983

----- week=2 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	-1.2014976	0.6687439	-2.0387424	-0.6067934
base	Analysis Value	4	2.2554203	0.5020783	1.9391633	2.9984983

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	1	-0.4892461	.	-0.4892461	-0.4892461
base	Analysis Value	1	2.1225589	.	2.1225589	2.1225589

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	-1.3835783	0.3400397	-1.6757716	-1.0103378
base	Analysis Value	3	2.4078058	0.5401109	1.9391633	2.9984983

----- week=6 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	-1.1599953	0.5263480	-1.6757716	-0.4892461
base	Analysis Value	4	2.3364941	0.4634882	1.9391633	2.9984983

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
1	-2.7294	.	.	-2.7294	-2.7294
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.7294
DF	t Value	Pr > t			
0	.	.			

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-3.6994	0.9259	0.5346	-4.4376	-2.6605
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.6994	-5.9996	-1.3993	0.9259	0.4821	5.8193
	DF	t Value	Pr > t		
	2	-6.92	0.0202		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-3.4569	0.8982	0.4491	-4.4376	-2.6605
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.4569	-4.8862 -2.0276	0.8982	0.5088	3.3491	
	DF	t Value	Pr > t		
	3	-7.70	0.0046		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
1	-2.6118	.	.	-2.6118	-2.6118
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.6118
DF	t Value	Pr > t			
0	.	.			

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-3.7914	0.7710	0.4451	-4.4631	-2.9495
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.7914	-5.7067 -1.8761	0.7710	0.4014	4.8457	
	DF	t Value	Pr > t		
	2	-8.52	0.0135		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-3.4965	0.8627	0.4313	-4.4631	-2.6118
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.4965	-4.8692 -2.1238	0.8627	0.4887	3.2164	
	DF	t Value	Pr > t		
	3	-8.11	0.0039		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	1	-1.2020769	.	-1.2020769	-1.2020769
base	Analysis Value	1	2.3589405	.	2.3589405	2.3589405

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	-2.9249409	0.2832610	-3.2191290	-2.6540454
base	Analysis Value	3	2.4036529	0.2153691	2.2066381	2.6335860

----- week=2 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	-2.4942249	0.8919396	-3.2191290	-1.2020769
base	Analysis Value	4	2.3924748	0.1772635	2.2066381	2.6335860

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	1	-0.8308433	.	-0.8308433	-0.8308433
base	Analysis Value	1	2.3589405	.	2.3589405	2.3589405

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	3	-2.6869488	0.3087162	-2.8849179	-2.3312312
base	Analysis Value	3	2.4640721	0.2266464	2.2066381	2.6335860

----- week=6 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	4	-2.2229224	0.9616751	-2.8849179	-0.8308433
base	Analysis Value	4	2.4377892	0.1923769	2.2066381	2.6335860

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
1	-3.5610	.	.	-3.5610	-3.5610
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.5610
DF	t Value	Pr > t			
0	.	.			

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-5.3286	0.2434	0.1405	-5.5899	-5.1083
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-5.3286	-5.9332	-4.7240	0.2434	0.1267	1.5296
	DF	t Value	Pr > t		
	2	-37.92	0.0007		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=2 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-4.8867	0.9059	0.4529	-5.5899	-3.5610
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.8867	-6.3281 -3.4453	0.9059	0.5132	3.3775	
	DF	t Value	Pr > t		
	3	-10.79	0.0017		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
1	-3.1898	.	.	-3.1898	-3.1898
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.1898
DF	t Value	Pr > t			
0	.	.			

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
3	-5.1510	0.2513	0.1451	-5.4369	-4.9648
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-5.1510	-5.7754 -4.5267	0.2513	0.1309	1.5796	
	DF	t Value	Pr > t		
	2	-35.50	0.0008		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.11 (Pharmacokinetic Population from PP)

----- week=6 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
4	-4.6607	1.0019	0.5009	-5.4369	-3.1898
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.6607	-6.2549 -3.0665	1.0019	0.5675 3.7355		
	DF	t Value	Pr > t		
	3	-9.30	0.0026		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	-1.2125857	0.4453183	-1.9031596	-0.3958394
base	Analysis Value	12	2.4996986	0.4325601	1.8689998	3.3250769

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	-1.1942658	0.6150555	-2.0387424	-0.3887946
base	Analysis Value	10	2.5071716	0.4198962	1.9391633	3.2411349

----- week=2 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	22	-1.2042585	0.5158379	-2.0387424	-0.3887946
base	Analysis Value	22	2.5030954	0.4166368	1.8689998	3.3250769

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	-0.9755541	0.3779986	-1.5228149	-0.4326120
base	Analysis Value	12	2.4996986	0.4325601	1.8689998	3.3250769

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	-1.2218321	0.4626663	-1.8251520	-0.4144139
base	Analysis Value	10	2.5396011	0.3840606	1.9391633	3.2411349

----- week=6 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	22	-1.0874986	0.4270100	-1.8251520	-0.4144139
base	Analysis Value	22	2.5178361	0.4020423	1.8689998	3.3250769

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-3.7123	0.5521	0.1594	-4.5453	-2.7294
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7123	-4.0631	-3.3615	0.5521	0.3911	0.9374
	DF	t Value	Pr > t		
	11	-23.29	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-3.7014	0.5605	0.1773	-4.4376	-2.6605
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7014	-4.1024	-3.3005	0.5605	0.3856	1.0233
	DF	t Value	Pr > t		
	9	-20.88	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
22	-3.7074	0.5425	0.1157	-4.5453	-2.6605
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7074	-3.9479	-3.4668	0.5425	0.4174	0.7753
	DF	t Value	Pr > t		
	21	-32.05	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-3.4753	0.4550	0.1313	-4.1650	-2.6118
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.4753	-3.7643 -3.1862	0.4550	0.3223 0.7725		
	DF	t Value	Pr > t		
	11	-26.46	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: C_{max}
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-3.7614	0.4588	0.1451	-4.4631	-2.9495
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7614	-4.0896	-3.4332	0.4588	0.3156	0.8376
	DF	t Value	Pr > t		
	9	-25.92	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: Cmax
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
22	-3.6053	0.4689	0.1000	-4.4631	-2.6118
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.6053	-3.8133 -3.3974	0.4689	0.3608 0.6702		
DF	t Value	Pr > t			
21	-36.06	<.0001			

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	-2.1092256	1.1126374	-4.0058147	-0.5495159
base	Analysis Value	12	2.5301425	0.3360421	1.9262423	2.9313930

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	-1.8424748	0.9164808	-3.2191290	-0.3094625
base	Analysis Value	10	2.5867930	0.3534275	2.1596881	3.3174591

----- week=2 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	22	-1.9879752	1.0133664	-4.0058147	-0.3094625
base	Analysis Value	22	2.5558927	0.3369239	1.9262423	3.3174591

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=B -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	-1.6319191	0.9697825	-3.9730608	-0.7751671
base	Analysis Value	12	2.5301425	0.3360421	1.9262423	2.9313930

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	-1.8677712	1.0375038	-3.5600428	-0.4532329
base	Analysis Value	10	2.6049187	0.3456786	2.1596881	3.3174591

----- week=6 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	22	-1.7391246	0.9840732	-3.9730608	-0.4532329
base	Analysis Value	22	2.5641317	0.3343871	1.9262423	3.3174591

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-4.6394	0.9879	0.2852	-5.9321	-3.1832
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-4.6394	-5.2671	-4.0117	0.9879	0.6999	1.6774
	DF	t Value	Pr > t		
	11	-16.27	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-4.4293	0.7308	0.2311	-5.5899	-3.4697
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-4.4293	-4.9521	-3.9065	0.7308	0.5027	1.3342
	DF	t Value	Pr > t		
	9	-19.17	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=2 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum	
22	-4.5439	0.8670	0.1848	-5.9321	-3.1832	
Mean	95% CL Mean	Std Dev	95% CL Std Dev			
-4.5439	-4.9283 -4.1595	0.8670	0.6670 1.2389			
		DF	t Value	Pr > t		
		21	-24.58	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-4.1621	0.8217	0.2372	-5.8993	-3.1898
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-4.1621	-4.6841	-3.6400	0.8217	0.5821	1.3951
	DF	t Value	Pr > t		
	11	-17.55	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum		
10	-4.4727	0.8485	0.2683	-5.7197	-3.0082		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-4.4727	-5.0797 -3.8657	0.8485	0.5837 1.5491				
DF	t Value	Pr > t					
9	-16.67	<.0001					

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Comparison of Baseline Adjusted Plasma Nicotine Pharmacokinetic Parameters: AUC0-180
for 14.2.7.12 (Pharmacokinetic Population from ITT)

----- week=6 treat=0 -----

The TTEST Procedure

Difference: AVAL - base

N	Mean	Std Dev	Std Err	Minimum	Maximum
22	-4.3033	0.8290	0.1768	-5.8993	-3.0082
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.3033	-4.6708 -3.9357	0.8290	0.6378 1.1847		
	DF	t Value	Pr > t		
	21	-24.35	<.0001		

Treat B: Non-mentholated; Treat D: Mentholated; Treat O: Combined
Base: Week -1 (UB Cigarettes); Weeks 2 and 6: VLN Cigarettes

Program: /CA24914/sas_prg/pksas/adam_statsttest.sas 12JUN2019 10:09

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	4.9047619	1.9210612	1.0000000	8.0000000
BASE	Baseline Value	21	5.3333333	1.7701224	1.0000000	8.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	5.0500000	1.8803982	1.0000000	8.0000000
BASE	Baseline Value	40	5.2000000	1.6044809	1.0000000	8.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	6.5000000	1.9002924	4.0000000	10.0000000
BASE	Baseline Value	10	5.8000000	1.7511901	4.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpds/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	5.2173913	2.2351840	1.0000000	10.0000000
BASE	Baseline Value	23	4.9565217	1.9418422	2.0000000	10.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.2105263	1.8731716	1.0000000	8.0000000
BASE	Baseline Value	19	5.0526316	1.4327008	2.0000000	7.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	13	4.2307692	2.0064000	1.0000000	8.0000000
BASE	Baseline Value	13	4.3076923	1.8878831	2.0000000	8.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.2105263	2.0433890	1.0000000	8.0000000
BASE	Baseline Value	19	5.2105263	1.7505221	1.0000000	7.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	5.3076923	1.9888352	1.0000000	8.0000000
BASE	Baseline Value	39	5.1794872	1.5873148	1.0000000	7.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	5.9000000	2.0789955	3.0000000	10.0000000
BASE	Baseline Value	10	5.9000000	1.7288403	4.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	4.8947368	1.9970739	2.0000000	10.0000000
BASE	Baseline Value	19	5.0526316	1.9571432	2.0000000	10.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	5.4000000	1.9841477	1.0000000	8.0000000
BASE	Baseline Value	20	5.1500000	1.4608937	2.0000000	7.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	3.7777778	1.2018504	2.0000000	6.0000000
BASE	Baseline Value	9	4.1111111	1.8333333	2.0000000	8.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.4286	1.0282	0.2244	-2.0000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4286	-0.8966 0.0394	1.0282	0.7866 1.4848		
DF	t Value	Pr > t			
20	-1.91	0.0706			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-0.1500	1.0754	0.1700	-2.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.1500	-0.4939	0.1939	1.0754	0.8809	1.3808
	DF	t Value	Pr > t		
	39	-0.88	0.3831		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	0.7000	1.2517	0.3958	-1.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.7000	-0.1954 1.5954	1.2517	0.8609 2.2851		
DF	t Value	Pr > t			
9	1.77	0.1108			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	0.2609	1.3218	0.2756	-2.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.2609	-0.3107	0.8324	1.3218	1.0222	1.8707
	DF	t Value	Pr > t		
	22	0.95	0.3542		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0.1579	1.0679	0.2450	-2.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.1579	-0.3568	0.6726	1.0679	0.8069	1.5792
	DF	t Value	Pr > t		
	18	0.64	0.5274		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
13	-0.0769	1.3205	0.3662	-2.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0769	-0.8749 0.7210	1.3205	0.9469 2.1797		
DF	t Value	Pr > t			
12	-0.21	0.8372			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0	0.7454	0.1710	-2.0000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0	-0.3593	0.3593	0.7454	0.5632	1.1023
DF	t Value	Pr > t			
18	0.00	1.0000			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	0.1282	1.0306	0.1650	-2.0000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.1282	-0.2059	0.4623	1.0306	0.8422	1.3282
	DF	t Value	Pr > t		
	38	0.78	0.4420		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	0	0.9428	0.2981	-1.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0	-0.6744	0.6744	0.9428	0.6485	1.7212
	DF	t Value	Pr > t		
	9	0.00	1.0000		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.1579	1.4245	0.3268	-4.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1579	-0.8445	0.5287	1.4245	1.0764	2.1066
DF	t Value	Pr > t			
18	-0.48	0.6348			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	0.2500	1.2513	0.2798	-1.0000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.2500	-0.3356 0.8356	1.2513	0.9516 1.8276		
DF	t Value	Pr > t			
19	0.89	0.3828			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-0.3333	1.8708	0.6236	-4.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3333	-1.7714	1.1047	1.8708	1.2637	3.5841
	DF	t Value	Pr > t		
	8	-0.53	0.6075		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDFTCDTQS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	65	1007 1010 1011 1015 1016 1017 1018 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2016 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	65
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	121
Number of Observations Used	121
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	489.84212683	
1	2	412.28685389	0.00043084
2	1	412.24061866	0.00000265
3	1	412.24034674	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	3.6288
UN(2,1)	subject	3.3065
UN(2,2)	subject	3.8624

Fit Statistics

-2 Res Log Likelihood	412.2
AIC (smaller is better)	418.2
AICC (smaller is better)	418.5
BIC (smaller is better)	424.8

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	77.60	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	61	3.12	0.0324
week	1	53	2.36	0.1305
treat*week	3	52.9	3.03	0.0371

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	1.5999	0.7143	62	2.24	0.0287	0.05	0.1720	3.0279
Week 2: VLN Mentholated vs UB Mentholated	-1.0518	0.6803	61.1	-1.55	0.1272	0.05	-2.4121	0.3084
Week 2: VLN Combined vs UB Combined	0.2740	0.4932	61.6	0.56	0.5805	0.05	-0.7120	1.2601
Week 2: VLN Combined	5.3677	0.3926	61.8	13.67	<.0001	0.05	4.5828	6.1526
Week 2: UB Combined	5.0937	0.2985	61.2	17.06	<.0001	0.05	4.4968	5.6905
Week 6: VLN Non-mentholated vs UB Non-mentholated	0.7734	0.7400	58.9	1.05	0.3002	0.05	-0.7073	2.2542
Week 6: VLN Mentholated vs UB Mentholated	-1.8169	0.7214	62	-2.52	0.0144	0.05	-3.2590	-0.3748
Week 6: VLN Combined vs UB Combined	-0.5217	0.5167	60.4	-1.01	0.3167	0.05	-1.5552	0.5117
Week 6: VLN Combined	4.7641	0.4143	61.7	11.50	<.0001	0.05	3.9359	5.5923
Week 6: UB Combined	5.2859	0.3088	57.9	17.12	<.0001	0.05	4.6677	5.9040

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	4.9048	0.4157	60.7	11.80	<.0001	0.05	4.0734	5.7361
treat*week	A	6	5.1717	0.4340	58.9	11.92	<.0001	0.05	4.3033	6.0401
treat*week	B	2	6.5047	0.5809	62.7	11.20	<.0001	0.05	5.3437	7.6657
treat*week	B	6	5.9451	0.5994	58.9	9.92	<.0001	0.05	4.7458	7.1445
treat*week	C	2	5.2826	0.4285	61.7	12.33	<.0001	0.05	4.4260	6.1393
treat*week	C	6	5.4000	0.4395	56.9	12.29	<.0001	0.05	4.5200	6.2800
treat*week	D	2	4.2308	0.5283	60.7	8.01	<.0001	0.05	3.1742	5.2874
treat*week	D	6	3.5831	0.5721	65	6.26	<.0001	0.05	2.4405	4.7257

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-0.2669	0.2151	52.4	-1.24	0.2200	0.05	-0.6984	0.1645
treat*week	A	2	B	2	-1.5999	0.7143	62	-2.24	0.0287	0.05	-3.0279	-0.1720
treat*week	A	2	B	6	-1.0404	0.7294	66.8	-1.43	0.1584	0.05	-2.4963	0.4156
treat*week	A	2	C	2	-0.3779	0.5970	61.2	-0.63	0.5291	0.05	-1.5716	0.8158
treat*week	A	2	C	6	-0.4952	0.6049	67	-0.82	0.4159	0.05	-1.7027	0.7122
treat*week	A	2	D	2	0.6740	0.6723	60.7	1.00	0.3200	0.05	-0.6704	2.0184
treat*week	A	2	D	6	1.3217	0.7072	72.4	1.87	0.0657	0.05	-0.08794	2.7313
treat*week	A	6	B	2	-1.3330	0.7251	69.6	-1.84	0.0703	0.05	-2.7794	0.1134
treat*week	A	6	B	6	-0.7734	0.7400	58.9	-1.05	0.3002	0.05	-2.2542	0.7073
treat*week	A	6	C	2	-0.1109	0.6099	69.1	-0.18	0.8562	0.05	-1.3276	1.1057
treat*week	A	6	C	6	-0.2283	0.6176	57.9	-0.37	0.7130	0.05	-1.4647	1.0081
treat*week	A	6	D	2	0.9409	0.6837	68.3	1.38	0.1733	0.05	-0.4233	2.3052
treat*week	A	6	D	6	1.5886	0.7181	62.8	2.21	0.0306	0.05	0.1535	3.0237

