



## PMI RESEARCH & DEVELOPMENT

### **Study ZRHM-REXA-08-US Clinical Study Report Appendix 15.1 Figures**

<b>Study Title:</b>	A randomized, controlled, open-label, 3-arm parallel group, multi-center study to demonstrate reductions in exposure to selected smoke constituents in apparently healthy smokers switching to the Tobacco Heating System 2.2 Menthol (THS 2.2 Menthol) or observing smoking abstinence, compared to continuing to use menthol conventional cigarettes, for 5 days in confinement and prolonged by 86 days in an ambulatory setting
<b>Study Number:</b>	ZRHM-REXA-08-US
<b>Product Name:</b>	Tobacco Heating System 2.2 Menthol (THS 2.2 Menthol)
<b>Study Initiated (first subject screened):</b>	17 December 2013
<b>Study Completed (last subject last visit):</b>	12 October 2014
<b>Principal Investigator and Affiliation:</b>	Dr William Lewis, Covance Dallas Site 1341 W. Mockingbird Ln., Suite 400E Dallas, TX 75247 Dr Frank Farmer, Covance Daytona Beach Site 1900 Mason Ave., Suite 140 Daytona Beach, FL 32117
<b>Sponsor:</b>	Philip Morris Products S.A. PMI Research & Development Quai Jeanrenaud 5 2000 Neuchâtel, Switzerland
<b>Sponsor Signatories:</b>	Christelle Haziza, PhD, Manager P1 Clinical Program, Clinical Scientist Guillaume de La Bourdonnaye, MEng, MSc, Biostatistician Andrea Donelli, Clinical Scientist Ruben Rosoky, MD PhD MFPM, Medical Safety Officer
<b>Version:</b>	1.0
<b>Date:</b>	25 May 2016

This study was conducted in accordance with Good Clinical Practice.

#### **Confidentiality Statement**

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This document is confidential. Disclosure of any of its contents to third parties is not permitted except by the prior written consent of Philip Morris Products S.A.

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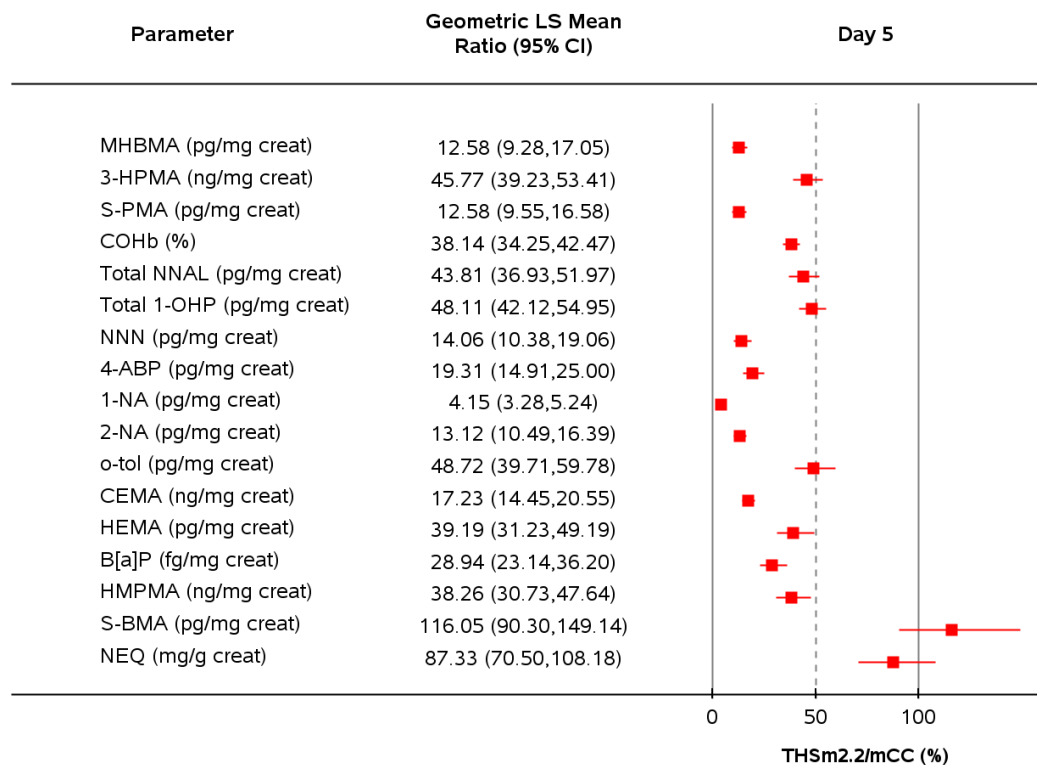


## 15.1 FIGURES



### **15.1.1 Primary Endpoints**



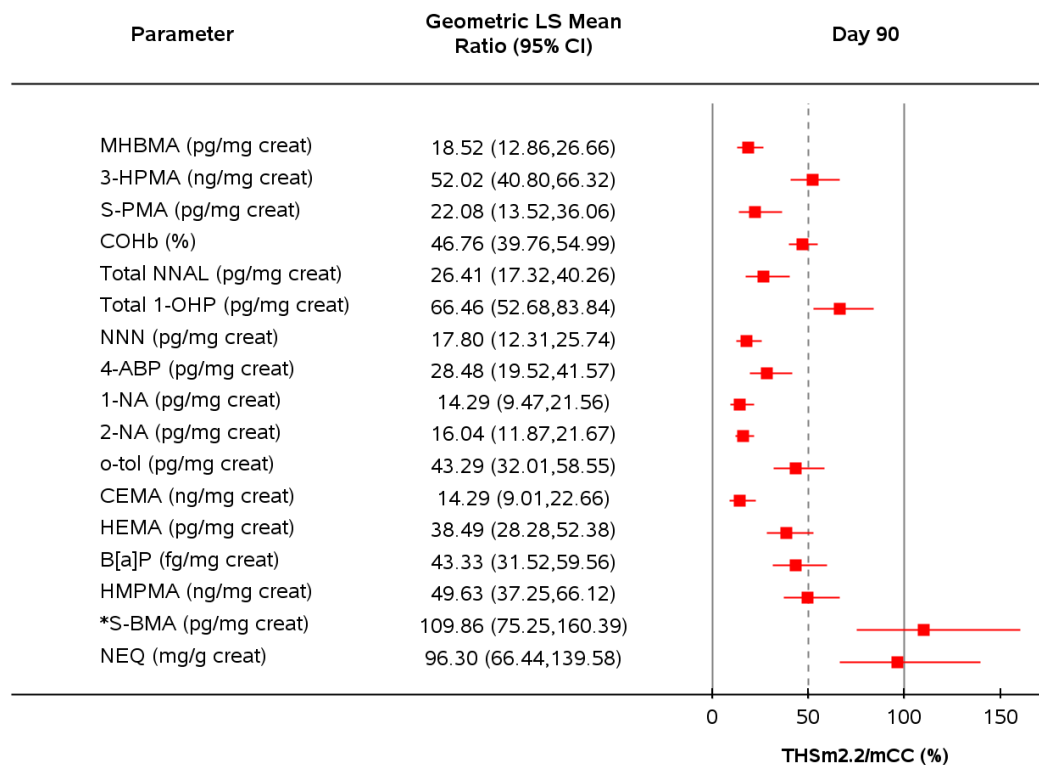
**Figure 15.1.1.1 Forest Plot of Statistical Analysis of Biomarkers of Exposure on Day 5 and Day 90 - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

\* The estimate or CI is outside of the reporting scale.