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.3 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.5596	0.3113	53.3	1.80	0.0779	0.05	-0.06477	1.1839
treat*week	B	2	C	2	1.2221	0.7219	62.4	1.69	0.0955	0.05	-0.2207	2.6649
treat*week	B	2	C	6	1.1047	0.7284	68.7	1.52	0.1340	0.05	-0.3486	2.5580
treat*week	B	2	D	2	2.2739	0.7852	61.8	2.90	0.0052	0.05	0.7041	3.8437
treat*week	B	2	D	6	2.9216	0.8153	73.9	3.58	0.0006	0.05	1.2970	4.5463
treat*week	B	6	C	2	0.6625	0.7368	67.5	0.90	0.3717	0.05	-0.8079	2.1329
treat*week	B	6	C	6	0.5451	0.7432	58.2	0.73	0.4662	0.05	-0.9424	2.0327
treat*week	B	6	D	2	1.7144	0.7990	68.1	2.15	0.0355	0.05	0.1201	3.3086
treat*week	B	6	D	6	2.3621	0.8286	61.7	2.85	0.0059	0.05	0.7056	4.0185
treat*week	C	2	C	6	-0.1174	0.2147	52.4	-0.55	0.5868	0.05	-0.5481	0.3133
treat*week	C	2	D	2	1.0518	0.6803	61.1	1.55	0.1272	0.05	-0.3084	2.4121
treat*week	C	2	D	6	1.6995	0.7148	73	2.38	0.0200	0.05	0.2750	3.1241
treat*week	C	6	D	2	1.1692	0.6872	67.2	1.70	0.0935	0.05	-0.2024	2.5408
treat*week	C	6	D	6	1.8169	0.7214	62	2.52	0.0144	0.05	0.3748	3.2590
treat*week	D	2	D	6	0.6477	0.3127	52.9	2.07	0.0432	0.05	0.02057	1.2748

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	4.9047619	1.9210612	1.0000000	8.0000000
BASE	Baseline Value	21	5.3333333	1.7701224	1.0000000	8.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	5.0500000	1.8803982	1.0000000	8.0000000
BASE	Baseline Value	40	5.2000000	1.6044809	1.0000000	8.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	47	6.2978723	1.6139998	3.0000000	10.0000000
BASE	Baseline Value	47	5.9574468	1.5597860	3.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	93	5.6559140	1.8147621	1.0000000	10.0000000
BASE	Baseline Value	92	5.5652174	1.6395145	2.0000000	10.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.2105263	1.8731716	1.0000000	8.0000000
BASE	Baseline Value	19	5.0526316	1.4327008	2.0000000	7.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	46	5.0000000	1.7888544	1.0000000	8.0000000
BASE	Baseline Value	45	5.1555556	1.6370089	2.0000000	8.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.2105263	2.0433890	1.0000000	8.0000000
BASE	Baseline Value	19	5.2105263	1.7505221	1.0000000	7.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	5.3076923	1.9888352	1.0000000	8.0000000
BASE	Baseline Value	39	5.1794872	1.5873148	1.0000000	7.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	6.0465116	1.6755026	3.0000000	10.0000000
BASE	Baseline Value	43	6.0697674	1.4863722	3.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	85	5.4000000	1.7808505	2.0000000	10.0000000
BASE	Baseline Value	84	5.6428571	1.5954971	2.0000000	10.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	5.4000000	1.9841477	1.0000000	8.0000000
BASE	Baseline Value	20	5.1500000	1.4608937	2.0000000	7.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	4.7380952	1.6536659	2.0000000	9.0000000
BASE	Baseline Value	41	5.1951220	1.6003048	2.0000000	8.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.4286	1.0282	0.2244	-2.0000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4286	-0.8966 0.0394	1.0282	0.7866 1.4848		
DF	t Value	Pr > t			
20	-1.91	0.0706			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
40	-0.1500	1.0754	0.1700	-2.0000	2.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.1500	-0.4939 0.1939	1.0754	0.8809 1.3808				
DF	t Value	Pr > t					
39	-0.88	0.3831					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	0.3404	1.0274	0.1499	-1.0000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.3404	0.0388	0.6421	1.0274	0.8537	1.2904
	DF	t Value	Pr > t		
	46	2.27	0.0278		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
92	0.1087	1.0839	0.1130	-2.0000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.1087	-0.1158	0.3332	1.0839	0.9467	1.2680
	DF	t Value	Pr > t		
	91	0.96	0.3387		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0.1579	1.0679	0.2450	-2.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.1579	-0.3568	0.6726	1.0679	0.8069	1.5792
	DF	t Value	Pr > t		
	18	0.64	0.5274		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
45	-0.1333	1.0996	0.1639	-2.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.1333	-0.4637	0.1970	1.0996	0.9103	1.3890
	DF	t Value	Pr > t		
	44	-0.81	0.4204		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0	0.7454	0.1710	-2.0000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0	-0.3593	0.3593	0.7454	0.5632	1.1023
DF	t Value	Pr > t			
18	0.00	1.0000			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	0.1282	1.0306	0.1650	-2.0000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.1282	-0.2059	0.4623	1.0306	0.8422	1.3282
	DF	t Value	Pr > t		
	38	0.78	0.4420		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-0.0233	1.1231	0.1713	-2.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0233	-0.3689 0.3224	1.1231	0.9260 1.4275		
DF	t Value	Pr > t			
42	-0.14	0.8926			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
84	-0.2381	1.2670	0.1382	-4.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.2381	-0.5131	0.0369	1.2670	1.1001	1.4940
	DF	t Value	Pr > t		
	83	-1.72	0.0887		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	0.2500	1.2513	0.2798	-1.0000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.2500	-0.3356 0.8356	1.2513	0.9516 1.8276		
DF	t Value	Pr > t			
19	0.89	0.3828			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (FTCDT) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.1.4 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-0.4634	1.3802	0.2155	-4.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4634	-0.8991 -0.0278	1.3802	1.1331 1.7659		
DF	t Value	Pr > t			
40	-2.15	0.0377			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDFTCDTQS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	136	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1018 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2016 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	136
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	257
Number of Observations Used	257
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1018.30583004	
1	3	871.09372356	0.00048087
2	1	870.99424089	0.00000156
3	1	870.99391714	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	3.1166
UN(2,1)	subject	2.7660
UN(2,2)	subject	3.3497

Fit Statistics

-2 Res Log Likelihood	871.0
AIC (smaller is better)	877.0
AICC (smaller is better)	877.1
BIC (smaller is better)	885.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	147.31	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	130	5.28	0.0018
week	1	117	0.75	0.3885
treat*week	3	117	2.92	0.0371

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	1.4457	0.4612	131	3.13	0.0021	0.05	0.5333	2.3582
Week 2: VLN Mentholated vs UB Mentholated	-0.2801	0.4752	132	-0.59	0.5566	0.05	-1.2200	0.6599
Week 2: VLN Combined vs UB Combined	0.5828	0.3311	132	1.76	0.0807	0.05	-0.07218	1.2378
Week 2: VLN Combined	5.6752	0.1817	131	31.23	<.0001	0.05	5.3158	6.0347
Week 2: UB Combined	5.0924	0.2768	132	18.40	<.0001	0.05	4.5449	5.6400
Week 6: VLN Non-mentholated vs UB Non-mentholated	0.8304	0.4848	127	1.71	0.0892	0.05	-0.1289	1.7897
Week 6: VLN Mentholated vs UB Mentholated	-0.7676	0.4921	123	-1.56	0.1214	0.05	-1.7417	0.2065
Week 6: VLN Combined vs UB Combined	0.03142	0.3454	125	0.09	0.9277	0.05	-0.6522	0.7150
Week 6: VLN Combined	5.3178	0.1908	128	27.87	<.0001	0.05	4.9402	5.6954
Week 6: UB Combined	5.2864	0.2879	125	18.36	<.0001	0.05	4.7165	5.8562

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	4.9048	0.3852	130	12.73	<.0001	0.05	4.1426	5.6669
treat*week	A	6	5.1727	0.4051	127	12.77	<.0001	0.05	4.3712	5.9743
treat*week	B	2	6.3505	0.2537	133	25.04	<.0001	0.05	5.8487	6.8522
treat*week	B	6	6.0031	0.2664	129	22.53	<.0001	0.05	5.4760	6.5302
treat*week	C	2	5.2801	0.3976	133	13.28	<.0001	0.05	4.4937	6.0664
treat*week	C	6	5.4000	0.4092	122	13.19	<.0001	0.05	4.5899	6.2101
treat*week	D	2	5.0000	0.2603	130	19.21	<.0001	0.05	4.4851	5.5149
treat*week	D	6	4.6324	0.2733	127	16.95	<.0001	0.05	4.0916	5.1733

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	-0.2680	0.2215	117	-1.21	0.2288	0.05	-0.7066	0.1707
treat*week	A	2	B	2	-1.4457	0.4612	131	-3.13	0.0021	0.05	-2.3582	-0.5333
treat*week	A	2	B	6	-1.0983	0.4684	150	-2.35	0.0203	0.05	-2.0238	-0.1729
treat*week	A	2	C	2	-0.3753	0.5536	132	-0.68	0.4990	0.05	-1.4704	0.7198
treat*week	A	2	C	6	-0.4952	0.5620	148	-0.88	0.3797	0.05	-1.6059	0.6154
treat*week	A	2	D	2	-0.09524	0.4649	130	-0.20	0.8380	0.05	-1.0150	0.8245
treat*week	A	2	D	6	0.2723	0.4723	150	0.58	0.5651	0.05	-0.6610	1.2057
treat*week	A	6	B	2	-1.1778	0.4779	147	-2.46	0.0149	0.05	-2.1223	-0.2332
treat*week	A	6	B	6	-0.8304	0.4848	127	-1.71	0.0892	0.05	-1.7897	0.1289
treat*week	A	6	C	2	-0.1074	0.5676	154	-0.19	0.8502	0.05	-1.2286	1.0139
treat*week	A	6	C	6	-0.2273	0.5758	125	-0.39	0.6937	0.05	-1.3669	0.9124
treat*week	A	6	D	2	0.1727	0.4815	146	0.36	0.7203	0.05	-0.7788	1.1243
treat*week	A	6	D	6	0.5403	0.4887	127	1.11	0.2710	0.05	-0.4267	1.5072

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (FTCDT)
for Table 14.2.9.1.5 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.3474	0.1503	119	2.31	0.0226	0.05	0.04971	0.6450
treat*week	B	2	C	2	1.0704	0.4716	133	2.27	0.0248	0.05	0.1376	2.0032
treat*week	B	2	C	6	0.9505	0.4815	142	1.97	0.0503	0.05	-0.00134	1.9023
treat*week	B	2	D	2	1.3505	0.3634	131	3.72	0.0003	0.05	0.6315	2.0694
treat*week	B	2	D	6	1.7180	0.3729	153	4.61	<.0001	0.05	0.9813	2.4547
treat*week	B	6	C	2	0.7230	0.4786	152	1.51	0.1329	0.05	-0.2224	1.6685
treat*week	B	6	C	6	0.6031	0.4883	124	1.24	0.2191	0.05	-0.3634	1.5696
treat*week	B	6	D	2	1.0031	0.3724	153	2.69	0.0079	0.05	0.2673	1.7389
treat*week	B	6	D	6	1.3707	0.3817	128	3.59	0.0005	0.05	0.6154	2.1259
treat*week	C	2	C	6	-0.1199	0.2212	117	-0.54	0.5887	0.05	-0.5580	0.3182
treat*week	C	2	D	2	0.2801	0.4752	132	0.59	0.5566	0.05	-0.6599	1.2200
treat*week	C	2	D	6	0.6476	0.4825	151	1.34	0.1815	0.05	-0.3056	1.6008
treat*week	C	6	D	2	0.4000	0.4850	142	0.82	0.4109	0.05	-0.5588	1.3588
treat*week	C	6	D	6	0.7676	0.4921	123	1.56	0.1214	0.05	-0.2065	1.7417
treat*week	D	2	D	6	0.3676	0.1490	117	2.47	0.0151	0.05	0.07251	0.6626

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	3.6952381	1.4773206	1.2000000	6.8000000
BASE	Baseline Value	21	3.6857143	1.2109029	1.6000000	6.4000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	3.9750000	1.6141601	1.0000000	7.0000000
BASE	Baseline Value	40	4.0500000	1.4118546	1.0000000	7.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	5.1800000	1.2053584	3.0000000	6.6000000
BASE	Baseline Value	10	4.4200000	2.2458851	1.4000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	4.2260870	1.8716102	1.0000000	7.0000000
BASE	Baseline Value	23	4.1652174	1.9759023	1.4000000	7.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	4.2842105	1.7401351	1.0000000	7.0000000
BASE	Baseline Value	19	4.4526316	1.5374468	1.0000000	7.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	13	3.4923077	1.9976910	1.0000000	7.0000000
BASE	Baseline Value	13	3.9692308	1.8107938	2.0000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	3.5368421	1.5720512	1.2000000	6.8000000
BASE	Baseline Value	19	3.6526316	1.2271776	1.6000000	6.4000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	3.8051282	1.5711124	1.0000000	7.0000000
BASE	Baseline Value	39	4.0717949	1.4168068	1.0000000	7.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	3.5600000	2.0062126	1.0000000	7.0000000
BASE	Baseline Value	10	4.4600000	2.1889622	1.8000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	2.8105263	1.7844684	1.0000000	7.0000000
BASE	Baseline Value	19	4.1894737	1.9736865	1.8000000	7.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	4.0600000	1.5668943	1.0000000	7.0000000
BASE	Baseline Value	20	4.4700000	1.4984553	1.0000000	7.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	1.9777778	1.0744508	1.0000000	4.6000000
BASE	Baseline Value	9	3.8888889	1.7835670	2.0000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	0.00952	1.3015	0.2840	-2.4000	2.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.00952	-0.5829 0.6020	1.3015	0.9957 1.8795		
DF	t Value	Pr > t			
20	0.03	0.9736			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-0.0750	1.1799	0.1866	-3.6000	2.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0750	-0.4524 0.3024	1.1799	0.9665 1.5150		
DF	t Value	Pr > t			
39	-0.40	0.6899			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	0.7600	1.4539	0.4598	-1.8000	2.8000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.7600	-0.2800 1.8000	1.4539	1.0000 2.6542		
DF	t Value	Pr > t			
9	1.65	0.1327			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	0.0609	1.5799	0.3294	-2.0000	4.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.0609	-0.6223	0.7441	1.5799	1.2219	2.2361
	DF	t Value	Pr > t		
	22	0.18	0.8551		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.1684	1.0568	0.2424	-3.6000	1.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1684	-0.6778 0.3409	1.0568	0.7985 1.5628		
DF	t Value	Pr > t			
18	-0.69	0.4961			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
13	-0.4769	1.5067	0.4179	-2.0000	4.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.4769	-1.3874	0.4336	1.5067	1.0805	2.4872
	DF	t Value	Pr > t		
	12	-1.14	0.2760		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.1158	1.2280	0.2817	-2.6000	3.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.1158	-0.7077	0.4761	1.2280	0.9279	1.8160
	DF	t Value	Pr > t		
	18	-0.41	0.6859		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-0.2667	1.0466	0.1676	-2.6000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2667	-0.6059 0.0726	1.0466	0.8554 1.3489		
DF	t Value	Pr > t			
38	-1.59	0.1199			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-0.9000	2.8709	0.9079	-5.4000	3.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9000	-2.9537 1.1537	2.8709	1.9747 5.2412		
DF	t Value	Pr > t			
9	-0.99	0.3474			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-1.3789	2.2587	0.5182	-5.4000	3.4000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-1.3789	-2.4676	-0.2903	2.2587	1.7067	3.3402
	DF	t Value	Pr > t		
	18	-2.66	0.0159		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.4100	0.8472	0.1894	-1.6000	2.2000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4100	-0.8065 -0.0135	0.8472	0.6443 1.2374		
DF	t Value	Pr > t			
19	-2.16	0.0434			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-1.9111	1.2654	0.4218	-3.8000	-0.2000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.9111	-2.8837 -0.9385	1.2654	0.8547 2.4241		
DF	t Value	Pr > t			
8	-4.53	0.0019			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDQSUF1QS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	65	1007 1010 1011 1015 1016 1017 1018 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2016 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	65
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	121
Number of Observations Used	121
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	450.68229804	
1	2	421.43942481	0.00000003
2	1	421.43942199	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	2.6843
UN(2,1)	subject	1.7186
UN(2,2)	subject	2.5508

Fit Statistics

-2 Res Log Likelihood	421.4
AIC (smaller is better)	427.4
AICC (smaller is better)	427.7
BIC (smaller is better)	434.0

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	29.24	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	61.2	3.18	0.0303
week	1	55.3	24.22	<.0001
treat*week	3	54.9	5.04	0.0037

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	1.6000	0.6215	61.5	2.57	0.0125	0.05	0.3574	2.8426
Week 2: VLN Mentholated vs UB Mentholated	-0.7756	0.5872	60.3	-1.32	0.1916	0.05	-1.9501	0.3990
Week 2: VLN Combined vs UB Combined	0.4122	0.4275	60.9	0.96	0.3388	0.05	-0.4427	1.2671
Week 2: VLN Combined	4.3938	0.3409	61.2	12.89	<.0001	0.05	3.7121	5.0755
Week 2: UB Combined	3.9816	0.2580	60.4	15.43	<.0001	0.05	3.4656	4.4975
Week 6: VLN Non-mentholated vs UB Non-mentholated	-0.01359	0.6121	57.1	-0.02	0.9824	0.05	-1.2392	1.2120
Week 6: VLN Mentholated vs UB Mentholated	-2.0800	0.6126	60.5	-3.40	0.0012	0.05	-3.3052	-0.8549
Week 6: VLN Combined vs UB Combined	-1.0468	0.4330	58.9	-2.42	0.0187	0.05	-1.9133	-0.1804
Week 6: VLN Combined	2.7349	0.3512	60.3	7.79	<.0001	0.05	2.0325	3.4373
Week 6: UB Combined	3.7817	0.2533	55.9	14.93	<.0001	0.05	3.2744	4.2891

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	3.6952	0.3575	59.7	10.34	<.0001	0.05	2.9800	4.4105
treat*week	A	6	3.5035	0.3592	57.2	9.75	<.0001	0.05	2.7843	4.2227
treat*week	B	2	5.2952	0.5084	62.3	10.42	<.0001	0.05	4.2791	6.3114
treat*week	B	6	3.4899	0.4956	57.1	7.04	<.0001	0.05	2.4974	4.4823
treat*week	C	2	4.2679	0.3720	61.1	11.47	<.0001	0.05	3.5241	5.0117
treat*week	C	6	4.0600	0.3571	54.6	11.37	<.0001	0.05	3.3442	4.7758
treat*week	D	2	3.4923	0.4544	59.7	7.69	<.0001	0.05	2.5833	4.4014
treat*week	D	6	1.9800	0.4977	63.2	3.98	0.0002	0.05	0.9854	2.9745

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.1918	0.3052	53.6	0.63	0.5325	0.05	-0.4203	0.8038
treat*week	A	2	B	2	-1.6000	0.6215	61.5	-2.57	0.0125	0.05	-2.8426	-0.3574
treat*week	A	2	B	6	0.2054	0.6111	79.7	0.34	0.7377	0.05	-1.0109	1.4216
treat*week	A	2	C	2	-0.5727	0.5159	60.4	-1.11	0.2714	0.05	-1.6045	0.4592
treat*week	A	2	C	6	-0.3648	0.5053	81.3	-0.72	0.4725	0.05	-1.3702	0.6406
treat*week	A	2	D	2	0.2029	0.5782	59.7	0.35	0.7268	0.05	-0.9538	1.3596
treat*week	A	2	D	6	1.7153	0.6128	88.2	2.80	0.0063	0.05	0.4975	2.9331
treat*week	A	6	B	2	-1.7918	0.6225	84.3	-2.88	0.0051	0.05	-3.0296	-0.5539
treat*week	A	6	B	6	0.01359	0.6121	57.1	0.02	0.9824	0.05	-1.2120	1.2392
treat*week	A	6	C	2	-0.7644	0.5171	85.7	-1.48	0.1430	0.05	-1.7924	0.2636
treat*week	A	6	C	6	-0.5565	0.5065	55.9	-1.10	0.2766	0.05	-1.5712	0.4582
treat*week	A	6	D	2	0.01116	0.5792	82.8	0.02	0.9847	0.05	-1.1409	1.1633
treat*week	A	6	D	6	1.5235	0.6138	61.3	2.48	0.0158	0.05	0.2963	2.7507

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	1.8053	0.4400	55.4	4.10	0.0001	0.05	0.9238	2.6869
treat*week	B	2	C	2	1.0273	0.6299	61.9	1.63	0.1080	0.05	-0.2320	2.2866
treat*week	B	2	C	6	1.2352	0.6213	82.5	1.99	0.0501	0.05	-0.00062	2.4711
treat*week	B	2	D	2	1.8029	0.6819	61.2	2.64	0.0104	0.05	0.4395	3.1663
treat*week	B	2	D	6	3.3153	0.7115	93.8	4.66	<.0001	0.05	1.9026	4.7279
treat*week	B	6	C	2	-0.7780	0.6197	81.5	-1.26	0.2129	0.05	-2.0109	0.4549
treat*week	B	6	C	6	-0.5701	0.6109	56.3	-0.93	0.3547	0.05	-1.7938	0.6535
treat*week	B	6	D	2	-0.00243	0.6724	83.5	-0.00	0.9971	0.05	-1.3397	1.3348
treat*week	B	6	D	6	1.5099	0.7024	60.3	2.15	0.0356	0.05	0.1051	2.9148
treat*week	C	2	C	6	0.2079	0.3067	52.8	0.68	0.5008	0.05	-0.4073	0.8231
treat*week	C	2	D	2	0.7756	0.5872	60.3	1.32	0.1916	0.05	-0.3990	1.9501
treat*week	C	2	D	6	2.2879	0.6214	89.8	3.68	0.0004	0.05	1.0535	3.5224
treat*week	C	6	D	2	0.5677	0.5779	80.6	0.98	0.3289	0.05	-0.5823	1.7177
treat*week	C	6	D	6	2.0800	0.6126	60.5	3.40	0.0012	0.05	0.8549	3.3052
treat*week	D	2	D	6	1.5123	0.4357	56.5	3.47	0.0010	0.05	0.6398	2.3849

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	3.6952381	1.4773206	1.2000000	6.8000000
BASE	Baseline Value	21	3.6857143	1.2109029	1.6000000	6.4000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	3.9750000	1.6141601	1.0000000	7.0000000
BASE	Baseline Value	40	4.0500000	1.4118546	1.0000000	7.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	47	5.3531915	1.5025849	1.6000000	7.0000000
BASE	Baseline Value	47	4.3234043	1.6673609	1.4000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	93	4.5290323	1.8825619	1.0000000	7.0000000
BASE	Baseline Value	92	4.1608696	1.6501053	1.0000000	7.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	4.2842105	1.7401351	1.0000000	7.0000000
BASE	Baseline Value	19	4.4526316	1.5374468	1.0000000	7.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	46	3.6869565	1.8717323	1.0000000	7.0000000
BASE	Baseline Value	45	3.9911111	1.6331540	1.0000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	3.5368421	1.5720512	1.2000000	6.8000000
BASE	Baseline Value	19	3.6526316	1.2271776	1.6000000	6.4000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	3.8051282	1.5711124	1.0000000	7.0000000
BASE	Baseline Value	39	4.0717949	1.4168068	1.0000000	7.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	4.3860465	1.6769561	1.0000000	7.0000000
BASE	Baseline Value	43	4.3906977	1.6987130	1.6000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	85	3.9011765	1.7516315	1.0000000	7.0000000
BASE	Baseline Value	84	4.1880952	1.6586687	1.0000000	7.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	4.0600000	1.5668943	1.0000000	7.0000000
BASE	Baseline Value	20	4.4700000	1.4984553	1.0000000	7.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	3.4047619	1.7047927	1.0000000	7.0000000
BASE	Baseline Value	41	3.9756098	1.6088475	1.0000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	0.00952	1.3015	0.2840	-2.4000	2.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.00952	-0.5829 0.6020	1.3015	0.9957 1.8795		
DF	t Value	Pr > t			
20	0.03	0.9736			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-0.0750	1.1799	0.1866	-3.6000	2.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.0750	-0.4524 0.3024	1.1799	0.9665 1.5150		
DF	t Value	Pr > t			
39	-0.40	0.6899			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	1.0298	1.6157	0.2357	-1.8000	5.4000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1.0298	0.5554	1.5042	1.6157	1.3426	2.0293
	DF	t Value	Pr > t		
	46	4.37	<.0001		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
92	0.3739	1.6794	0.1751	-3.6000	5.4000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.3739	0.0261	0.7217	1.6794	1.4669	1.9646
	DF	t Value	Pr > t		
	91	2.14	0.0354		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.1684	1.0568	0.2424	-3.6000	1.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1684	-0.6778 0.3409	1.0568	0.7985 1.5628		
DF	t Value	Pr > t			
18	-0.69	0.4961			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
45	-0.3111	1.4713	0.2193	-3.6000	4.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.3111	-0.7531 0.1309	1.4713	1.2180 1.8585				
DF	t Value	Pr > t					
44	-1.42	0.1631					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.1158	1.2280	0.2817	-2.6000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1158	-0.7077 0.4761	1.2280	0.9279 1.8160		
DF	t Value	Pr > t			
18	-0.41	0.6859			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-0.2667	1.0466	0.1676	-2.6000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2667	-0.6059 0.0726	1.0466	0.8554 1.3489		
DF	t Value	Pr > t			
38	-1.59	0.1199			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-0.00465	2.0417	0.3114	-5.4000	3.6000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.00465	-0.6330	0.6237	2.0417	1.6835	2.5950
DF	t Value	Pr > t			
42	-0.01	0.9882			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
84	-0.2810	1.9687	0.2148	-6.0000	5.2000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.2810	-0.7082	0.1463	1.9687	1.7094	2.3215
	DF	t Value	Pr > t		
	83	-1.31	0.1945		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.4100	0.8472	0.1894	-1.6000	2.2000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4100	-0.8065 -0.0135	0.8472	0.6443 1.2374		
DF	t Value	Pr > t			
19	-2.16	0.0434			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF1) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-0.5707	1.8701	0.2921	-6.0000	5.2000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5707	-1.1610 0.0195	1.8701	1.5353 2.3927		
DF	t Value	Pr > t			
40	-1.95	0.0577			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDQSUF1QS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	136	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1018 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2016 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	136
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	257
Number of Observations Used	257
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	986.83003004	
1	2	940.23498521	0.00000001
2	1	940.23498248	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	2.7812
UN(2,1)	subject	1.5910
UN(2,2)	subject	2.7528

Fit Statistics

-2 Res Log Likelihood	940.2
AIC (smaller is better)	946.2
AICC (smaller is better)	946.3
BIC (smaller is better)	955.0

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	46.60	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	130	7.01	0.0002
week	1	121	8.85	0.0035
treat*week	3	121	2.77	0.0448

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	1.6946	0.4369	130	3.88	0.0002	0.05	0.8304	2.5588
Week 2: VLN Mentholated vs UB Mentholated	-0.5833	0.4522	132	-1.29	0.1994	0.05	-1.4778	0.3113
Week 2: VLN Combined vs UB Combined	0.5557	0.3144	131	1.77	0.0795	0.05	-0.06624	1.1776
Week 2: VLN Combined	4.5384	0.1724	131	26.33	<.0001	0.05	4.1974	4.8794
Week 2: UB Combined	3.9827	0.2629	131	15.15	<.0001	0.05	3.4626	4.5028
Week 6: VLN Non-mentholated vs UB Non-mentholated	0.8027	0.4495	126	1.79	0.0765	0.05	-0.08680	1.6921
Week 6: VLN Mentholated vs UB Mentholated	-0.6654	0.4487	122	-1.48	0.1407	0.05	-1.5538	0.2229
Week 6: VLN Combined vs UB Combined	0.06863	0.3176	124	0.22	0.8293	0.05	-0.5599	0.6972
Week 6: VLN Combined	3.8521	0.1770	126	21.77	<.0001	0.05	3.5019	4.2023
Week 6: UB Combined	3.7835	0.2637	123	14.35	<.0001	0.05	3.2616	4.3055

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	3.6952	0.3639	130	10.15	<.0001	0.05	2.9753	4.4152
treat*week	A	6	3.5070	0.3748	125	9.36	<.0001	0.05	2.7652	4.2488
treat*week	B	2	5.3898	0.2417	132	22.30	<.0001	0.05	4.9118	5.8679
treat*week	B	6	4.3097	0.2480	127	17.37	<.0001	0.05	3.8188	4.8005
treat*week	C	2	4.2702	0.3795	133	11.25	<.0001	0.05	3.5195	5.0209
treat*week	C	6	4.0600	0.3710	120	10.94	<.0001	0.05	3.3255	4.7945
treat*week	D	2	3.6870	0.2459	130	14.99	<.0001	0.05	3.2005	4.1734
treat*week	D	6	3.3946	0.2524	125	13.45	<.0001	0.05	2.8950	3.8942

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.1882	0.3484	121	0.54	0.5900	0.05	-0.5016	0.8780
treat*week	A	2	B	2	-1.6946	0.4369	130	-3.88	0.0002	0.05	-2.5588	-0.8304
treat*week	A	2	B	6	-0.6145	0.4404	186	-1.40	0.1646	0.05	-1.4833	0.2544
treat*week	A	2	C	2	-0.5750	0.5258	131	-1.09	0.2762	0.05	-1.6151	0.4652
treat*week	A	2	C	6	-0.3648	0.5197	190	-0.70	0.4836	0.05	-1.3899	0.6603
treat*week	A	2	D	2	0.008282	0.4392	130	0.02	0.9850	0.05	-0.8606	0.8772
treat*week	A	2	D	6	0.3007	0.4429	186	0.68	0.4981	0.05	-0.5731	1.1744
treat*week	A	6	B	2	-1.8828	0.4460	179	-4.22	<.0001	0.05	-2.7628	-1.0028
treat*week	A	6	B	6	-0.8027	0.4495	126	-1.79	0.0765	0.05	-1.6921	0.08680
treat*week	A	6	C	2	-0.7632	0.5334	200	-1.43	0.1540	0.05	-1.8150	0.2886
treat*week	A	6	C	6	-0.5530	0.5274	123	-1.05	0.2964	0.05	-1.5969	0.4909
treat*week	A	6	D	2	-0.1799	0.4483	179	-0.40	0.6886	0.05	-1.0645	0.7046
treat*week	A	6	D	6	0.1124	0.4519	125	0.25	0.8039	0.05	-0.7819	1.0068

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF1)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	1.0801	0.2351	125	4.59	<.0001	0.05	0.6149	1.5454
treat*week	B	2	C	2	1.1196	0.4499	132	2.49	0.0141	0.05	0.2296	2.0096
treat*week	B	2	C	6	1.3298	0.4428	173	3.00	0.0031	0.05	0.4559	2.2038
treat*week	B	2	D	2	1.7029	0.3448	131	4.94	<.0001	0.05	1.0208	2.3849
treat*week	B	2	D	6	1.9953	0.3495	198	5.71	<.0001	0.05	1.3061	2.6844
treat*week	B	6	C	2	0.03948	0.4534	187	0.09	0.9307	0.05	-0.8549	0.9339
treat*week	B	6	C	6	0.2497	0.4463	122	0.56	0.5768	0.05	-0.6337	1.1331
treat*week	B	6	D	2	0.6227	0.3493	198	1.78	0.0761	0.05	-0.06602	1.3115
treat*week	B	6	D	6	0.9151	0.3539	126	2.59	0.0109	0.05	0.2147	1.6155
treat*week	C	2	C	6	0.2102	0.3501	119	0.60	0.5494	0.05	-0.4830	0.9035
treat*week	C	2	D	2	0.5833	0.4522	132	1.29	0.1994	0.05	-0.3113	1.4778
treat*week	C	2	D	6	0.8756	0.4558	187	1.92	0.0562	0.05	-0.02354	1.7748
treat*week	C	6	D	2	0.3730	0.4451	173	0.84	0.4031	0.05	-0.5055	1.2516
treat*week	C	6	D	6	0.6654	0.4487	122	1.48	0.1407	0.05	-0.2229	1.5538
treat*week	D	2	D	6	0.2924	0.2345	121	1.25	0.2150	0.05	-0.1720	0.7567

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	2.6952381	0.9952267	1.0000000	5.0000000
BASE	Baseline Value	21	2.9619048	1.0170920	1.2000000	5.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	3.0050000	1.2097785	1.0000000	5.6000000
BASE	Baseline Value	40	3.3200000	1.3249480	1.0000000	6.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	3.1800000	1.6178175	1.0000000	5.4000000
BASE	Baseline Value	10	3.1800000	1.9309180	1.0000000	6.6000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	2.8608696	1.6585150	1.0000000	6.8000000
BASE	Baseline Value	23	3.0260870	1.7922098	1.0000000	7.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	3.3473684	1.3545678	1.0000000	5.6000000
BASE	Baseline Value	19	3.7157895	1.5294382	1.0000000	6.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	13	2.6153846	1.7116494	1.0000000	6.8000000
BASE	Baseline Value	13	2.9076923	1.7485525	1.4000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	2.6736842	0.9982441	1.0000000	4.6000000
BASE	Baseline Value	19	2.9684211	1.0672148	1.2000000	5.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	2.9846154	1.2047141	1.0000000	5.6000000
BASE	Baseline Value	39	3.3435897	1.3368846	1.0000000	6.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	2.3800000	1.2308985	1.0000000	4.2000000
BASE	Baseline Value	10	3.2200000	1.8890327	1.0000000	6.6000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	1.9894737	1.2119290	1.0000000	4.4000000
BASE	Baseline Value	19	2.9157895	1.6510142	1.0000000	6.6000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	3.2800000	1.3304530	1.0000000	5.6000000
BASE	Baseline Value	20	3.7000000	1.4903196	1.0000000	6.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	1.5555556	1.0944303	1.0000000	4.4000000
BASE	Baseline Value	9	2.5777778	1.3691035	1.4000000	5.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.2667	0.7933	0.1731	-1.4000	1.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2667	-0.6278 0.0944	0.7933	0.6069 1.1456		
DF	t Value	Pr > t			
20	-1.54	0.1391			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-0.3150	0.7468	0.1181	-2.6000	1.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3150	-0.5538 -0.0762	0.7468	0.6118 0.9589		
DF	t Value	Pr > t			
39	-2.67	0.0111			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	0	1.1235	0.3553	-2.0000	1.6000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0	-0.8037	0.8037	1.1235	0.7728	2.0510
	DF	t Value	Pr > t		
	9	0.00	1.0000		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	-0.1652	1.0386	0.2166	-2.0000	2.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1652	-0.6144 0.2839	1.0386	0.8033 1.4700		
DF	t Value	Pr > t			
22	-0.76	0.4536			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.3684	0.7095	0.1628	-2.6000	0.2000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3684	-0.7104 -0.0265	0.7095	0.5361 1.0492		
DF	t Value	Pr > t			
18	-2.26	0.0362			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
13	-0.2923	0.9954	0.2761	-1.6000	2.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2923	-0.8938 0.3092	0.9954	0.7138 1.6431		
DF	t Value	Pr > t			
12	-1.06	0.3105			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.2947	1.0250	0.2351	-2.4000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2947	-0.7887 0.1993	1.0250	0.7745 1.5157		
DF	t Value	Pr > t			
18	-1.25	0.2261			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-0.3590	0.8635	0.1383	-2.4000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3590	-0.6389 -0.0791	0.8635	0.7057 1.1129		
DF	t Value	Pr > t			
38	-2.60	0.0133			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-0.8400	2.1885	0.6921	-5.6000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.8400	-2.4055 0.7255	2.1885	1.5053 3.9953		
DF	t Value	Pr > t			
9	-1.21	0.2557			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.9263	1.6868	0.3870	-5.6000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.9263	-1.7393 -0.1133	1.6868	1.2746 2.4945		
DF	t Value	Pr > t			
18	-2.39	0.0278			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.4200	0.6986	0.1562	-2.4000	0.6000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4200	-0.7469 -0.0931	0.6986	0.5313 1.0203		
DF	t Value	Pr > t			
19	-2.69	0.0145			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
9	-1.0222	0.9972	0.3324	-3.0000	-0.2000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-1.0222	-1.7888 -0.2557	0.9972	0.6736 1.9104				
DF	t Value	Pr > t					
8	-3.08	0.0152					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDQSUF2QS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	65	1007 1010 1011 1015 1016 1017 1018 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2016 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	65
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	121
Number of Observations Used	121
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	398.49561423	
1	2	363.75232343	0.00203070
2	1	363.58029206	0.00004253
3	1	363.57692741	0.00000002
4	1	363.57692568	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	1.8634
UN(2,1)	subject	1.1829
UN(2,2)	subject	1.4873