Appendix 15.2.3.2 and 15.2.3.4

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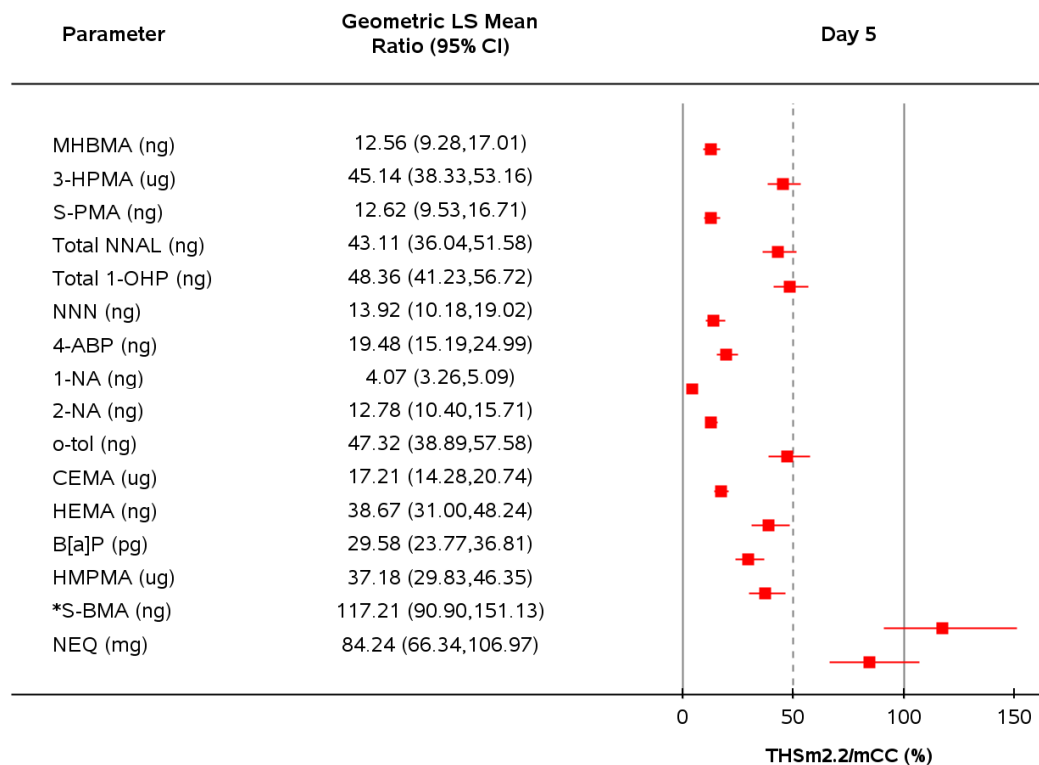
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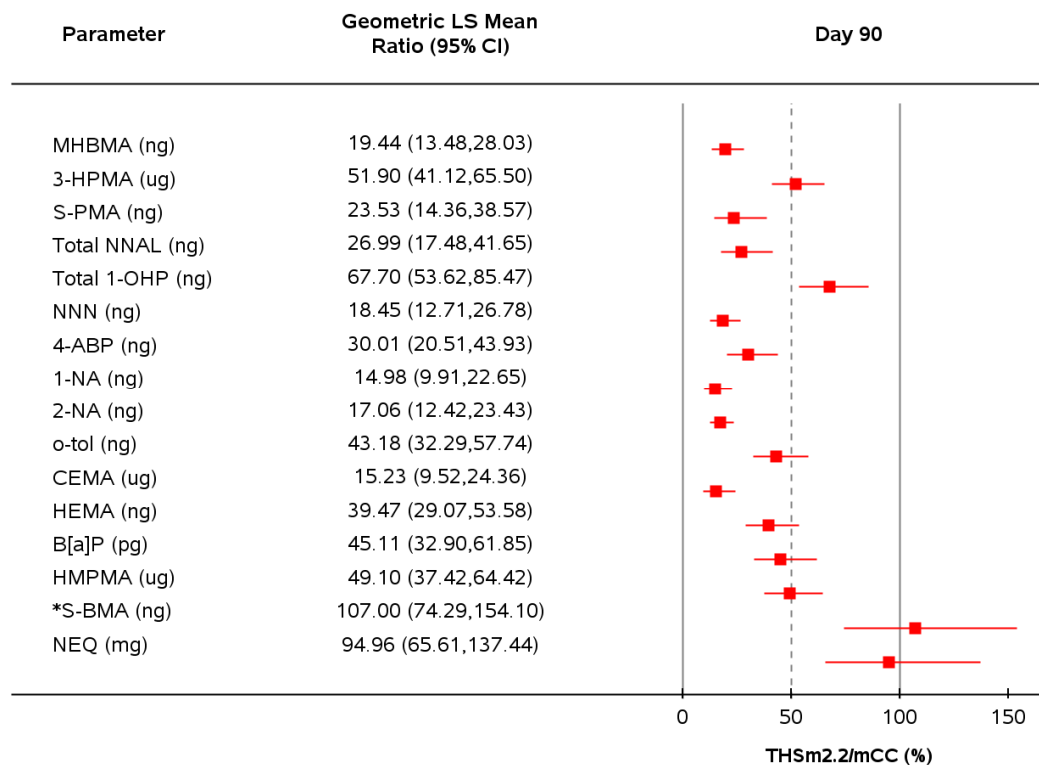
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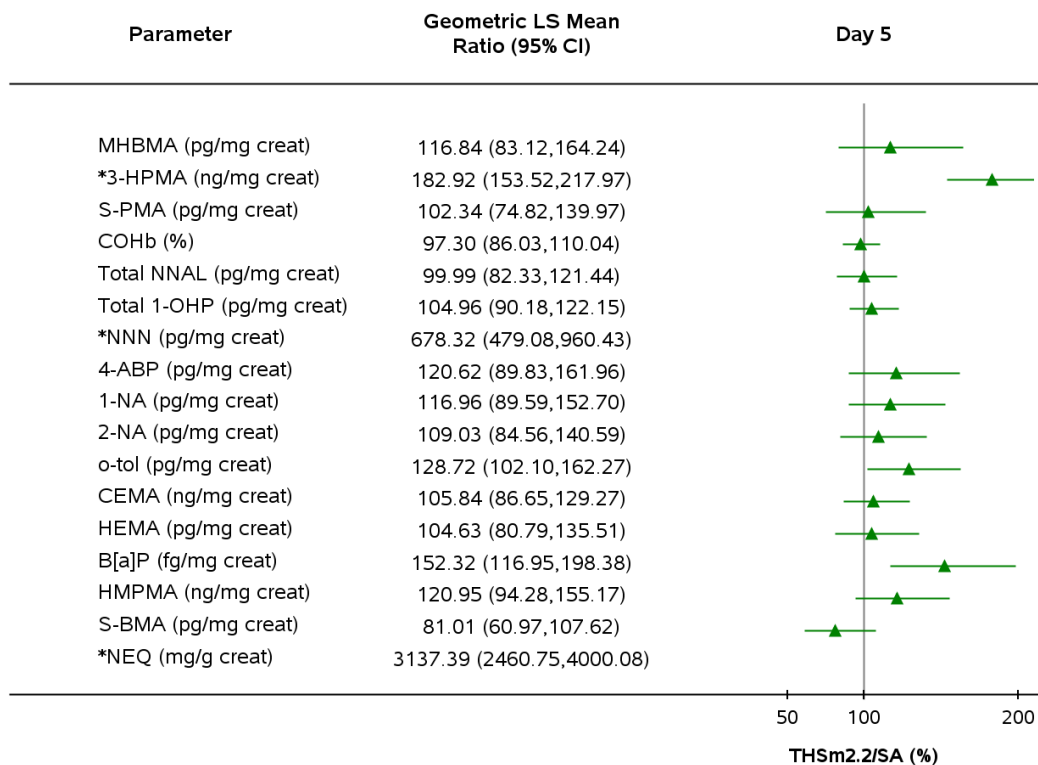