Fit Statistics

-2 Res Log Likelihood	363.6
AIC (smaller is better)	369.6
AICC (smaller is better)	369.8
BIC (smaller is better)	376.1

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	34.92	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	59.6	2.60	0.0605
week	1	53.2	13.28	0.0006
treat*week	3	52.7	3.54	0.0206

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	0.5274	0.5166	62.2	1.02	0.3113	0.05	-0.5052	1.5599
Week 2: VLN Mentholated vs UB Mentholated	-0.7454	0.4889	61	-1.52	0.1325	0.05	-1.7230	0.2323
Week 2: VLN Combined vs UB Combined	-0.1090	0.3556	61.6	-0.31	0.7602	0.05	-0.8200	0.6020
Week 2: VLN Combined	2.9190	0.2835	61.9	10.30	<.0001	0.05	2.3523	3.4857
Week 2: UB Combined	3.0280	0.2147	61.1	14.10	<.0001	0.05	2.5987	3.4573
Week 6: VLN Non-mentholated vs UB Non-mentholated	-0.4030	0.4657	54	-0.87	0.3907	0.05	-1.3367	0.5307
Week 6: VLN Mentholated vs UB Mentholated	-1.6300	0.4637	57.8	-3.51	0.0009	0.05	-2.5584	-0.7017
Week 6: VLN Combined vs UB Combined	-1.0165	0.3286	55.9	-3.09	0.0031	0.05	-1.6749	-0.3582
Week 6: VLN Combined	1.9571	0.2660	57.6	7.36	<.0001	0.05	1.4247	2.4896
Week 6: UB Combined	2.9737	0.1930	52.8	15.41	<.0001	0.05	2.5865	3.3609

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	2.6952	0.2979	60.4	9.05	<.0001	0.05	2.0995	3.2910
treat*week	A	6	2.6673	0.2733	54.1	9.76	<.0001	0.05	2.1195	3.2152
treat*week	B	2	3.2226	0.4221	63.1	7.64	<.0001	0.05	2.3792	4.0660
treat*week	B	6	2.2643	0.3771	54	6.00	<.0001	0.05	1.5082	3.0204
treat*week	C	2	3.3608	0.3093	61.8	10.86	<.0001	0.05	2.7424	3.9791
treat*week	C	6	3.2800	0.2727	51.4	12.03	<.0001	0.05	2.7326	3.8274
treat*week	D	2	2.6154	0.3786	60.4	6.91	<.0001	0.05	1.8582	3.3726
treat*week	D	6	1.6500	0.3751	61.1	4.40	<.0001	0.05	0.9000	2.4000

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.02792	0.2253	51.6	0.12	0.9019	0.05	-0.4242	0.4801
treat*week	A	2	B	2	-0.5274	0.5166	62.2	-1.02	0.3113	0.05	-1.5599	0.5052
treat*week	A	2	B	6	0.4309	0.4806	75.8	0.90	0.3727	0.05	-0.5263	1.3882
treat*week	A	2	C	2	-0.6655	0.4294	61.1	-1.55	0.1264	0.05	-1.5242	0.1932
treat*week	A	2	C	6	-0.5848	0.4039	76.7	-1.45	0.1517	0.05	-1.3890	0.2195
treat*week	A	2	D	2	0.07985	0.4817	60.4	0.17	0.8689	0.05	-0.8837	1.0434
treat*week	A	2	D	6	1.0453	0.4790	84.4	2.18	0.0319	0.05	0.09284	1.9977
treat*week	A	6	B	2	-0.5553	0.5028	79.6	-1.10	0.2728	0.05	-1.5560	0.4454
treat*week	A	6	B	6	0.4030	0.4657	54	0.87	0.3907	0.05	-0.5307	1.3367
treat*week	A	6	C	2	-0.6934	0.4127	80.7	-1.68	0.0968	0.05	-1.5147	0.1278
treat*week	A	6	C	6	-0.6127	0.3861	52.8	-1.59	0.1185	0.05	-1.3871	0.1617
treat*week	A	6	D	2	0.05194	0.4669	77.7	0.11	0.9117	0.05	-0.8777	0.9816
treat*week	A	6	D	6	1.0174	0.4641	58.7	2.19	0.0323	0.05	0.08866	1.9461

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.3 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.9583	0.3263	52.5	2.94	0.0049	0.05	0.3037	1.6129
treat*week	B	2	C	2	-0.1382	0.5233	62.7	-0.26	0.7926	0.05	-1.1839	0.9076
treat*week	B	2	C	6	-0.05739	0.5025	78.1	-0.11	0.9094	0.05	-1.0577	0.9430
treat*week	B	2	D	2	0.6072	0.5670	61.9	1.07	0.2883	0.05	-0.5262	1.7406
treat*week	B	2	D	6	1.5726	0.5646	88.3	2.79	0.0065	0.05	0.4506	2.6947
treat*week	B	6	C	2	-1.0965	0.4878	77.5	-2.25	0.0274	0.05	-2.0676	-0.1253
treat*week	B	6	C	6	-1.0157	0.4654	53.1	-2.18	0.0335	0.05	-1.9491	-0.08227
treat*week	B	6	D	2	-0.3511	0.5344	78.7	-0.66	0.5131	0.05	-1.4148	0.7126
treat*week	B	6	D	6	0.6143	0.5319	57.6	1.15	0.2529	0.05	-0.4505	1.6792
treat*week	C	2	C	6	0.08076	0.2275	49.7	0.35	0.7241	0.05	-0.3763	0.5378
treat*week	C	2	D	2	0.7454	0.4889	61	1.52	0.1325	0.05	-0.2323	1.7230
treat*week	C	2	D	6	1.7108	0.4862	86	3.52	0.0007	0.05	0.7443	2.6773
treat*week	C	6	D	2	0.6646	0.4666	76	1.42	0.1584	0.05	-0.2647	1.5939
treat*week	C	6	D	6	1.6300	0.4637	57.8	3.51	0.0009	0.05	0.7017	2.5584
treat*week	D	2	D	6	0.9654	0.3194	55.9	3.02	0.0038	0.05	0.3255	1.6054

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	2.6952381	0.9952267	1.0000000	5.0000000
BASE	Baseline Value	21	2.9619048	1.0170920	1.2000000	5.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	3.0050000	1.2097785	1.0000000	5.6000000
BASE	Baseline Value	40	3.3200000	1.3249480	1.0000000	6.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	47	3.8553191	1.5246965	1.0000000	7.0000000
BASE	Baseline Value	47	3.1446809	1.5051807	1.0000000	6.6000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	93	3.2473118	1.6925406	1.0000000	7.0000000
BASE	Baseline Value	92	3.0173913	1.5660273	1.0000000	7.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	3.3473684	1.3545678	1.0000000	5.6000000
BASE	Baseline Value	19	3.7157895	1.5294382	1.0000000	6.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	46	2.6260870	1.6430912	1.0000000	7.0000000
BASE	Baseline Value	45	2.8844444	1.6334508	1.0000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	2.6736842	0.9982441	1.0000000	4.6000000
BASE	Baseline Value	19	2.9684211	1.0672148	1.2000000	5.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	2.9846154	1.2047141	1.0000000	5.6000000
BASE	Baseline Value	39	3.3435897	1.3368846	1.0000000	6.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	3.2279070	1.5384478	1.0000000	7.0000000
BASE	Baseline Value	43	3.2093023	1.5386782	1.0000000	6.6000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	85	2.7952941	1.5910393	1.0000000	7.0000000
BASE	Baseline Value	84	3.0142857	1.5488155	1.0000000	7.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	3.2800000	1.3304530	1.0000000	5.6000000
BASE	Baseline Value	20	3.7000000	1.4903196	1.0000000	6.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	2.3523810	1.5376952	1.0000000	7.0000000
BASE	Baseline Value	41	2.8097561	1.5517417	1.0000000	7.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.2667	0.7933	0.1731	-1.4000	1.4000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2667	-0.6278 0.0944	0.7933	0.6069 1.1456		
DF	t Value	Pr > t			
20	-1.54	0.1391			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
40	-0.3150	0.7468	0.1181	-2.6000	1.4000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.3150	-0.5538 -0.0762	0.7468	0.6118 0.9589				
DF	t Value	Pr > t					
39	-2.67	0.0111					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	0.7106	1.2967	0.1891	-2.0000	3.8000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.7106	0.3299 1.0914	1.2967	1.0775 1.6286		
DF	t Value	Pr > t			
46	3.76	0.0005			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
92	0.2239	1.2776	0.1332	-3.0000	3.8000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.2239	-0.0407	0.4885	1.2776	1.1160	1.4946
	DF	t Value	Pr > t		
	91	1.68	0.0962		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.3684	0.7095	0.1628	-2.6000	0.2000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.3684	-0.7104	-0.0265	0.7095	0.5361	1.0492
	DF	t Value	Pr > t		
	18	-2.26	0.0362		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
45	-0.2844	1.0492	0.1564	-3.0000	3.4000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.2844	-0.5997	0.0308	1.0492	0.8686	1.3254
	DF	t Value	Pr > t		
	44	-1.82	0.0758		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.2947	1.0250	0.2351	-2.4000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.2947	-0.7887	0.1993	1.0250	0.7745	1.5157
	DF	t Value	Pr > t		
	18	-1.25	0.2261		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-0.3590	0.8635	0.1383	-2.4000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3590	-0.6389 -0.0791	0.8635	0.7057 1.1129		
DF	t Value	Pr > t			
38	-2.60	0.0133			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	0.0186	1.9048	0.2905	-5.6000	5.6000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.0186	-0.5676	0.6048	1.9048	1.5706	2.4210
	DF	t Value	Pr > t		
	42	0.06	0.9492		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
84	-0.2095	1.6568	0.1808	-5.6000	5.6000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2095	-0.5691 0.1500	1.6568	1.4386 1.9537		
DF	t Value	Pr > t			
83	-1.16	0.2498			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.4200	0.6986	0.1562	-2.4000	0.6000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4200	-0.7469 -0.0931	0.6986	0.5313 1.0203		
DF	t Value	Pr > t			
19	-2.69	0.0145			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (QSUF2) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.2.4 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
41	-0.4488	1.3310	0.2079	-4.8000	4.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.4488	-0.8689 -0.0287	1.3310	1.0928 1.7030		
DF	t Value	Pr > t			
40	-2.16	0.0369			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDQSUF2QS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	136	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1018 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2016 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	136
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	257
Number of Observations Used	257
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	921.45412240	
1	2	849.46483190	0.00012914
2	1	849.43887617	0.00000021
3	1	849.43883479	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	2.1840
UN(2,1)	subject	1.4869
UN(2,2)	subject	2.1267

Fit Statistics

-2 Res Log Likelihood	849.4
AIC (smaller is better)	855.4
AICC (smaller is better)	855.5
BIC (smaller is better)	864.2

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	72.02	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	129	5.21	0.0020
week	1	118	5.91	0.0166
treat*week	3	118	2.49	0.0637

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	1.1941	0.3868	130	3.09	0.0025	0.05	0.4290	1.9593
Week 2: VLN Mentholated vs UB Mentholated	-0.7331	0.3997	132	-1.83	0.0689	0.05	-1.5237	0.05755
Week 2: VLN Combined vs UB Combined	0.2305	0.2781	131	0.83	0.4086	0.05	-0.3196	0.7806
Week 2: VLN Combined	3.2577	0.1525	131	21.36	<.0001	0.05	2.9560	3.5595
Week 2: UB Combined	3.0272	0.2325	131	13.02	<.0001	0.05	2.5672	3.4872
Week 6: VLN Non-mentholated vs UB Non-mentholated	0.4892	0.3919	125	1.25	0.2143	0.05	-0.2864	1.2649
Week 6: VLN Mentholated vs UB Mentholated	-0.9066	0.3936	120	-2.30	0.0230	0.05	-1.6859	-0.1274
Week 6: VLN Combined vs UB Combined	-0.2087	0.2777	123	-0.75	0.4538	0.05	-0.7584	0.3410
Week 6: VLN Combined	2.7647	0.1543	125	17.92	<.0001	0.05	2.4594	3.0701
Week 6: UB Combined	2.9734	0.2309	122	12.88	<.0001	0.05	2.5163	3.4306

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	2.6952	0.3225	129	8.36	<.0001	0.05	2.0572	3.3333
treat*week	A	6	2.6669	0.3270	125	8.15	<.0001	0.05	2.0196	3.3141
treat*week	B	2	3.8894	0.2135	132	18.22	<.0001	0.05	3.4670	4.3117
treat*week	B	6	3.1561	0.2160	126	14.61	<.0001	0.05	2.7287	3.5835
treat*week	C	2	3.3591	0.3351	133	10.03	<.0001	0.05	2.6964	4.0219
treat*week	C	6	3.2800	0.3261	119	10.06	<.0001	0.05	2.6343	3.9257
treat*week	D	2	2.6261	0.2179	129	12.05	<.0001	0.05	2.1950	3.0572
treat*week	D	6	2.3734	0.2204	124	10.77	<.0001	0.05	1.9371	2.8096

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.02838	0.2633	118	0.11	0.9144	0.05	-0.4931	0.5499
treat*week	A	2	B	2	-1.1941	0.3868	130	-3.09	0.0025	0.05	-1.9593	-0.4290
treat*week	A	2	B	6	-0.4608	0.3881	170	-1.19	0.2367	0.05	-1.2270	0.3053
treat*week	A	2	C	2	-0.6639	0.4650	131	-1.43	0.1558	0.05	-1.5838	0.2560
treat*week	A	2	C	6	-0.5848	0.4586	171	-1.28	0.2040	0.05	-1.4900	0.3205
treat*week	A	2	D	2	0.06915	0.3892	129	0.18	0.8593	0.05	-0.7009	0.8392
treat*week	A	2	D	6	0.3219	0.3906	170	0.82	0.4111	0.05	-0.4492	1.0929
treat*week	A	6	B	2	-1.2225	0.3906	166	-3.13	0.0021	0.05	-1.9936	-0.4514
treat*week	A	6	B	6	-0.4892	0.3919	125	-1.25	0.2143	0.05	-1.2649	0.2864
treat*week	A	6	C	2	-0.6923	0.4682	180	-1.48	0.1410	0.05	-1.6161	0.2316
treat*week	A	6	C	6	-0.6131	0.4618	122	-1.33	0.1868	0.05	-1.5274	0.3011
treat*week	A	6	D	2	0.04077	0.3930	166	0.10	0.9175	0.05	-0.7351	0.8167
treat*week	A	6	D	6	0.2935	0.3944	124	0.74	0.4582	0.05	-0.4871	1.0740

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (QSUF2)
for Table 14.2.9.2.5 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.7333	0.1781	121	4.12	<.0001	0.05	0.3806	1.0859
treat*week	B	2	C	2	0.5302	0.3973	133	1.33	0.1843	0.05	-0.2557	1.3161
treat*week	B	2	C	6	0.6094	0.3898	159	1.56	0.1200	0.05	-0.1604	1.3791
treat*week	B	2	D	2	1.2633	0.3051	131	4.14	<.0001	0.05	0.6598	1.8668
treat*week	B	2	D	6	1.5160	0.3069	179	4.94	<.0001	0.05	0.9104	2.1215
treat*week	B	6	C	2	-0.2031	0.3986	173	-0.51	0.6111	0.05	-0.9899	0.5837
treat*week	B	6	C	6	-0.1239	0.3911	121	-0.32	0.7519	0.05	-0.8982	0.6504
treat*week	B	6	D	2	0.5300	0.3068	179	1.73	0.0858	0.05	-0.07538	1.1354
treat*week	B	6	D	6	0.7827	0.3086	125	2.54	0.0124	0.05	0.1720	1.3934
treat*week	C	2	C	6	0.07914	0.2644	116	0.30	0.7652	0.05	-0.4445	0.6028
treat*week	C	2	D	2	0.7331	0.3997	132	1.83	0.0689	0.05	-0.05755	1.5237
treat*week	C	2	D	6	0.9858	0.4010	172	2.46	0.0150	0.05	0.1942	1.7774
treat*week	C	6	D	2	0.6539	0.3922	159	1.67	0.0974	0.05	-0.1207	1.4285
treat*week	C	6	D	6	0.9066	0.3936	120	2.30	0.0230	0.05	0.1274	1.6859
treat*week	D	2	D	6	0.2527	0.1772	118	1.43	0.1566	0.05	-0.09827	0.6037