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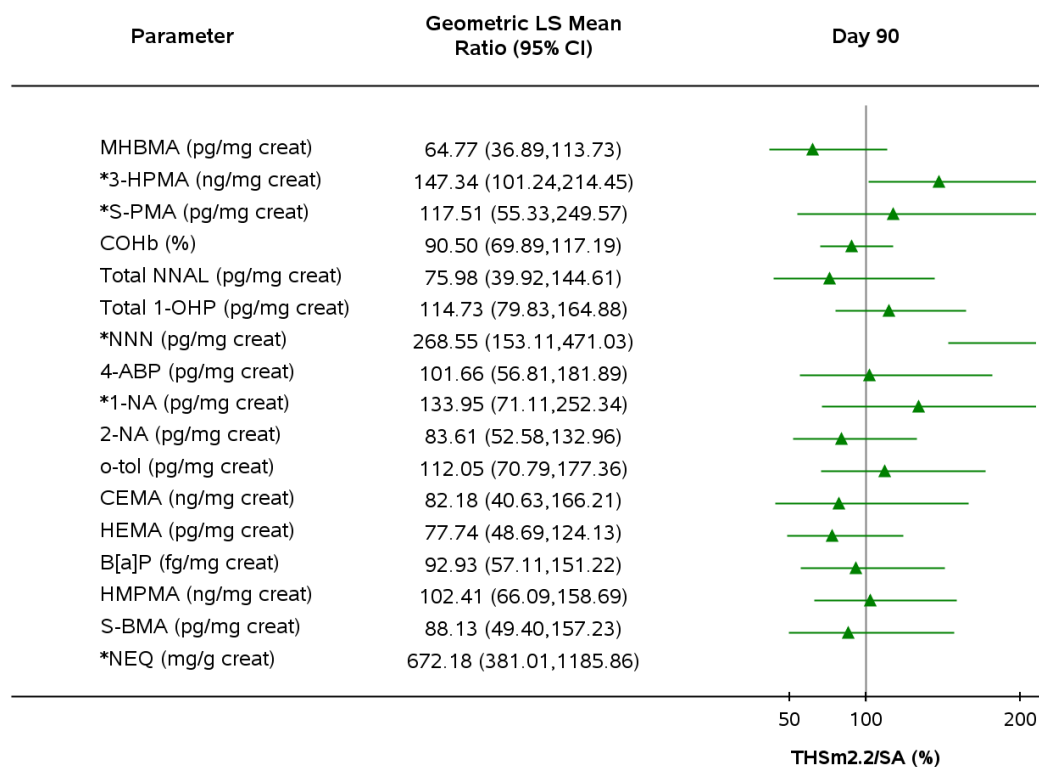
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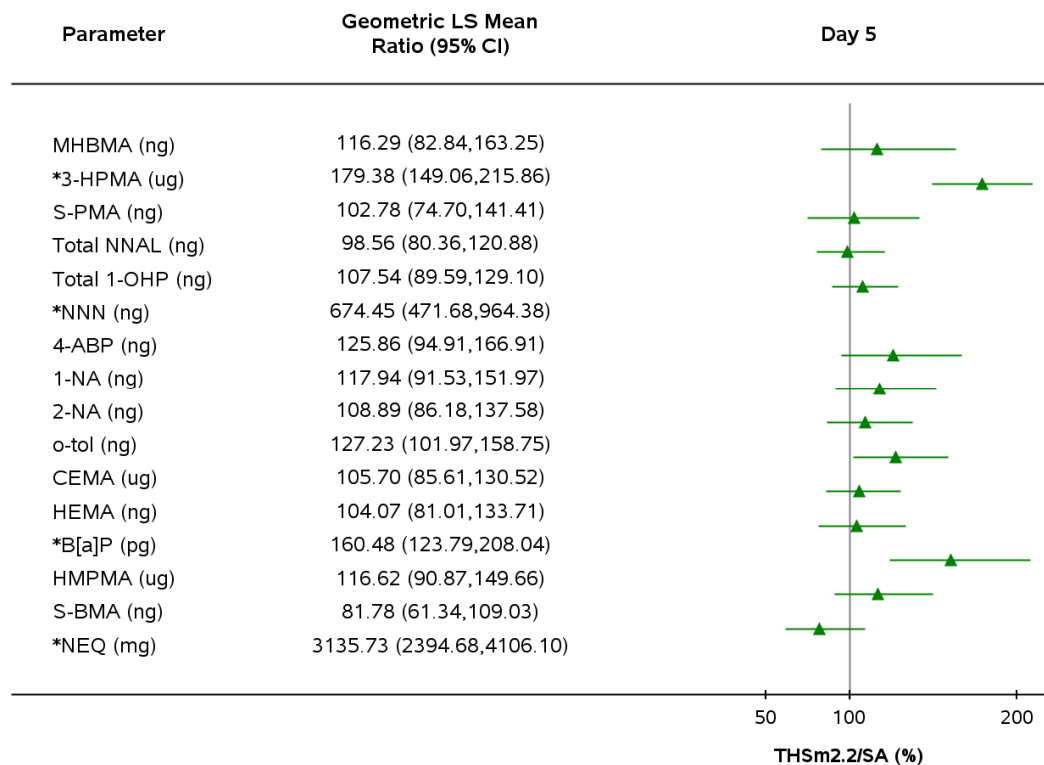
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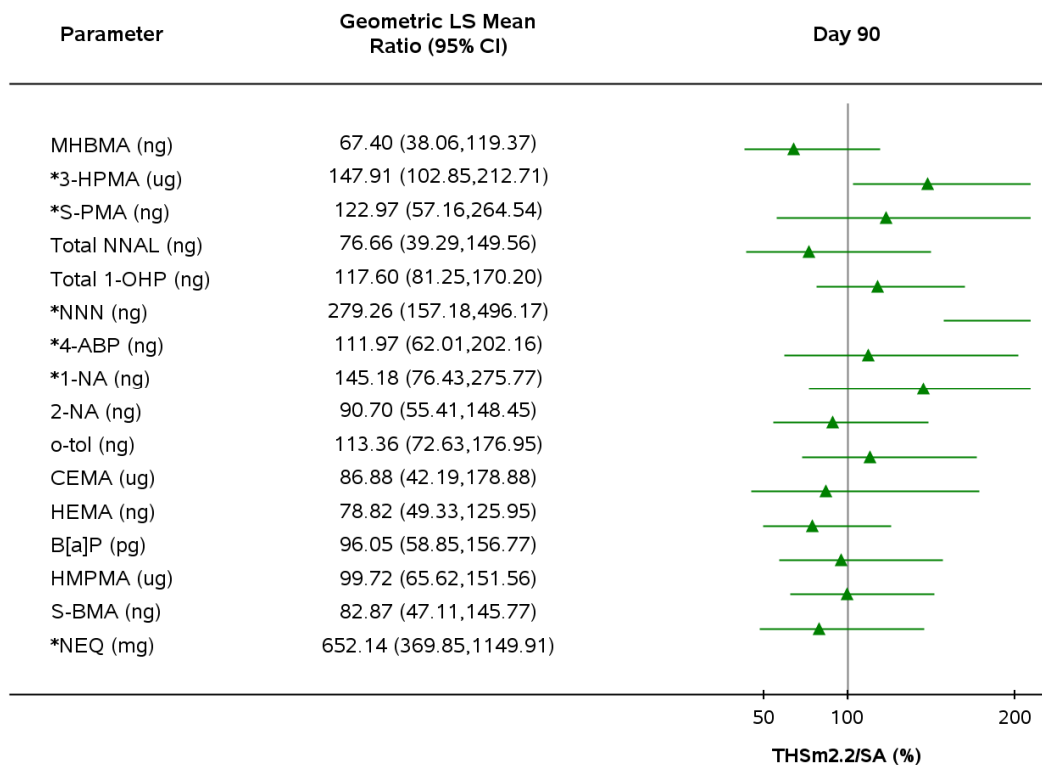