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	9.0000000	6.9354164	0	25.0000000
BASE	Baseline Value	21	9.2857143	7.6559967	0	26.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	8.5500000	7.9030990	0	34.0000000
BASE	Baseline Value	40	9.6250000	8.5024506	0	36.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	12.2000000	9.6701143	3.0000000	29.0000000
BASE	Baseline Value	10	11.0000000	8.3666003	2.0000000	23.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	13.2173913	10.7912276	0	33.0000000
BASE	Baseline Value	23	10.4782609	9.3218685	1.0000000	33.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	8.0526316	9.0214170	0	34.0000000
BASE	Baseline Value	19	10.0000000	9.5510325	0	36.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	13	14.0000000	11.9093801	0	33.0000000
BASE	Baseline Value	13	10.0769231	10.3155347	1.0000000	33.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	8.2631579	7.5265612	0	25.0000000
BASE	Baseline Value	19	8.8421053	7.9320948	0	26.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	7.8717949	7.3311860	0	27.0000000
BASE	Baseline Value	39	9.7435897	8.7980798	0	36.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	6.2000000	5.9029183	0	15.0000000
BASE	Baseline Value	10	11.1000000	8.3059550	2.0000000	23.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.4736842	6.4495342	0	20.0000000
BASE	Baseline Value	19	10.6842105	8.6477526	1.0000000	33.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	7.5000000	7.3161681	0	27.0000000
BASE	Baseline Value	20	10.6000000	9.6757973	0	36.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	6.7777778	7.3616876	0	20.0000000
BASE	Baseline Value	9	10.2222222	9.4970756	1.0000000	33.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.2857	6.2140	1.3560	-13.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2857	-3.1143 2.5429	6.2140	4.7541 8.9735		
DF	t Value	Pr > t			
20	-0.21	0.8353			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-1.0750	6.1285	0.9690	-19.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.0750	-3.0350	0.8850	6.1285	5.0202	7.8692
DF	t Value	Pr > t			
39	-1.11	0.2741			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	1.2000	7.4207	2.3466	-15.0000	13.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
1.2000	-4.1084	6.5084	7.4207	5.1042	13.5473
	DF	t Value	Pr > t		
	9	0.51	0.6214		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	2.7391	10.4369	2.1762	-15.0000	27.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
2.7391	-1.7741	7.2524	10.4369	8.0718	14.7719
	DF	t Value	Pr > t		
	22	1.26	0.2213		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-1.9474	6.0780	1.3944	-19.0000	10.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-1.9474	-4.8768	0.9821	6.0780	4.5926	8.9882
	DF	t Value	Pr > t		
	18	-1.40	0.1795		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
13	3.9231	12.4463	3.4520	-12.0000	27.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
3.9231	-3.5981	11.4443	12.4463	8.9251	20.5455
	DF	t Value	Pr > t		
	12	1.14	0.2779		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.5789	7.4186	1.7019	-20.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5789	-4.1546	2.9967	7.4186	5.6056	10.9708
DF	t Value	Pr > t			
18	-0.34	0.7377			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-1.8718	6.1008	0.9769	-20.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.8718	-3.8495 0.1059	6.1008	4.9859 7.8626		
	DF	t Value	Pr > t		
	38	-1.92	0.0629		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-4.9000	6.3500	2.0080	-18.0000	1.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-4.9000	-9.4425	-0.3575	6.3500	4.3677	11.5926
	DF	t Value	Pr > t		
	9	-2.44	0.0374		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-4.2105	7.3453	1.6851	-19.0000	14.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.2105	-7.7508 -0.6702	7.3453	5.5502 10.8624		
	DF	t Value	Pr > t		
	18	-2.50	0.0224		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-3.1000	4.3637	0.9758	-11.0000	8.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.1000	-5.1423	-1.0577	4.3637	3.3186	6.3735
	DF	t Value	Pr > t		
	19	-3.18	0.0050		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-3.4444	8.6474	2.8825	-19.0000	14.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.4444	-10.0914	3.2025	8.6474	5.8410	16.5665
DF	t Value	Pr > t			
8	-1.19	0.2663			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDMNWSTQS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	65	1007 1010 1011 1015 1016 1017 1018 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2016 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	65
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	121
Number of Observations Used	121
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	819.81134876	
1	2	773.87611664	0.00000991
2	1	773.87327505	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	84.5470
UN(2,1)	subject	48.3801
UN(2,2)	subject	50.3363

Fit Statistics

-2 Res Log Likelihood	773.9
AIC (smaller is better)	779.9
AICC (smaller is better)	780.1
BIC (smaller is better)	786.4

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	45.94	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	61.8	0.28	0.8366
week	1	58.2	19.73	<.0001
treat*week	3	57.7	3.71	0.0164

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNVST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	3.3806	3.4746	61.3	0.97	0.3344	0.05	-3.5666	10.3278
Week 2: VLN Mentholated vs UB Mentholated	5.4162	3.2916	60	1.65	0.1051	0.05	-1.1680	12.0004
Week 2: VLN Combined vs UB Combined	4.3984	2.3931	60.7	1.84	0.0710	0.05	-0.3874	9.1842
Week 2: VLN Combined	13.1903	1.9072	60.9	6.92	<.0001	0.05	9.3765	17.0041
Week 2: UB Combined	8.7919	1.4454	60.2	6.08	<.0001	0.05	5.9008	11.6830
Week 6: VLN Non-mentholated vs UB Non-mentholated	-2.0217	2.7028	59.8	-0.75	0.4574	0.05	-7.4285	3.3852
Week 6: VLN Mentholated vs UB Mentholated	-0.5315	2.6816	63.5	-0.20	0.8435	0.05	-5.8895	4.8265
Week 6: VLN Combined vs UB Combined	-1.2766	1.9037	61.6	-0.67	0.5050	0.05	-5.0825	2.5293
Week 6: VLN Combined	6.5448	1.5383	63.3	4.25	<.0001	0.05	3.4710	9.6185
Week 6: UB Combined	7.8213	1.1215	58.5	6.97	<.0001	0.05	5.5768	10.0659

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	9.0000	2.0065	59.4	4.49	<.0001	0.05	4.9856	13.0144
treat*week	A	6	8.1427	1.5858	59.9	5.13	<.0001	0.05	4.9706	11.3148
treat*week	B	2	12.3806	2.8367	62.2	4.36	<.0001	0.05	6.7106	18.0506
treat*week	B	6	6.1210	2.1887	59.7	2.80	0.0069	0.05	1.7425	10.4995
treat*week	C	2	8.5838	2.0811	60.9	4.12	0.0001	0.05	4.4222	12.7454
treat*week	C	6	7.5000	1.5864	57.2	4.73	<.0001	0.05	4.3234	10.6766
treat*week	D	2	14.0000	2.5502	59.4	5.49	<.0001	0.05	8.8977	19.1023
treat*week	D	6	6.9685	2.1620	66.7	3.22	0.0020	0.05	2.6527	11.2844

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.8573	1.3903	56.6	0.62	0.5400	0.05	-1.9272	3.6418
treat*week	A	2	B	2	-3.3806	3.4746	61.3	-0.97	0.3344	0.05	-10.3278	3.5666
treat*week	A	2	B	6	2.8790	2.9693	78.6	0.97	0.3352	0.05	-3.0316	8.7897
treat*week	A	2	C	2	0.4162	2.8909	60.2	0.14	0.8860	0.05	-5.3660	6.1985
treat*week	A	2	C	6	1.5000	2.5579	75.6	0.59	0.5593	0.05	-3.5949	6.5949
treat*week	A	2	D	2	-5.0000	3.2449	59.4	-1.54	0.1287	0.05	-11.4922	1.4922
treat*week	A	2	D	6	2.0315	2.9497	85.9	0.69	0.4929	0.05	-3.8324	7.8953
treat*week	A	6	B	2	-4.2379	3.2498	75.4	-1.30	0.1962	0.05	-10.7113	2.2355
treat*week	A	6	B	6	2.0217	2.7028	59.8	0.75	0.4574	0.05	-3.3852	7.4285
treat*week	A	6	C	2	-0.4411	2.6164	78.6	-0.17	0.8666	0.05	-5.6494	4.7672
treat*week	A	6	C	6	0.6427	2.2431	58.5	0.29	0.7755	0.05	-3.8465	5.1319
treat*week	A	6	D	2	-5.8573	3.0030	74	-1.95	0.0549	0.05	-11.8409	0.1263
treat*week	A	6	D	6	1.1742	2.6812	64.4	0.44	0.6629	0.05	-4.1816	6.5299

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.3 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	6.2596	2.0207	56.9	3.10	0.0030	0.05	2.2130	10.3062
treat*week	B	2	C	2	3.7968	3.5182	61.7	1.08	0.2847	0.05	-3.2366	10.8302
treat*week	B	2	C	6	4.8806	3.2501	74.4	1.50	0.1374	0.05	-1.5949	11.3561
treat*week	B	2	D	2	-1.6194	3.8145	60.9	-0.42	0.6727	0.05	-9.2471	6.0082
treat*week	B	2	D	6	5.4121	3.5667	84.6	1.52	0.1329	0.05	-1.6798	12.5040
treat*week	B	6	C	2	-2.4628	3.0202	79.9	-0.82	0.4172	0.05	-8.4733	3.5477
treat*week	B	6	C	6	-1.3790	2.7032	58.9	-0.51	0.6119	0.05	-6.7884	4.0304
treat*week	B	6	D	2	-7.8790	3.3607	78.2	-2.34	0.0216	0.05	-14.5694	-1.1886
treat*week	B	6	D	6	-0.8475	3.0765	63.3	-0.28	0.7838	0.05	-6.9950	5.2999
treat*week	C	2	C	6	1.0838	1.4177	54.2	0.76	0.4479	0.05	-1.7583	3.9258
treat*week	C	2	D	2	-5.4162	3.2916	60	-1.65	0.1051	0.05	-12.0004	1.1680
treat*week	C	2	D	6	1.6153	3.0009	87	0.54	0.5918	0.05	-4.3494	7.5799
treat*week	C	6	D	2	-6.5000	3.0034	72.8	-2.16	0.0337	0.05	-12.4860	-0.5140
treat*week	C	6	D	6	0.5315	2.6816	63.5	0.20	0.8435	0.05	-4.8265	5.8895
treat*week	D	2	D	6	7.0315	1.9326	61.9	3.64	0.0006	0.05	3.1681	10.8948

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	9.0000000	6.9354164	0	25.0000000
BASE	Baseline Value	21	9.2857143	7.6559967	0	26.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	8.5500000	7.9030990	0	34.0000000
BASE	Baseline Value	40	9.6250000	8.5024506	0	36.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	47	16.0212766	9.7434245	2.0000000	35.0000000
BASE	Baseline Value	47	12.5744681	8.2058958	0	30.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	93	12.2688172	9.8798651	0	35.0000000
BASE	Baseline Value	92	10.1304348	8.0372996	0	33.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	8.0526316	9.0214170	0	34.0000000
BASE	Baseline Value	19	10.0000000	9.5510325	0	36.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	46	8.4347826	8.5313856	0	33.0000000
BASE	Baseline Value	45	7.5777778	7.0822726	0	33.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	8.2631579	7.5265612	0	25.0000000
BASE	Baseline Value	19	8.8421053	7.9320948	0	26.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	7.8717949	7.3311860	0	27.0000000
BASE	Baseline Value	39	9.7435897	8.7980798	0	36.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	13.4418605	10.0149943	0	46.0000000
BASE	Baseline Value	43	12.8139535	9.3254792	0	38.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	85	9.4705882	9.2241766	0	46.0000000
BASE	Baseline Value	84	10.1547619	8.4361443	0	38.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	7.5000000	7.3161681	0	27.0000000
BASE	Baseline Value	20	10.6000000	9.6757973	0	36.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	5.4047619	6.1725574	0	20.0000000
BASE	Baseline Value	41	7.3658537	6.3865331	0	33.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.2857	6.2140	1.3560	-13.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.2857	-3.1143	2.5429	6.2140	4.7541	8.9735
DF	t Value	Pr > t			
20	-0.21	0.8353			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-1.0750	6.1285	0.9690	-19.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.0750	-3.0350	0.8850	6.1285	5.0202	7.8692
DF	t Value	Pr > t			
39	-1.11	0.2741			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	3.4468	9.3989	1.3710	-18.0000	28.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
3.4468	0.6872	6.2064	9.3989	7.8103	11.8049
	DF	t Value	Pr > t		
	46	2.51	0.0155		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
92	2.1848	8.7152	0.9086	-18.0000	28.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
2.1848	0.3799	3.9896	8.7152	7.6122	10.1949
DF	t Value	Pr > t			
91	2.40	0.0182			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-1.9474	6.0780	1.3944	-19.0000	10.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-1.9474	-4.8768	0.9821	6.0780	4.5926	8.9882
	DF	t Value	Pr > t		
	18	-1.40	0.1795		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
45	0.8667	7.8265	1.1667	-14.0000	27.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.8667	-1.4847 3.2180	7.8265	6.4792 9.8865		
	DF	t Value	Pr > t		
	44	0.74	0.4615		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.5789	7.4186	1.7019	-20.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5789	-4.1546	2.9967	7.4186	5.6056	10.9708
DF	t Value	Pr > t			
18	-0.34	0.7377			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-1.8718	6.1008	0.9769	-20.0000	11.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.8718	-3.8495	0.1059	6.1008	4.9859	7.8626
DF	t Value	Pr > t			
38	-1.92	0.0629			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
43	0.6279	9.9140	1.5119	-21.0000	26.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.6279	-2.4232 3.6790	9.9140	8.1745 12.6008				
DF	t Value	Pr > t					
42	0.42	0.6800					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
84	-0.6310	8.3533	0.9114	-21.0000	26.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.6310	-2.4437 1.1818	8.3533	7.2531 9.8501		
DF	t Value	Pr > t			
83	-0.69	0.4907			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-3.1000	4.3637	0.9758	-11.0000	8.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.1000	-5.1423 -1.0577	4.3637	3.3186 6.3735		
DF	t Value	Pr > t			
19	-3.18	0.0050			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (MNWST) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.3.4 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	-1.9512	6.1723	0.9640	-19.0000	14.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-1.9512	-3.8994 -0.00299	6.1723	5.0676 7.8975				
DF	t Value	Pr > t					
40	-2.02	0.0497					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDMNWSTQS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	136	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1018 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2016 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	136
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	257
Number of Observations Used	257
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1797.96937345	
1	2	1742.33292248	0.00055607
2	1	1741.94487268	0.00001187
3	1	1741.93713334	0.00000001

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	82.1286
UN(2,1)	subject	46.9497
UN(2,2)	subject	65.2863

Fit Statistics

-2 Res Log Likelihood	1741.9
AIC (smaller is better)	1747.9
AICC (smaller is better)	1748.0
BIC (smaller is better)	1756.7

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	56.03	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	125	9.36	<.0001
week	1	118	6.65	0.0111
treat*week	3	118	0.57	0.6350

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNMST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	7.4311	2.3727	122	3.13	0.0022	0.05	2.7341	12.1281
Week 2: VLN Mentholated vs UB Mentholated	-0.01527	2.4539	124	-0.01	0.9950	0.05	-4.8723	4.8418
Week 2: VLN Combined vs UB Combined	3.7079	1.7067	123	2.17	0.0317	0.05	0.3296	7.0863
Week 2: VLN Combined	12.4330	0.9360	123	13.28	<.0001	0.05	10.5801	14.2858
Week 2: UB Combined	8.7250	1.4271	123	6.11	<.0001	0.05	5.9001	11.5500
Week 6: VLN Non-mentholated vs UB Non-mentholated	5.4641	2.1792	127	2.51	0.0134	0.05	1.1520	9.7762
Week 6: VLN Mentholated vs UB Mentholated	-1.7514	2.1828	123	-0.80	0.4239	0.05	-6.0721	2.5693
Week 6: VLN Combined vs UB Combined	1.8563	1.5422	125	1.20	0.2310	0.05	-1.1958	4.9085
Week 6: VLN Combined	9.6777	0.8579	128	11.28	<.0001	0.05	7.9801	11.3754
Week 6: UB Combined	7.8214	1.2815	124	6.10	<.0001	0.05	5.2850	10.3578

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	9.0000	1.9776	121	4.55	<.0001	0.05	5.0849	12.9151
treat*week	A	6	8.1428	1.8179	127	4.48	<.0001	0.05	4.5454	11.7402
treat*week	B	2	16.4311	1.3111	124	12.53	<.0001	0.05	13.8361	19.0262
treat*week	B	6	13.6069	1.2017	129	11.32	<.0001	0.05	11.2293	15.9845
treat*week	C	2	8.4500	2.0582	125	4.11	<.0001	0.05	4.3765	12.5236
treat*week	C	6	7.5000	1.8067	121	4.15	<.0001	0.05	3.9232	11.0768
treat*week	D	2	8.4348	1.3362	121	6.31	<.0001	0.05	5.7895	11.0800
treat*week	D	6	5.7486	1.2248	126	4.69	<.0001	0.05	3.3248	8.1724

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.8572	1.6566	118	0.52	0.6058	0.05	-2.4233	4.1377
treat*week	A	2	B	2	-7.4311	2.3727	122	-3.13	0.0022	0.05	-12.1281	-2.7341
treat*week	A	2	B	6	-4.6069	2.3141	165	-1.99	0.0482	0.05	-9.1759	-0.03786
treat*week	A	2	C	2	0.5500	2.8543	123	0.19	0.8475	0.05	-5.0999	6.1998
treat*week	A	2	C	6	1.5000	2.6787	176	0.56	0.5762	0.05	-3.7864	6.7864
treat*week	A	2	D	2	0.5652	2.3867	121	0.24	0.8132	0.05	-4.1597	5.2902
treat*week	A	2	D	6	3.2514	2.3262	165	1.40	0.1641	0.05	-1.3416	7.8444
treat*week	A	6	B	2	-8.2883	2.2414	178	-3.70	0.0003	0.05	-12.7114	-3.8652
treat*week	A	6	B	6	-5.4641	2.1792	127	-2.51	0.0134	0.05	-9.7762	-1.1520
treat*week	A	6	C	2	-0.3072	2.7461	185	-0.11	0.9110	0.05	-5.7250	5.1105
treat*week	A	6	C	6	0.6428	2.5630	124	0.25	0.8024	0.05	-4.4301	5.7157
treat*week	A	6	D	2	-0.2920	2.2562	177	-0.13	0.8972	0.05	-4.7444	4.1604
treat*week	A	6	D	6	2.3942	2.1921	127	1.09	0.2768	0.05	-1.9435	6.7320