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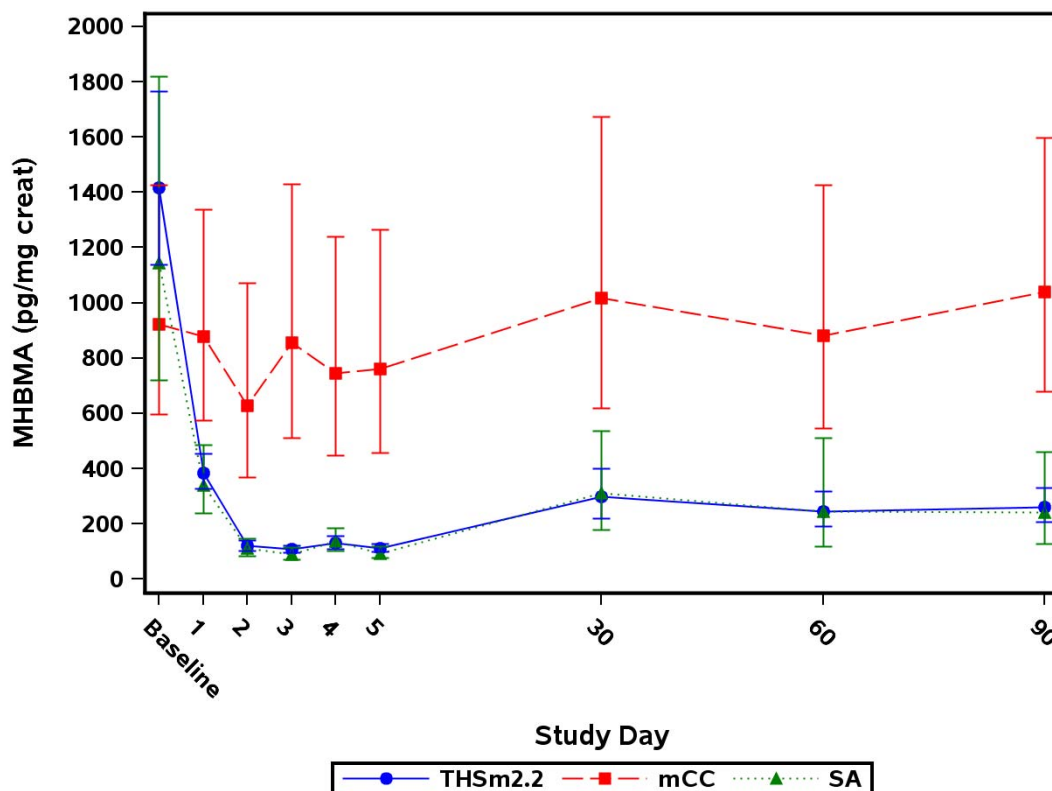
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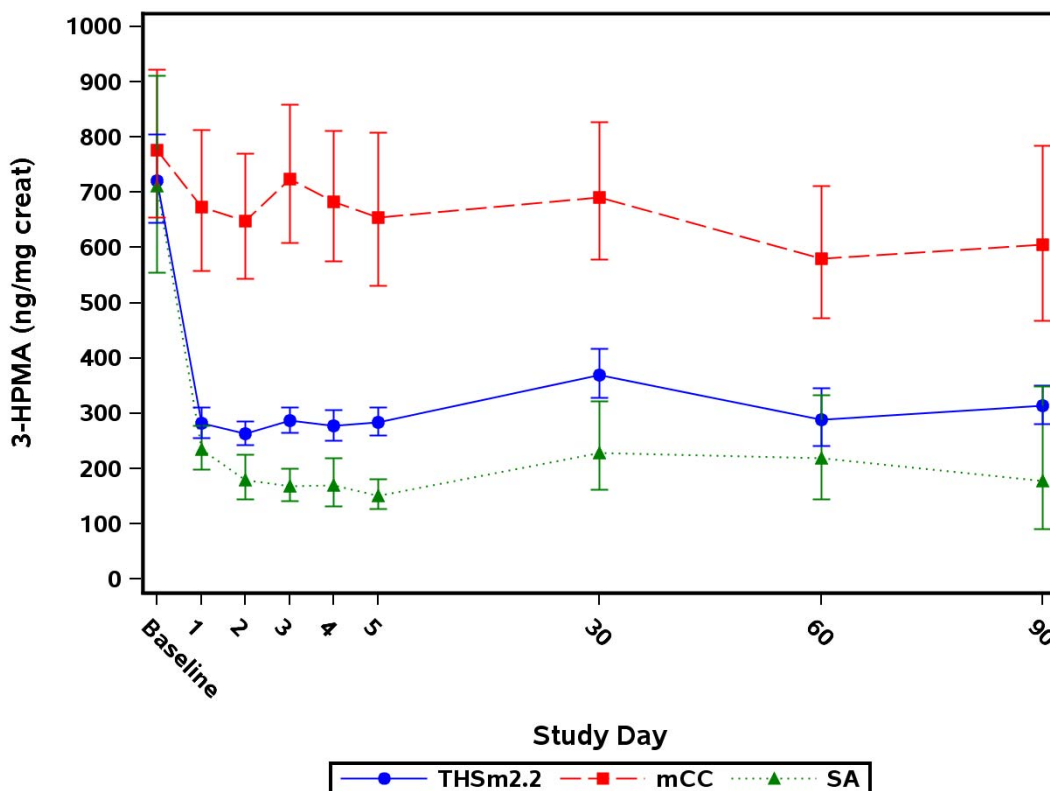
**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