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
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Statistical Comparisons of Questionnaire Parameter (MNWST)
for Table 14.2.9.3.5 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	2.8242	1.1197	121	2.52	0.0130	0.05	0.6076	5.0409
treat*week	B	2	C	2	7.9811	2.4403	124	3.27	0.0014	0.05	3.1512	12.8110
treat*week	B	2	C	6	8.9311	2.2323	171	4.00	<.0001	0.05	4.5246	13.3376
treat*week	B	2	D	2	7.9963	1.8720	123	4.27	<.0001	0.05	4.2907	11.7020
treat*week	B	2	D	6	10.6825	1.7942	185	5.95	<.0001	0.05	7.1427	14.2224
treat*week	B	6	C	2	5.1568	2.3833	167	2.16	0.0319	0.05	0.4515	9.8622
treat*week	B	6	C	6	6.1069	2.1699	124	2.81	0.0057	0.05	1.8120	10.4018
treat*week	B	6	D	2	5.1721	1.7971	183	2.88	0.0045	0.05	1.6265	8.7177
treat*week	B	6	D	6	7.8583	1.7159	128	4.58	<.0001	0.05	4.4630	11.2536
treat*week	C	2	C	6	0.9500	1.6749	116	0.57	0.5717	0.05	-2.3675	4.2676
treat*week	C	2	D	2	0.01527	2.4539	124	0.01	0.9950	0.05	-4.8418	4.8723
treat*week	C	2	D	6	2.7015	2.3951	167	1.13	0.2610	0.05	-2.0271	7.4300
treat*week	C	6	D	2	-0.9348	2.2472	170	-0.42	0.6779	0.05	-5.3707	3.5011
treat*week	C	6	D	6	1.7514	2.1828	123	0.80	0.4239	0.05	-2.5693	6.0721
treat*week	D	2	D	6	2.6862	1.1155	118	2.41	0.0176	0.05	0.4772	4.8952

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsststatsmixedITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	7.0000000	2.6832816	1.0000000	10.0000000
BASE	Baseline Value	21	7.5714286	2.2488092	3.0000000	10.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	6.9000000	2.3837054	1.0000000	10.0000000
BASE	Baseline Value	40	7.0750000	2.2347776	2.0000000	10.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	5.3000000	2.8303906	1.0000000	10.0000000
BASE	Baseline Value	10	7.4000000	2.2705848	4.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	4.6086957	2.7755283	1.0000000	10.0000000
BASE	Baseline Value	23	6.8260870	2.1245785	3.0000000	10.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.7894737	2.0703984	3.0000000	10.0000000
BASE	Baseline Value	19	6.5263158	2.1439429	2.0000000	10.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	13	4.0769231	2.7221786	1.0000000	9.0000000
BASE	Baseline Value	13	6.3846154	1.9806759	3.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.8947368	2.5362864	2.0000000	10.0000000
BASE	Baseline Value	19	7.5789474	2.2190035	3.0000000	10.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	6.7435897	2.1240224	2.0000000	10.0000000
BASE	Baseline Value	39	7.0512821	2.1878699	2.0000000	10.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	4.0000000	3.5590261	1.0000000	10.0000000
BASE	Baseline Value	10	7.7000000	2.1108187	4.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	3.3157895	3.1632022	1.0000000	10.0000000
BASE	Baseline Value	19	7.2631579	2.0232566	3.0000000	10.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	6.6000000	1.6982964	3.0000000	10.0000000
BASE	Baseline Value	20	6.5500000	2.0894472	2.0000000	10.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	2.5555556	2.6509956	1.0000000	9.0000000
BASE	Baseline Value	9	6.7777778	1.9220938	3.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.5714	1.6605	0.3623	-4.0000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5714	-1.3273 0.1844	1.6605	1.2704 2.3978		
DF	t Value	Pr > t			
20	-1.58	0.1305			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-0.1750	1.8521	0.2928	-4.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1750	-0.7673 0.4173	1.8521	1.5171 2.3781		
DF	t Value	Pr > t			
39	-0.60	0.5536			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-2.1000	3.7845	1.1968	-7.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-2.1000	-4.8072	0.6072	3.7845	2.6031	6.9090
	DF	t Value	Pr > t		
	9	-1.75	0.1132		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	-2.2174	3.2045	0.6682	-7.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-2.2174	-3.6031 -0.8317	3.2045	2.4783 4.5355		
DF	t Value	Pr > t			
22	-3.32	0.0031			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0.2632	1.9956	0.4578	-3.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.2632	-0.6987	1.2250	1.9956	1.5079	2.9512
	DF	t Value	Pr > t		
	18	0.57	0.5725		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined

Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined

Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
13	-2.3077	2.8397	0.7876	-7.0000	2.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-2.3077	-4.0237	-0.5917	2.8397	2.0363	4.6877
	DF	t Value	Pr > t		
	12	-2.93	0.0126		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.6842	1.9164	0.4396	-6.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.6842	-1.6079	0.2395	1.9164	1.4480	2.8340
DF	t Value	Pr > t			
18	-1.56	0.1371			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
39	-0.3077	2.0281	0.3248	-6.0000	5.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.3077	-0.9651 0.3498	2.0281	1.6575 2.6138				
DF	t Value	Pr > t					
38	-0.95	0.3494					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-3.7000	5.0563	1.5990	-9.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.7000	-7.3171	-0.0829	5.0563	3.4779	9.2309
	DF	t Value	Pr > t		
	9	-2.31	0.0459		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-3.9474	3.8941	0.8934	-9.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.9474	-5.8242 -2.0705	3.8941	2.9424 5.7586		
DF	t Value	Pr > t			
18	-4.42	0.0003			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	0.0500	2.1145	0.4728	-3.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.0500	-0.9396 1.0396	2.1145	1.6080 3.0884		
DF	t Value	Pr > t			
19	0.11	0.9169			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.2 (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-4.2222	2.2791	0.7597	-7.0000	-1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-4.2222	-5.9741 -2.4703	2.2791	1.5395 4.3663		
DF	t Value	Pr > t			
8	-5.56	0.0005			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttest.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDPHRS001QS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	65	1007 1010 1011 1015 1016 1017 1018 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2016 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2251 2257 2259
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	65
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	121
Number of Observations Used	121
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	551.70585787	
1	2	529.71475566	0.00000818
2	1	529.71342666	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	6.4155
UN(2,1)	subject	3.6485
UN(2,2)	subject	6.2571

Fit Statistics

-2 Res Log Likelihood	529.7
AIC (smaller is better)	535.7
AICC (smaller is better)	535.9
BIC (smaller is better)	542.2

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	21.99	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	62.4	7.67	0.0002
week	1	57.1	3.62	0.0620
treat*week	3	56.7	0.69	0.5635

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-1.7642	0.9640	61.5	-1.83	0.0721	0.05	-3.6914	0.1631
Week 2: VLN Mentholated vs UB Mentholated	-2.6941	0.9088	60.5	-2.96	0.0043	0.05	-4.5117	-0.8765
Week 2: VLN Combined vs UB Combined	-2.2291	0.6624	61.1	-3.37	0.0013	0.05	-3.5537	-0.9046
Week 2: VLN Combined	4.6564	0.5285	61.3	8.81	<.0001	0.05	3.5997	5.7131
Week 2: UB Combined	6.8855	0.3994	60.6	17.24	<.0001	0.05	6.0869	7.6842
Week 6: VLN Non-mentholated vs UB Non-mentholated	-2.7645	0.9634	57.5	-2.87	0.0057	0.05	-4.6932	-0.8357
Week 6: VLN Mentholated vs UB Mentholated	-3.5584	0.9708	60.2	-3.67	0.0005	0.05	-5.5001	-1.6167
Week 6: VLN Combined vs UB Combined	-3.1614	0.6838	58.9	-4.62	<.0001	0.05	-4.5298	-1.7930
Week 6: VLN Combined	3.5710	0.5563	60	6.42	<.0001	0.05	2.4582	4.6838
Week 6: UB Combined	6.7324	0.3977	56.5	16.93	<.0001	0.05	5.9359	7.5289

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	7.0000	0.5527	60	12.66	<.0001	0.05	5.8944	8.1056
treat*week	A	6	6.8648	0.5654	57.5	12.14	<.0001	0.05	5.7328	7.9968
treat*week	B	2	5.2358	0.7898	62.3	6.63	<.0001	0.05	3.6573	6.8144
treat*week	B	6	4.1003	0.7800	57.4	5.26	<.0001	0.05	2.5387	5.6620
treat*week	C	2	6.7711	0.5766	61.3	11.74	<.0001	0.05	5.6182	7.9239
treat*week	C	6	6.6000	0.5593	55.3	11.80	<.0001	0.05	5.4792	7.7208
treat*week	D	2	4.0769	0.7025	60	5.80	<.0001	0.05	2.6717	5.4821
treat*week	D	6	3.0416	0.7934	62.1	3.83	0.0003	0.05	1.4556	4.6276

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.1352	0.5270	55.1	0.26	0.7985	0.05	-0.9208	1.1912
treat*week	A	2	B	2	1.7642	0.9640	61.5	1.83	0.0721	0.05	-0.1631	3.6914
treat*week	A	2	B	6	2.8997	0.9560	84.4	3.03	0.0032	0.05	0.9988	4.8006
treat*week	A	2	C	2	0.2289	0.7987	60.6	0.29	0.7754	0.05	-1.3684	1.8263
treat*week	A	2	C	6	0.4000	0.7864	87.6	0.51	0.6123	0.05	-1.1628	1.9628
treat*week	A	2	D	2	2.9231	0.8939	60	3.27	0.0018	0.05	1.1351	4.7111
treat*week	A	2	D	6	3.9584	0.9670	91.6	4.09	<.0001	0.05	2.0378	5.8790
treat*week	A	6	B	2	1.6290	0.9713	89.7	1.68	0.0970	0.05	-0.3008	3.5587
treat*week	A	6	B	6	2.7645	0.9634	57.5	2.87	0.0057	0.05	0.8357	4.6932
treat*week	A	6	C	2	0.09374	0.8076	92	0.12	0.9078	0.05	-1.5101	1.6976
treat*week	A	6	C	6	0.2648	0.7953	56.5	0.33	0.7404	0.05	-1.3281	1.8578
treat*week	A	6	D	2	2.7879	0.9018	88.9	3.09	0.0027	0.05	0.9960	4.5797
treat*week	A	6	D	6	3.8232	0.9743	60.8	3.92	0.0002	0.05	1.8748	5.7715

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.3 (PP Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	1.1355	0.7573	57.4	1.50	0.1393	0.05	-0.3808	2.6518
treat*week	B	2	C	2	-1.5352	0.9778	61.9	-1.57	0.1215	0.05	-3.4899	0.4195
treat*week	B	2	C	6	-1.3642	0.9678	87.8	-1.41	0.1622	0.05	-3.2875	0.5591
treat*week	B	2	D	2	1.1589	1.0570	61.3	1.10	0.2772	0.05	-0.9545	3.2723
treat*week	B	2	D	6	2.1942	1.1195	99.5	1.96	0.0528	0.05	-0.02697	4.4154
treat*week	B	6	C	2	-2.6707	0.9700	86.4	-2.75	0.0072	0.05	-4.5988	-0.7426
treat*week	B	6	C	6	-2.4997	0.9598	56.7	-2.60	0.0117	0.05	-4.4219	-0.5775
treat*week	B	6	D	2	0.02341	1.0497	89.5	0.02	0.9823	0.05	-2.0622	2.1090
treat*week	B	6	D	6	1.0587	1.1126	60	0.95	0.3451	0.05	-1.1669	3.2843
treat*week	C	2	C	6	0.1711	0.5296	54.3	0.32	0.7479	0.05	-0.8905	1.2327
treat*week	C	2	D	2	2.6941	0.9088	60.5	2.96	0.0043	0.05	0.8765	4.5117
treat*week	C	2	D	6	3.7294	0.9808	93.6	3.80	0.0003	0.05	1.7819	5.6770
treat*week	C	6	D	2	2.5231	0.8980	86.6	2.81	0.0061	0.05	0.7381	4.3080
treat*week	C	6	D	6	3.5584	0.9708	60.2	3.67	0.0005	0.05	1.6167	5.5001
treat*week	D	2	D	6	1.0353	0.7495	58.3	1.38	0.1724	0.05	-0.4648	2.5354

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixed.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	7.0000000	2.6832816	1.0000000	10.0000000
BASE	Baseline Value	21	7.5714286	2.2488092	3.0000000	10.0000000

----- week=2 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	40	6.9000000	2.3837054	1.0000000	10.0000000
BASE	Baseline Value	40	7.0750000	2.2347776	2.0000000	10.0000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	47	4.0425532	3.0213548	1.0000000	10.0000000
BASE	Baseline Value	47	7.5744681	2.0720152	3.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	93	3.7419355	2.8813615	1.0000000	10.0000000
BASE	Baseline Value	92	7.2826087	2.1551170	2.0000000	10.0000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.7894737	2.0703984	3.0000000	10.0000000
BASE	Baseline Value	19	6.5263158	2.1439429	2.0000000	10.0000000

----- week=2 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	46	3.4347826	2.7296900	1.0000000	10.0000000
BASE	Baseline Value	45	6.9777778	2.2206560	2.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	6.8947368	2.5362864	2.0000000	10.0000000
BASE	Baseline Value	19	7.5789474	2.2190035	3.0000000	10.0000000

----- week=6 treat=AC -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	6.7435897	2.1240224	2.0000000	10.0000000
BASE	Baseline Value	39	7.0512821	2.1878699	2.0000000	10.0000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	3.5581395	2.7886020	1.0000000	10.0000000
BASE	Baseline Value	43	7.8139535	1.9055785	3.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=BD -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	85	3.3882353	2.8288232	1.0000000	10.0000000
BASE	Baseline Value	84	7.4761905	2.0737963	2.0000000	10.0000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	6.6000000	1.6982964	3.0000000	10.0000000
BASE	Baseline Value	20	6.5500000	2.0894472	2.0000000	10.0000000

----- week=6 treat=D -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	3.2142857	2.8926797	1.0000000	10.0000000
BASE	Baseline Value	41	7.1219512	2.2044854	2.0000000	10.0000000

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	-0.5714	1.6605	0.3623	-4.0000	3.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5714	-1.3273 0.1844	1.6605	1.2704 2.3978		
DF	t Value	Pr > t			
20	-1.58	0.1305			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
40	-0.1750	1.8521	0.2928	-4.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.1750	-0.7673 0.4173	1.8521	1.5171 2.3781		
DF	t Value	Pr > t			
39	-0.60	0.5536			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
47	-3.5319	3.7408	0.5457	-9.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.5319	-4.6303	-2.4336	3.7408	3.1085	4.6984
	DF	t Value	Pr > t		
	46	-6.47	<.0001		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
92	-3.5761	3.4362	0.3582	-9.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-3.5761	-4.2877	-2.8645	3.4362	3.0013	4.0196
	DF	t Value	Pr > t		
	91	-9.98	<.0001		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0.2632	1.9956	0.4578	-3.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.2632	-0.6987	1.2250	1.9956	1.5079	2.9512
	DF	t Value	Pr > t		
	18	0.57	0.5725		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
45	-3.6222	3.1282	0.4663	-9.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-3.6222	-4.5620 -2.6824	3.1282	2.5897 3.9516		
DF	t Value	Pr > t			
44	-7.77	<.0001			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	-0.6842	1.9164	0.4396	-6.0000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.6842	-1.6079 0.2395	1.9164	1.4480 2.8340		
DF	t Value	Pr > t			
18	-1.56	0.1371			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=AC -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
39	-0.3077	2.0281	0.3248	-6.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.3077	-0.9651 0.3498	2.0281	1.6575 2.6138		
DF	t Value	Pr > t			
38	-0.95	0.3494			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-4.2558	3.6193	0.5519	-9.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-4.2558	-5.3697	-3.1419	3.6193	2.9843	4.6002
	DF	t Value	Pr > t		
	42	-7.71	<.0001		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=BD -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
84	-4.0714	3.4634	0.3779	-9.0000	5.0000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-4.0714	-4.8230	-3.3198	3.4634	3.0072	4.0839
	DF	t Value	Pr > t		
	83	-10.77	<.0001		

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	0.0500	2.1145	0.4728	-3.0000	5.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.0500	-0.9396 1.0396	2.1145	1.6080 3.0884		
DF	t Value	Pr > t			
19	0.11	0.9169			

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Summary of Questionnaire Parameter (PHRS001) at Weeks 2 and 6 Versus Week -1 by Study Product Groups
for Table 14.2.9.4.4 (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	-3.8780	3.3256	0.5194	-9.0000	4.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-3.8780	-4.9277 -2.8284	3.3256	2.7304 4.2551				
DF	t Value	Pr > t					
40	-7.47	<.0001					

Treat A: UB non-mentholated; Treat B: VLN non-mentholated; Treat AC: UB combined
Treat C: UB mentholated; Treat D: VLN mentholated; Treat BD: VLN Combined
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsttestITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDPHRS001QS
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	136	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1018 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2016 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2251 2257 2259 2269 2272
treat	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	136
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	257
Number of Observations Used	257
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	1228.57401445	
1	2	1153.46337690	0.00000058
2	1	1153.46317543	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated, C = UB Mentholated, D = VIN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	7.5699
UN(2,1)	subject	4.9567
UN(2,2)	subject	6.9368