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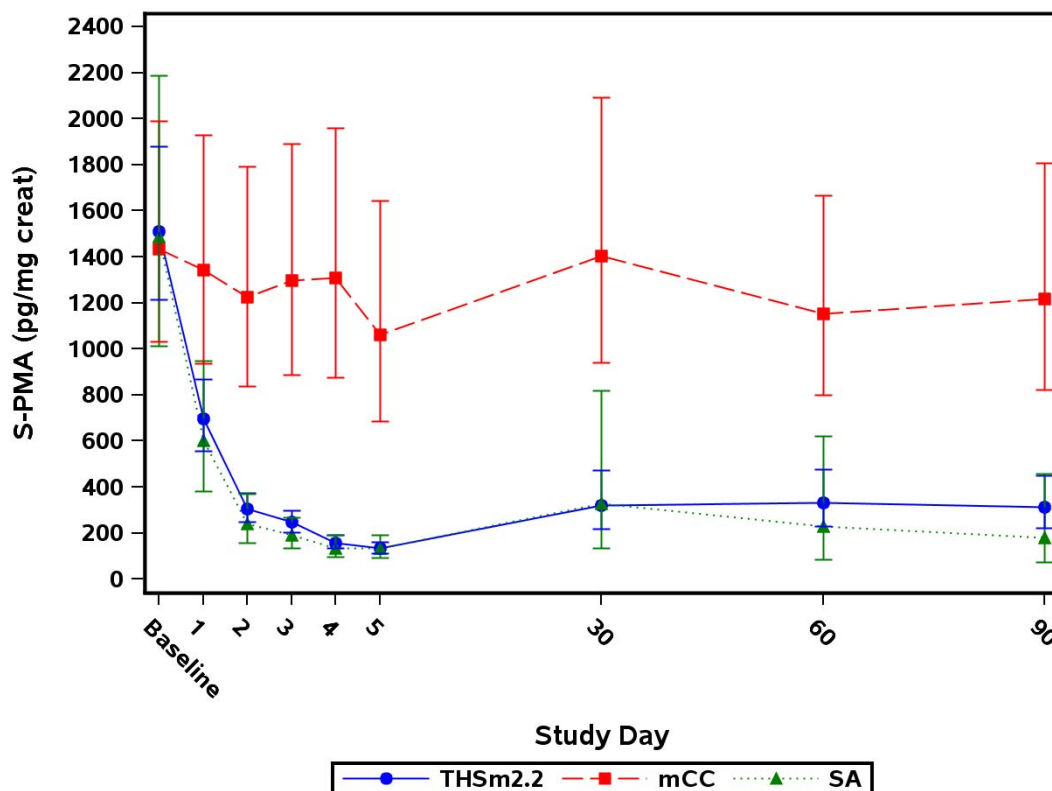
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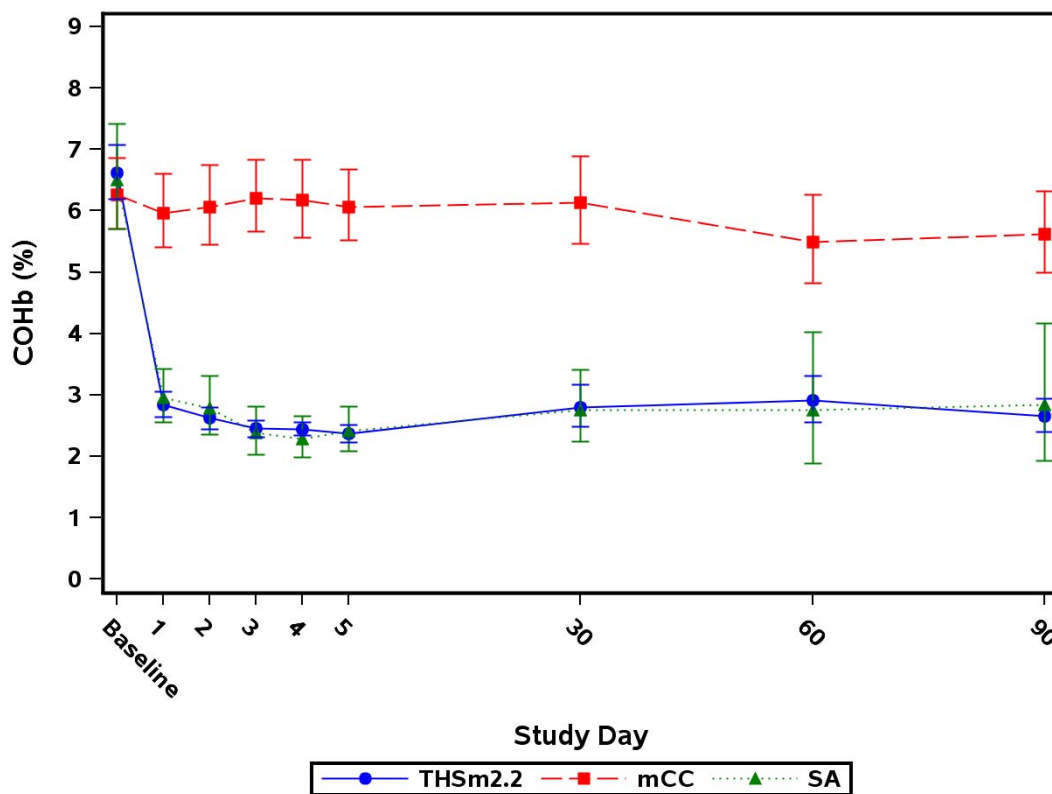
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**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