Fit Statistics

-2 Res Log Likelihood	1153.5
AIC (smaller is better)	1159.5
AICC (smaller is better)	1159.6
BIC (smaller is better)	1168.2

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	75.11	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
treat	3	132	15.98	<.0001
week	1	121	1.30	0.2556
treat*week	3	122	0.48	0.6983

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	
treat*week	A	2	-1
treat*week	A	6	
treat*week	B	2	1
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	-1
treat*week	C	6	
treat*week	D	2	1
treat*week	D	6	

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	-0.5
treat*week	A	6	
treat*week	B	2	0.5
treat*week	B	6	
treat*week	C	2	-0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: VLN
Combined vs UB Combined

Effect	treat	week	Row1
treat*week	C	6	0.5
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 2: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		
treat	D		0.5
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	0.5
treat*week	D	6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 2: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	1
week		6	
treat*week	A	2	0.5
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
Intercept			
treat	A		-1
treat	B		1
treat	C		
treat	D		
week		2	
week		6	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Non-mentholated vs UB Non-mentholated

Effect	treat	week	Row1
treat*week	A	2	
treat*week	A	6	-1
treat*week	B	2	
treat*week	B	6	1
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
Intercept			
treat	A		
treat	B		
treat	C		-1
treat	D		1
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	
treat*week	C	6	-1

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN
Mentholated vs UB Mentholated

Effect	treat	week	Row1
treat*week	D	2	
treat*week	D	6	1

Coefficients for Week 6: VLN
Combined vs UB Combined

Effect	treat	week	Row1
Intercept			
treat	A		-0.5
treat	B		0.5
treat	C		-0.5
treat	D		0.5
week		2	
week		6	
treat*week	A	2	
treat*week	A	6	-0.5
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	-0.5
treat*week	D	2	
treat*week	D	6	0.5

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: VLN Combined

Effect	treat	week	Row1
Intercept			1
treat	A		
treat	B		0.5
treat	C		
treat	D		0.5
week		2	
week		6	1
treat*week	A	2	
treat*week	A	6	
treat*week	B	2	
treat*week	B	6	0.5
treat*week	C	2	
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	0.5

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
Intercept			1
treat	A		0.5
treat	B		
treat	C		0.5
treat	D		
week		2	
week		6	1
treat*week	A	2	

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Coefficients for Week 6: UB Combined

Effect	treat	week	Row1
treat*week	A	6	0.5
treat*week	B	2	
treat*week	B	6	
treat*week	C	2	0.5
treat*week	C	6	
treat*week	D	2	
treat*week	D	6	

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	-2.8972	0.7201	130	-4.02	<.0001	0.05	-4.3218	-1.4726
Week 2: VLN Mentholated vs UB Mentholated	-3.3321	0.7442	132	-4.48	<.0001	0.05	-4.8042	-1.8600
Week 2: VLN Combined vs UB Combined	-3.1147	0.5178	131	-6.02	<.0001	0.05	-4.1389	-2.0904
Week 2: VLN Combined	3.7688	0.2840	131	13.27	<.0001	0.05	3.2070	4.3306
Week 2: UB Combined	6.8835	0.4329	131	15.90	<.0001	0.05	6.0270	7.7399
Week 6: VLN Non-mentholated vs UB Non-mentholated	-3.3420	0.7081	130	-4.72	<.0001	0.05	-4.7429	-1.9411
Week 6: VLN Mentholated vs UB Mentholated	-3.2257	0.7109	125	-4.54	<.0001	0.05	-4.6327	-1.8188
Week 6: VLN Combined vs UB Combined	-3.2839	0.5017	128	-6.55	<.0001	0.05	-4.2766	-2.2911
Week 6: VLN Combined	3.4463	0.2788	130	12.36	<.0001	0.05	2.8948	3.9978
Week 6: UB Combined	6.7301	0.4171	127	16.13	<.0001	0.05	5.9047	7.5556

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Least Squares Means

Effect	treat	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	7.0000	0.6004	130	11.66	<.0001	0.05	5.8122	8.1878
treat*week	A	6	6.8603	0.5909	130	11.61	<.0001	0.05	5.6913	8.0293
treat*week	B	2	4.1028	0.3976	132	10.32	<.0001	0.05	3.3164	4.8892
treat*week	B	6	3.5183	0.3902	131	9.02	<.0001	0.05	2.7463	4.2903
treat*week	C	2	6.7669	0.6239	133	10.85	<.0001	0.05	5.5328	8.0010
treat*week	C	6	6.6000	0.5889	124	11.21	<.0001	0.05	5.4343	7.7657
treat*week	D	2	3.4348	0.4057	130	8.47	<.0001	0.05	2.6322	4.2374
treat*week	D	6	3.3743	0.3982	129	8.47	<.0001	0.05	2.5864	4.1621

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	A	2	A	6	0.1397	0.4874	122	0.29	0.7748	0.05	-0.8251	1.1046
treat*week	A	2	B	2	2.8972	0.7201	130	4.02	<.0001	0.05	1.4726	4.3218
treat*week	A	2	B	6	3.4817	0.7161	171	4.86	<.0001	0.05	2.0682	4.8952
treat*week	A	2	C	2	0.2331	0.8659	131	0.27	0.7882	0.05	-1.4798	1.9460
treat*week	A	2	C	6	0.4000	0.8410	175	0.48	0.6349	0.05	-1.2599	2.0599
treat*week	A	2	D	2	3.5652	0.7246	130	4.92	<.0001	0.05	2.1317	4.9988
treat*week	A	2	D	6	3.6257	0.7204	170	5.03	<.0001	0.05	2.2036	5.0479
treat*week	A	6	B	2	2.7575	0.7122	172	3.87	0.0002	0.05	1.3518	4.1632
treat*week	A	6	B	6	3.3420	0.7081	130	4.72	<.0001	0.05	1.9411	4.7429
treat*week	A	6	C	2	0.09337	0.8593	184	0.11	0.9136	0.05	-1.6020	1.7887
treat*week	A	6	C	6	0.2603	0.8343	127	0.31	0.7556	0.05	-1.3906	1.9112
treat*week	A	6	D	2	3.4255	0.7167	172	4.78	<.0001	0.05	2.0108	4.8402
treat*week	A	6	D	6	3.4860	0.7125	129	4.89	<.0001	0.05	2.0763	4.8957

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparisons of Questionnaire Parameter (PHRS001)
for Table 14.2.9.4.5 (ITT Population)

The Mixed Procedure

Differences of Least Squares Means

Effect	treat	week	_treat	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
treat*week	B	2	B	6	0.5845	0.3297	124	1.77	0.0787	0.05	-0.06798	1.2370
treat*week	B	2	C	2	-2.6641	0.7398	133	-3.60	0.0004	0.05	-4.1274	-1.2008
treat*week	B	2	C	6	-2.4972	0.7106	165	-3.51	0.0006	0.05	-3.9001	-1.0943
treat*week	B	2	D	2	0.6680	0.5680	131	1.18	0.2417	0.05	-0.4556	1.7917
treat*week	B	2	D	6	0.7286	0.5627	183	1.29	0.1970	0.05	-0.3817	1.8388
treat*week	B	6	C	2	-3.2486	0.7359	173	-4.41	<.0001	0.05	-4.7011	-1.7961
treat*week	B	6	C	6	-3.0817	0.7065	126	-4.36	<.0001	0.05	-4.4798	-1.6836
treat*week	B	6	D	2	0.08351	0.5629	182	0.15	0.8822	0.05	-1.0271	1.1941
treat*week	B	6	D	6	0.1440	0.5575	130	0.26	0.7966	0.05	-0.9590	1.2471
treat*week	C	2	C	6	0.1669	0.4903	120	0.34	0.7342	0.05	-0.8040	1.1378
treat*week	C	2	D	2	3.3321	0.7442	132	4.48	<.0001	0.05	1.8600	4.8042
treat*week	C	2	D	6	3.3927	0.7402	173	4.58	<.0001	0.05	1.9317	4.8536
treat*week	C	6	D	2	3.1652	0.7151	165	4.43	<.0001	0.05	1.7532	4.5772
treat*week	C	6	D	6	3.2257	0.7109	125	4.54	<.0001	0.05	1.8188	4.6327
treat*week	D	2	D	6	0.06053	0.3281	121	0.18	0.8539	0.05	-0.5889	0.7100

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated, C = UB Mentholated, D = VLN Mentholated
Program: /CA24914/sas_prg/pksas/pd_cpd_qs/adam_qsstatsmixedITT.sas 13JUN2019 4:37

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	5.4047619	1.2060167	2.7000000	7.5000000
BASE	Baseline Value	21	5.3380952	1.2567721	2.7000000	8.8000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	11	6.9909091	1.8769414	4.3000000	10.8000000
BASE	Baseline Value	11	6.2181818	1.4055733	4.6000000	8.4000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	5.5850000	2.0602184	3.7000000	13.1000000
BASE	Baseline Value	20	5.4100000	1.3222389	3.3000000	7.6000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=D -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	12	5.4500000	2.2960440	3.0000000	11.6000000
BASE	Baseline Value	12	5.6333333	1.3989173	2.4000000	7.8000000

----- week=2 treat=N -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	5.4926829	1.6588234	2.7000000	13.1000000
BASE	Baseline Value	41	5.3731707	1.2733861	2.7000000	8.8000000

----- week=2 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	23	6.1869565	2.2037786	3.0000000	11.6000000
BASE	Baseline Value	23	5.9130435	1.4020454	2.4000000	8.4000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.5578947	1.3230083	2.5000000	7.8000000
BASE	Baseline Value	19	5.3157895	1.2755231	2.7000000	8.8000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	10	5.8100000	1.7685210	3.8000000	9.1000000
BASE	Baseline Value	10	6.3800000	1.3693470	4.8000000	8.4000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	4.6100000	1.2586124	3.2000000	7.4000000
BASE	Baseline Value	20	5.4100000	1.3222389	3.3000000	7.6000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=D -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	9	5.0555556	2.4546441	2.4000000	9.9000000
BASE	Baseline Value	9	5.8000000	1.5668440	2.4000000	7.8000000

----- week=6 treat=N -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	5.0717949	1.3607174	2.5000000	7.8000000
BASE	Baseline Value	39	5.3641026	1.2833934	2.7000000	8.8000000

----- week=6 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.4526316	2.0955955	2.4000000	9.9000000
BASE	Baseline Value	19	6.1052632	1.4550577	2.4000000	8.4000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
21	0.0667	1.0283	0.2244	-1.7000	2.0000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.0667	-0.4014 0.5347	1.0283	0.7867 1.4849				
DF	t Value	Pr > t					
20	0.30	0.7694					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
11	0.7727	1.1646	0.3511	-1.8000	2.6000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.7727	-0.00963	1.5551	1.1646	0.8137	2.0437
DF	t Value	Pr > t			
10	2.20	0.0524			

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	0.1750	1.7806	0.3981	-1.9000	6.7000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.1750	-0.6583 1.0083	1.7806	1.3541 2.6006		
DF	t Value	Pr > t			
19	0.44	0.6652			

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

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Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
12	-0.1833	1.7023	0.4914	-2.8000	3.8000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.1833	-1.2649	0.8983	1.7023	1.2059	2.8903
	DF	t Value	Pr > t		
	11	-0.37	0.7162		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=N -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	0.1195	1.4274	0.2229	-1.9000	6.7000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.1195	-0.3310 0.5701	1.4274	1.1720 1.8264				
DF	t Value	Pr > t					
40	0.54	0.5949					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=2 treat=0 -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
23	0.2739	1.5178	0.3165	-2.8000	3.8000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.2739	-0.3824	0.9303	1.5178	1.1739	2.1483
	DF	t Value	Pr > t		
	22	0.87	0.3961		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
19	0.2421	0.9822	0.2253	-1.8000	2.2000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.2421	-0.2313	0.7155	0.9822	0.7422	1.4526
	DF	t Value	Pr > t		
	18	1.07	0.2968		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
10	-0.5700	0.9429	0.2982	-1.8000	0.7000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.5700	-1.2445	0.1045	0.9429	0.6485	1.7213
	DF	t Value	Pr > t		
	9	-1.91	0.0882		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.8000	1.0623	0.2375	-3.8000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.8000	-1.2972 -0.3028	1.0623	0.8078 1.5515		
DF	t Value	Pr > t			
19	-3.37	0.0032			

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
9	-0.7444	1.6749	0.5583	-2.8000	2.1000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
-0.7444	-2.0319	0.5430	1.6749	1.1313	3.2087
	DF	t Value	Pr > t		
	8	-1.33	0.2191		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=N -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
39	-0.2923	1.1400	0.1826	-3.8000	2.2000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.2923	-0.6619 0.0772	1.1400	0.9317 1.4693				
DF	t Value	Pr > t					
38	-1.60	0.1176					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (PP Population)

----- week=6 treat=0 -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
19	-0.6526	1.3036	0.2991	-2.8000	2.1000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.6526	-1.2809 -0.0243	1.3036	0.9850 1.9278				
DF	t Value	Pr > t					
18	-2.18	0.0426					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest.sas 12JUN2019 9:17

SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for PP Population

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDCOHB
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Class Level Information

Class	Levels	Values
subject	64	1007 1010 1011 1015 1016 1017 1021 1032 1036 1037 1045 1046 1051 1054 1059 1063 1064 1066 1069 1070 1072 1075 1077 1079 1089 1098 1106 1108 1109 1114 1115 2002 2007 2008 2010 2015 2018 2021 2023 2025 2028 2029 2050 2052 2059 2100 2110 2113 2119 2120 2122 2125 2140 2143 2158 2164 2170 2175 2212 2215 2247 2251 2257 2259
group	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated,
C = UB Mentholated, D = VLN Mentholated,

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsmixed.sas 12JUN2019 9:17

SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for PP Population

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	64
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	122
Number of Observations Used	122
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	406.70145122	
1	2	385.95708854	0.00003883
2	1	385.95362106	0.00000001
3	1	385.95361979	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,
C = UB Mentholated, D = VIN Mentholated,

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for PP Population

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	2.1137
UN(2,1)	subject	0.8231
UN(2,2)	subject	1.2520

Fit Statistics

-2 Res Log Likelihood	386.0
AIC (smaller is better)	392.0
AICC (smaller is better)	392.2
BIC (smaller is better)	398.4

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	20.75	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
group	3	61.9	1.16	0.3327
week	1	61.3	14.11	0.0004
group*week	3	60.9	3.97	0.0119

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,

C = UB Mentholated, D = VIN Mentholated,

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsmixed.sas 12JUN2019 9:17

SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for PP Population

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	0.7061	0.5411	60	1.30	0.1969	0.05	-0.3763	1.7885
Week 2: VLN Mentholated vs UB Mentholated	-0.3583	0.5309	60	-0.67	0.5023	0.05	-1.4202	0.7036
Week 2: VLN Combined vs UB Combined	0.1739	0.3790	60	0.46	0.6481	0.05	-0.5843	0.9320
Week 2: VLN Combined	0.2947	0.3034	60	0.97	0.3354	0.05	-0.3123	0.9017
Week 2: UB Combined	0.1208	0.2271	60	0.53	0.5967	0.05	-0.3335	0.5751
Week 6: VLN Non-mentholated vs UB Non-mentholated	-0.7974	0.4324	57.9	-1.84	0.0703	0.05	-1.6631	0.06822
Week 6: VLN Mentholated vs UB Mmentholated	0.04041	0.4401	59.3	0.09	0.9271	0.05	-0.8401	0.9209
Week 6: VLN Combined vs UB Combined	-0.3785	0.3085	58.6	-1.23	0.2247	0.05	-0.9959	0.2389
Week 6: VLN Combined	-0.6506	0.2518	59.3	-2.58	0.0123	0.05	-1.1545	-0.1468
Week 6: UB Combined	-0.2721	0.1782	57.1	-1.53	0.1323	0.05	-0.6290	0.08473

Least Squares Means

Effect	group	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
group*week	A	2	0.06667	0.3173	60	0.21	0.8343	0.05	-0.5679	0.7013
group*week	A	6	0.2558	0.2539	58	1.01	0.3179	0.05	-0.2524	0.7639
group*week	B	2	0.7727	0.4384	60	1.76	0.0830	0.05	-0.1041	1.6496
group*week	B	6	-0.5417	0.3501	57.9	-1.55	0.1273	0.05	-1.2425	0.1591
group*week	C	2	0.1750	0.3251	60	0.54	0.5924	0.05	-0.4753	0.8253
group*week	C	6	-0.8000	0.2502	56.2	-3.20	0.0023	0.05	-1.3012	-0.2988
group*week	D	2	-0.1833	0.4197	60	-0.44	0.6638	0.05	-1.0228	0.6562
group*week	D	6	-0.7596	0.3620	60.5	-2.10	0.0401	0.05	-1.4837	-0.03550