Note: COHb on Day 5 represents the evening sample collected.

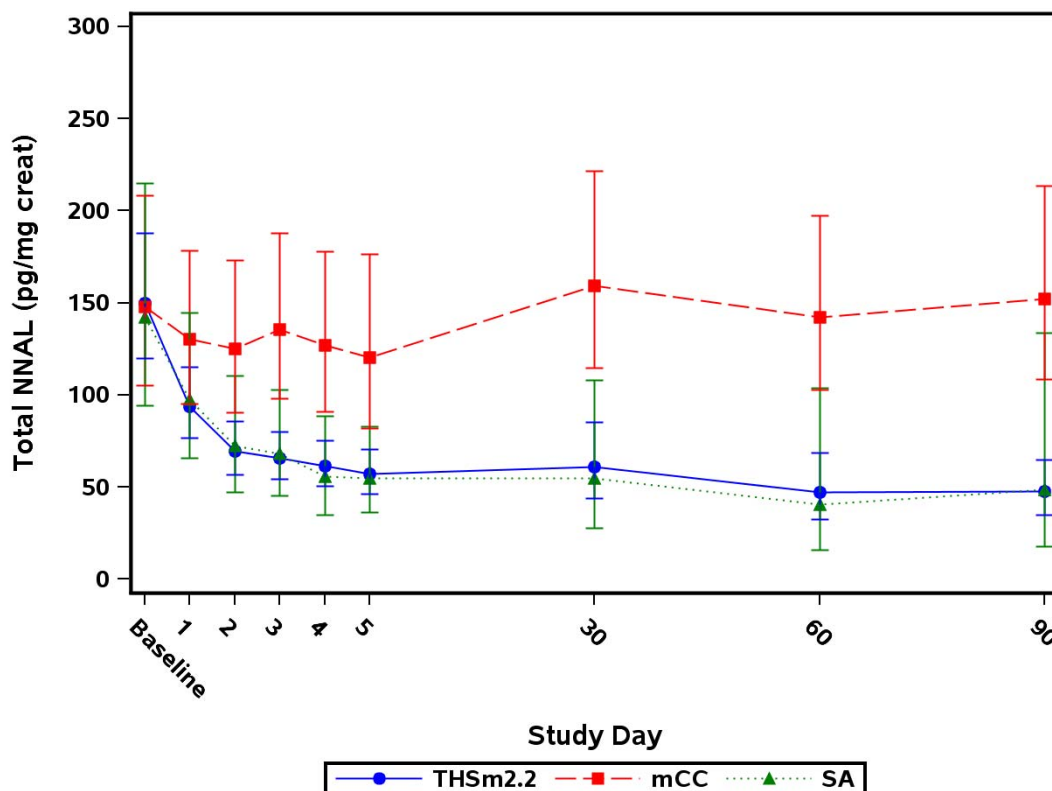
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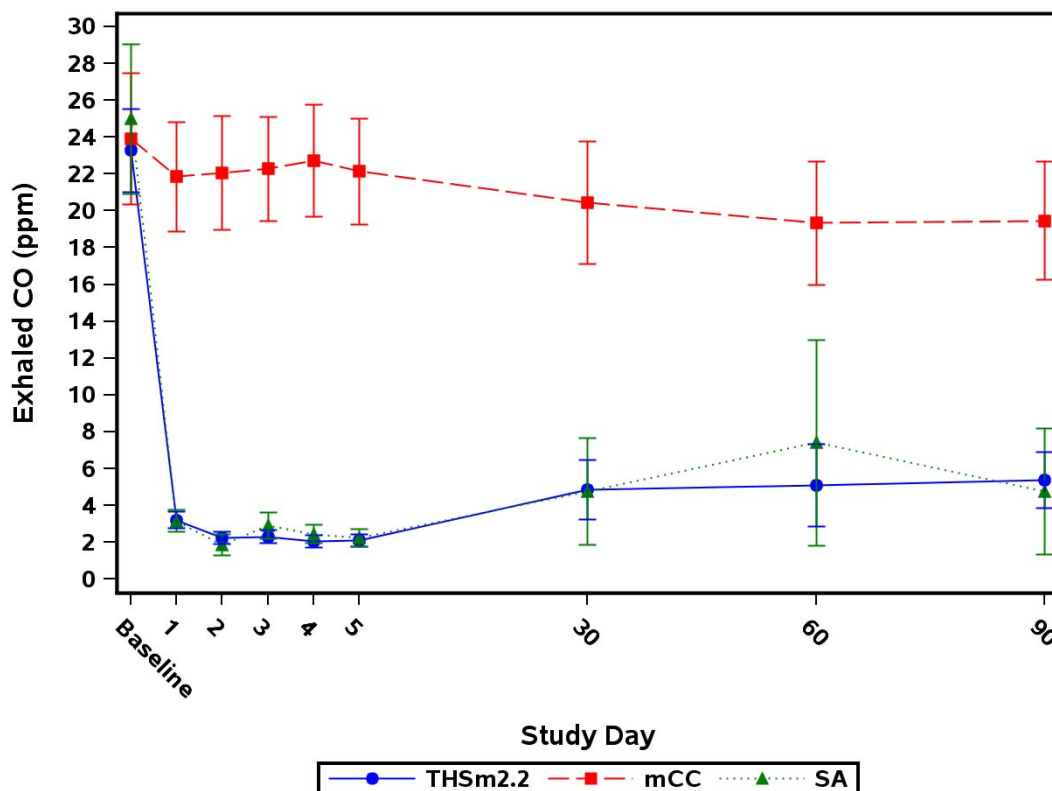
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**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

Note: CO on Baseline and Days 1- 5 represent the evening sample collected.