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated,

C = UB Mentholated, D = VLN Mentholated,

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsmixed.sas 12JUN2019 9:17

SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for PP Population

The Mixed Procedure

Differences of Least Squares Means

Effect	group	week	_group	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
group*week	A	2	A	6	-0.1891	0.2945	60.3	-0.64	0.5232	0.05	-0.7781	0.3999
group*week	A	2	B	2	-0.7061	0.5411	60	-1.30	0.1969	0.05	-1.7885	0.3763
group*week	A	2	B	6	0.6083	0.4725	94.7	1.29	0.2010	0.05	-0.3297	1.5463
group*week	A	2	C	2	-0.1083	0.4542	60	-0.24	0.8123	0.05	-1.0170	0.8003
group*week	A	2	C	6	0.8667	0.4040	91.2	2.14	0.0346	0.05	0.06411	1.6692
group*week	A	2	D	2	0.2500	0.5261	60	0.48	0.6364	0.05	-0.8024	1.3024
group*week	A	2	D	6	0.8263	0.4814	98.9	1.72	0.0892	0.05	-0.1289	1.7814
group*week	A	6	B	2	-0.5170	0.5066	83.8	-1.02	0.3104	0.05	-1.5243	0.4904
group*week	A	6	B	6	0.7974	0.4324	57.9	1.84	0.0703	0.05	-0.06822	1.6631
group*week	A	6	C	2	0.08077	0.4125	92.8	0.20	0.8452	0.05	-0.7383	0.8999
group*week	A	6	C	6	1.0558	0.3564	57.1	2.96	0.0044	0.05	0.3421	1.7695
group*week	A	6	D	2	0.4391	0.4905	85.3	0.90	0.3732	0.05	-0.5361	1.4143
group*week	A	6	D	6	1.0154	0.4422	59.7	2.30	0.0252	0.05	0.1308	1.8999
group*week	B	2	B	6	1.3144	0.4063	60.2	3.24	0.0020	0.05	0.5017	2.1271
group*week	B	2	C	2	0.5977	0.5457	60	1.10	0.2778	0.05	-0.4939	1.6894
group*week	B	2	C	6	1.5727	0.5047	82.4	3.12	0.0025	0.05	0.5687	2.5767
group*week	B	2	D	2	0.9561	0.6069	60	1.58	0.1204	0.05	-0.2579	2.1700
group*week	B	2	D	6	1.5323	0.5685	97.4	2.70	0.0083	0.05	0.4040	2.6606
group*week	B	6	C	2	-0.7167	0.4778	95	-1.50	0.1369	0.05	-1.6652	0.2318
group*week	B	6	C	6	0.2583	0.4303	57.4	0.60	0.5507	0.05	-0.6032	1.1199
group*week	B	6	D	2	-0.3583	0.5465	94.1	-0.66	0.5136	0.05	-1.4435	0.7268
group*week	B	6	D	6	0.2179	0.5036	59.3	0.43	0.6668	0.05	-0.7897	1.2256
group*week	C	2	C	6	0.9750	0.2932	57.7	3.33	0.0015	0.05	0.3880	1.5620
group*week	C	2	D	2	0.3583	0.5309	60	0.67	0.5023	0.05	-0.7036	1.4202
group*week	C	2	D	6	0.9346	0.4866	99.3	1.92	0.0576	0.05	-0.03087	1.9000
group*week	C	6	D	2	-0.6167	0.4886	83.7	-1.26	0.2104	0.05	-1.5884	0.3550
group*week	C	6	D	6	-0.04041	0.4401	59.3	-0.09	0.9271	0.05	-0.9209	0.8401

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,

C = UB Mentholated, D = VIN Mentholated,

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsmixed.sas 12JUN2019 9:17

SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for PP Population

The Mixed Procedure

Differences of Least Squares Means

Effect	group	week	_group	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
group*week	D	2	D	6	0.5763	0.4124	64.6	1.40	0.1671	0.05	-0.2474	1.3999

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,
C = UB Mentholated, D = VIN Mentholated,

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsmixed.sas 12JUN2019 9:17

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	21	5.4047619	1.2060167	2.7000000	7.5000000
BASE	Baseline Value	21	5.3380952	1.2567721	2.7000000	8.8000000

----- week=2 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	49	7.0959184	2.7942619	2.3000000	19.5000000
BASE	Baseline Value	49	6.1591837	1.7981377	1.3000000	12.2000000

----- week=2 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	5.5850000	2.0602184	3.7000000	13.1000000
BASE	Baseline Value	20	5.4100000	1.3222389	3.3000000	7.6000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=D -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	45	5.5488889	2.1669650	2.6000000	11.6000000
BASE	Baseline Value	45	5.7222222	1.5273103	2.4000000	8.7000000

----- week=2 treat=N -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	41	5.4926829	1.6588234	2.7000000	13.1000000
BASE	Baseline Value	41	5.3731707	1.2733861	2.7000000	8.8000000

----- week=2 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	94	6.3553191	2.6182411	2.3000000	19.5000000
BASE	Baseline Value	94	5.9500000	1.6794616	1.3000000	12.2000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=A -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	19	5.5578947	1.3230083	2.5000000	7.8000000
BASE	Baseline Value	19	5.3157895	1.2755231	2.7000000	8.8000000

----- week=6 treat=B -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	43	5.9744186	1.9298523	3.1000000	11.9000000
BASE	Baseline Value	43	6.4232558	1.6856308	3.7000000	12.2000000

----- week=6 treat=C -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	20	4.6100000	1.2586124	3.2000000	7.4000000
BASE	Baseline Value	20	5.4100000	1.3222389	3.3000000	7.6000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=D -----

The MEANS Procedure

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	42	4.6333333	1.8977094	2.4000000	9.9000000
BASE	Baseline Value	42	5.7642857	1.5666994	2.4000000	8.7000000

----- week=6 treat=N -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	39	5.0717949	1.3607174	2.5000000	7.8000000
BASE	Baseline Value	39	5.3641026	1.2833934	2.7000000	8.8000000

----- week=6 treat=O -----

Variable	Label	N	Mean	Std Dev	Minimum	Maximum
AVAL	Analysis Value	85	5.3117647	2.0186282	2.4000000	11.9000000
BASE	Baseline Value	85	6.0976471	1.6518371	2.4000000	12.2000000

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
21	0.0667	1.0283	0.2244	-1.7000	2.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.0667	-0.4014 0.5347	1.0283	0.7867 1.4849		
	DF	t Value	Pr > t		
	20	0.30	0.7694		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
49	0.9367	1.6534	0.2362	-2.5000	7.3000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.9367	0.4618	1.4116	1.6534	1.3788	2.0655
	DF	t Value	Pr > t		
	48	3.97	0.0002		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	0.1750	1.7806	0.3981	-1.9000	6.7000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
0.1750	-0.6583	1.0083	1.7806	1.3541	2.6006
	DF	t Value	Pr > t		
	19	0.44	0.6652		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
45	-0.1733	1.6299	0.2430	-3.1000	3.8000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.1733	-0.6630 0.3163	1.6299	1.3493 2.0589				
DF	t Value	Pr > t					
44	-0.71	0.4794					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=N -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
41	0.1195	1.4274	0.2229	-1.9000	6.7000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.1195	-0.3310 0.5701	1.4274	1.1720 1.8264				
DF	t Value	Pr > t					
40	0.54	0.5949					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=2 treat=0 -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
94	0.4053	1.7259	0.1780	-3.1000	7.3000
Mean	95% CL Mean		Std Dev	95% CL Std Dev	
0.4053	0.0518	0.7588	1.7259	1.5095	2.0152
	DF	t Value	Pr > t		
	93	2.28	0.0251		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=A -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
19	0.2421	0.9822	0.2253	-1.8000	2.2000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
0.2421	-0.2313 0.7155	0.9822	0.7422 1.4526				
DF	t Value	Pr > t					
18	1.07	0.2968					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=B -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
43	-0.4488	1.4715	0.2244	-3.2000	3.7000
	Mean	95% CL Mean	Std Dev	95% CL Std Dev	
	-0.4488	-0.9017 0.00403	1.4715	1.2133 1.8703	
		DF	t Value	Pr > t	
		42	-2.00	0.0520	

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

Program: /CA24914/sas_prg/pksas/pdblood/adam_bloodstatsttest_ITT.sas 12JUN2019 9:18

Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=C -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
20	-0.8000	1.0623	0.2375	-3.8000	1.0000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.8000	-1.2972 -0.3028	1.0623	0.8078 1.5515		
DF	t Value	Pr > t			
19	-3.37	0.0032			

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

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Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=D -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
42	-1.1310	1.6139	0.2490	-4.7000	2.1000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-1.1310	-1.6339 -0.6280	1.6139	1.3279 2.0580		
	DF	t Value	Pr > t		
	41	-4.54	<.0001		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

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Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=N -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum		
39	-0.2923	1.1400	0.1826	-3.8000	2.2000		
Mean	95% CL Mean	Std Dev	95% CL Std Dev				
-0.2923	-0.6619 0.0772	1.1400	0.9317 1.4693				
DF	t Value	Pr > t					
38	-1.60	0.1176					

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

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Statistical Comparison of Blood COHb at Weeks 2 and 6 Versus Week -1 by Study Product Group (ITT Population)

----- week=6 treat=0 -----

The TTEST Procedure

Difference: AVAL - BASE

N	Mean	Std Dev	Std Err	Minimum	Maximum
85	-0.7859	1.5722	0.1705	-4.7000	3.7000
Mean	95% CL Mean	Std Dev	95% CL Std Dev		
-0.7859	-1.1250 -0.4468	1.5722	1.3662 1.8519		
	DF	t Value	Pr > t		
	84	-4.61	<.0001		

Treat A: UB Non-Mentholated; Treat B: VLN Non-Mentholated; Treat N: UB Combined

Treat C: UB Mentholated; Treat D: VLN Mentholated; Treat O: VLN Combined

Base: Week -1 (UB Cigarettes);

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Model Information

Data Set	WORK.MIXEDCOHB
Dependent Variable	AVAL
Covariance Structure	Unstructured
Subject Effect	subject
Estimation Method	REML
Residual Variance Method	None
Fixed Effects SE Method	Kenward-Roger
Degrees of Freedom Method	Kenward-Roger

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,
C = UB Mentholated, D = VIN Mentholated,

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Class Level Information

Class	Levels	Values
subject	135	1001 1002 1003 1007 1008 1010 1011 1013 1014 1015 1016 1017 1019 1020 1021 1023 1029 1032 1034 1035 1036 1037 1038 1042 1045 1046 1050 1051 1052 1053 1054 1055 1056 1058 1059 1060 1063 1064 1066 1069 1070 1071 1072 1074 1075 1077 1078 1079 1082 1083 1084 1086 1088 1089 1092 1094 1095 1096 1097 1098 1099 1100 1101 1103 1105 1106 1107 1108 1109 1112 1114 1115 2002 2003 2007 2008 2009 2010 2011 2014 2015 2017 2018 2020 2021 2023 2025 2028 2029 2039 2050 2052 2057 2058 2059 2060 2064 2066 2067 2076 2086 2088 2092 2099 2100 2108 2110 2113 2119 2120 2122 2125 2126 2136 2140 2143 2158 2159 2164 2168 2170 2175 2211 2212 2213 2215 2220 2235 2244 2247 2251 2257 2259 2269 2272
group	4	A B C D
week	2	2 6

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated,

C = UB Mentholated, D = VLN Mentholated,

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Dimensions

Covariance Parameters	3
Columns in X	15
Columns in Z	0
Subjects	135
Max Obs Per Subject	2

Number of Observations

Number of Observations Read	259
Number of Observations Used	259
Number of Observations Not Used	0

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	943.59645816	
1	2	902.62433589	0.00000250
2	1	902.62378296	0.00000000

Convergence criteria met.

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,

C = UB Mentholated, D = VIN Mentholated,

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Estimate
UN(1,1)	subject	2.5151
UN(2,1)	subject	1.1478
UN(2,2)	subject	1.9465

Fit Statistics

-2 Res Log Likelihood	902.6
AIC (smaller is better)	908.6
AICC (smaller is better)	908.7
BIC (smaller is better)	917.3

Null Model Likelihood Ratio Test

DF	Chi-Square	Pr > ChiSq
2	40.97	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
group	3	132	4.04	0.0087
week	1	127	31.64	<.0001
group*week	3	127	5.49	0.0014

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,

C = UB Mentholated, D = VIN Mentholated,

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Estimates

Label	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
Week 2: VLN Non-mentholated vs UB Non-mentholated	0.8701	0.4136	131	2.10	0.0373	0.05	0.05179	1.6883
Week 2: VLN Mentholated vs UB Mentholated	-0.3483	0.4262	131	-0.82	0.4152	0.05	-1.1915	0.4948
Week 2: VLN Combined vs UB Combined	0.2609	0.2970	131	0.88	0.3813	0.05	-0.3266	0.8483
Week 2: VLN Combined	0.3817	0.1637	131	2.33	0.0213	0.05	0.05782	0.7056
Week 2: UB Combined	0.1208	0.2478	131	0.49	0.6266	0.05	-0.3693	0.6109
Week 6: VLN Non-mentholated vs UB Non-mentholated	-0.7454	0.3792	128	-1.97	0.0515	0.05	-1.4957	0.004926
Week 6: VLN Mentholated vs UB Mmentholated	-0.3351	0.3780	124	-0.89	0.3771	0.05	-1.0832	0.4131
Week 6: VLN Combined vs UB Combined	-0.5402	0.2677	126	-2.02	0.0457	0.05	-1.0700	-0.01045
Week 6: VLN Combined	-0.8112	0.1495	127	-5.43	<.0001	0.05	-1.1070	-0.5154
Week 6: UB Combined	-0.2709	0.2221	125	-1.22	0.2247	0.05	-0.7104	0.1686

Least Squares Means

Effect	group	week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
group*week	A	2	0.06667	0.3461	131	0.19	0.8475	0.05	-0.6180	0.7513
group*week	A	6	0.2581	0.3161	127	0.82	0.4157	0.05	-0.3674	0.8837
group*week	B	2	0.9367	0.2266	131	4.13	<.0001	0.05	0.4885	1.3849
group*week	B	6	-0.4873	0.2094	128	-2.33	0.0215	0.05	-0.9015	-0.07297
group*week	C	2	0.1750	0.3546	131	0.49	0.6225	0.05	-0.5265	0.8765
group*week	C	6	-0.8000	0.3120	123	-2.56	0.0115	0.05	-1.4175	-0.1825
group*week	D	2	-0.1733	0.2364	131	-0.73	0.4648	0.05	-0.6410	0.2944
group*week	D	6	-1.1351	0.2134	126	-5.32	<.0001	0.05	-1.5574	-0.7127

Note: A = UB Non-Mentholated, B = VLN Non-Mentholated,

C = UB Mentholated, D = VLN Mentholated,

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at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Differences of Least Squares Means

Effect	group	week	_group	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
group*week	A	2	A	6	-0.1915	0.3323	129	-0.58	0.5655	0.05	-0.8488	0.4659
group*week	A	2	B	2	-0.8701	0.4136	131	-2.10	0.0373	0.05	-1.6883	-0.05179
group*week	A	2	B	6	0.5539	0.4045	186	1.37	0.1725	0.05	-0.2441	1.3519
group*week	A	2	C	2	-0.1083	0.4955	131	-0.22	0.8273	0.05	-1.0886	0.8719
group*week	A	2	C	6	0.8667	0.4659	201	1.86	0.0643	0.05	-0.05208	1.7854
group*week	A	2	D	2	0.2400	0.4191	131	0.57	0.5679	0.05	-0.5891	1.0691
group*week	A	2	D	6	1.2017	0.4066	186	2.96	0.0035	0.05	0.3996	2.0039
group*week	A	6	B	2	-0.6786	0.3889	194	-1.74	0.0826	0.05	-1.4457	0.08847
group*week	A	6	B	6	0.7454	0.3792	128	1.97	0.0515	0.05	-0.00493	1.4957
group*week	A	6	C	2	0.08312	0.4751	206	0.17	0.8613	0.05	-0.8535	1.0197
group*week	A	6	C	6	1.0581	0.4441	125	2.38	0.0187	0.05	0.1791	1.9371
group*week	A	6	D	2	0.4315	0.3948	196	1.09	0.2757	0.05	-0.3470	1.2099
group*week	A	6	D	6	1.3932	0.3814	127	3.65	0.0004	0.05	0.6384	2.1480
group*week	B	2	B	6	1.4240	0.2198	130	6.48	<.0001	0.05	0.9891	1.8589
group*week	B	2	C	2	0.7617	0.4208	131	1.81	0.0726	0.05	-0.07074	1.5942
group*week	B	2	C	6	1.7367	0.3856	188	4.50	<.0001	0.05	0.9761	2.4973
group*week	B	2	D	2	1.1101	0.3274	131	3.39	0.0009	0.05	0.4623	1.7578
group*week	B	2	D	6	2.0718	0.3113	205	6.66	<.0001	0.05	1.4581	2.6855
group*week	B	6	C	2	-0.6623	0.4118	184	-1.61	0.1095	0.05	-1.4748	0.1502
group*week	B	6	C	6	0.3127	0.3757	125	0.83	0.4068	0.05	-0.4309	1.0564
group*week	B	6	D	2	-0.3139	0.3158	207	-0.99	0.3214	0.05	-0.9365	0.3087
group*week	B	6	D	6	0.6478	0.2990	127	2.17	0.0321	0.05	0.05619	1.2395
group*week	C	2	C	6	0.9750	0.3291	124	2.96	0.0037	0.05	0.3236	1.6264
group*week	C	2	D	2	0.3483	0.4262	131	0.82	0.4152	0.05	-0.4948	1.1915
group*week	C	2	D	6	1.3101	0.4139	184	3.17	0.0018	0.05	0.4935	2.1267
group*week	C	6	D	2	-0.6267	0.3914	190	-1.60	0.1110	0.05	-1.3988	0.1454
group*week	C	6	D	6	0.3351	0.3780	124	0.89	0.3771	0.05	-0.4131	1.0832

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,

C = UB Mentholated, D = VIN Mentholated,

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SAS output for : Statistical Comparison of COHB Absolute Change From Baseline Among Study Product Groups
at Weeks 2 and 6 for ITT Population

The Mixed Procedure

Differences of Least Squares Means

Effect	group	week	_group	_week	Estimate	Standard Error	DF	t Value	Pr > t	Alpha	Lower	Upper
group*week	D	2	D	6	0.9617	0.2246	127	4.28	<.0001	0.05	0.5174	1.4061

Note: A = UB Non-Mentholated, B = VIN Non-Mentholated,
C = UB Mentholated, D = VIN Mentholated,

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