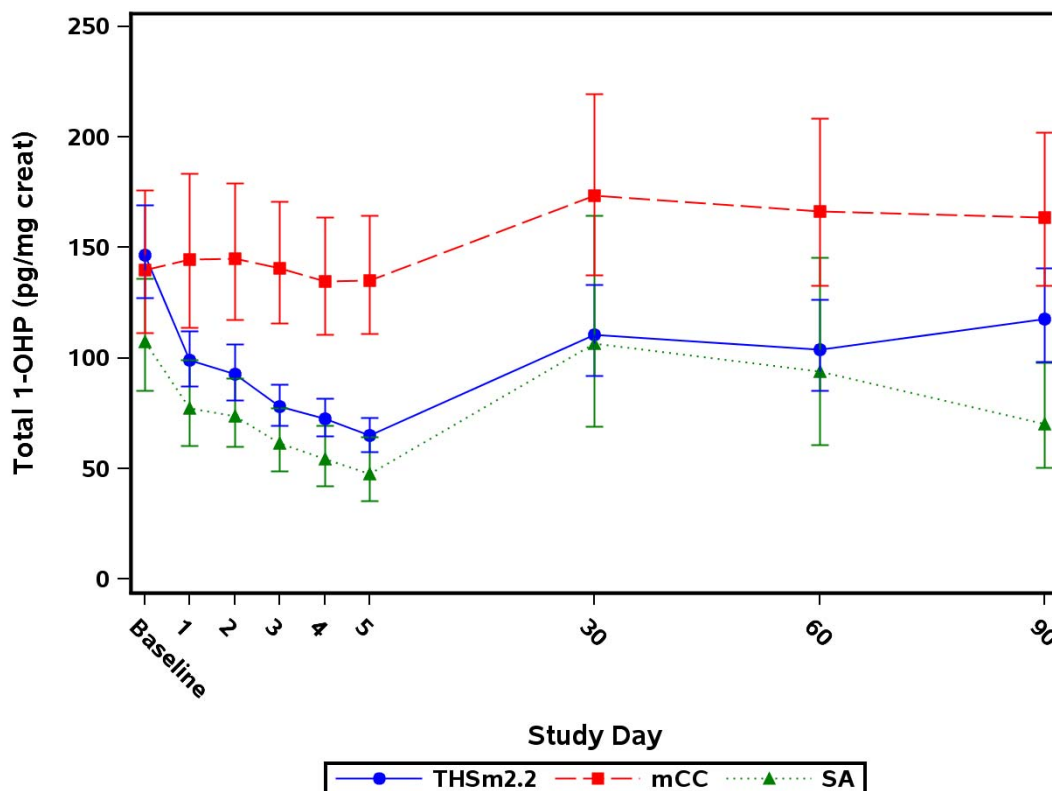
Note: Arithmetic mean and 95% CI are plotted for Exhaled CO (ppm).

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

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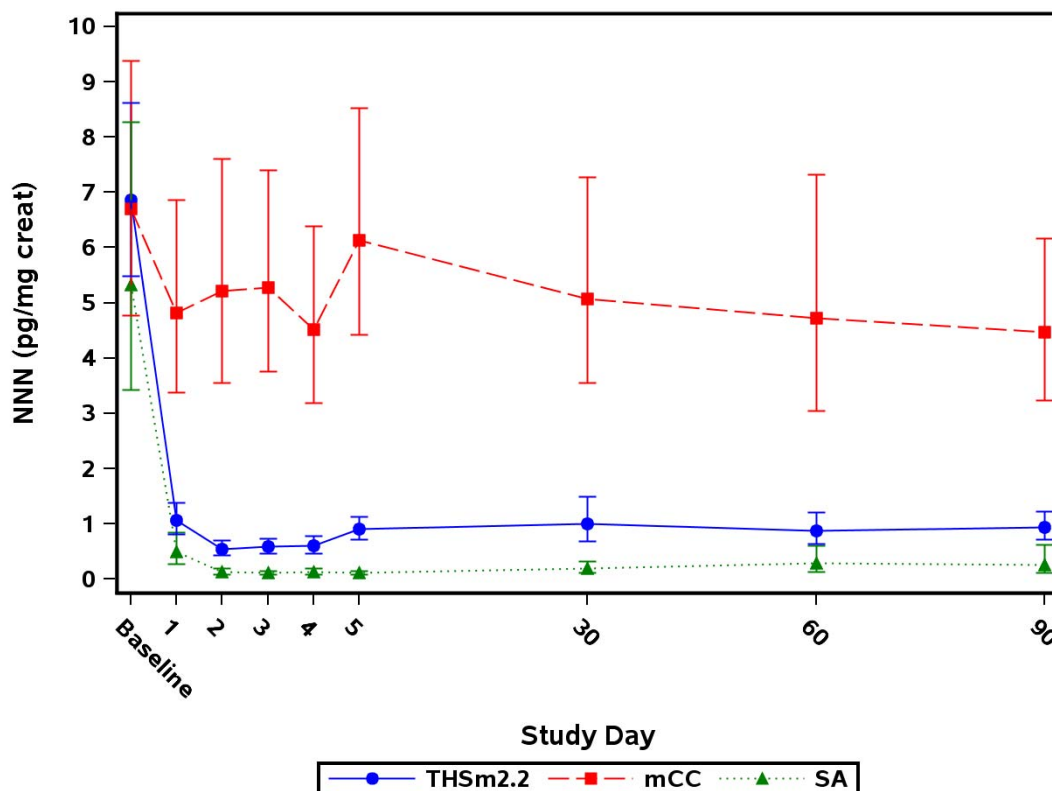
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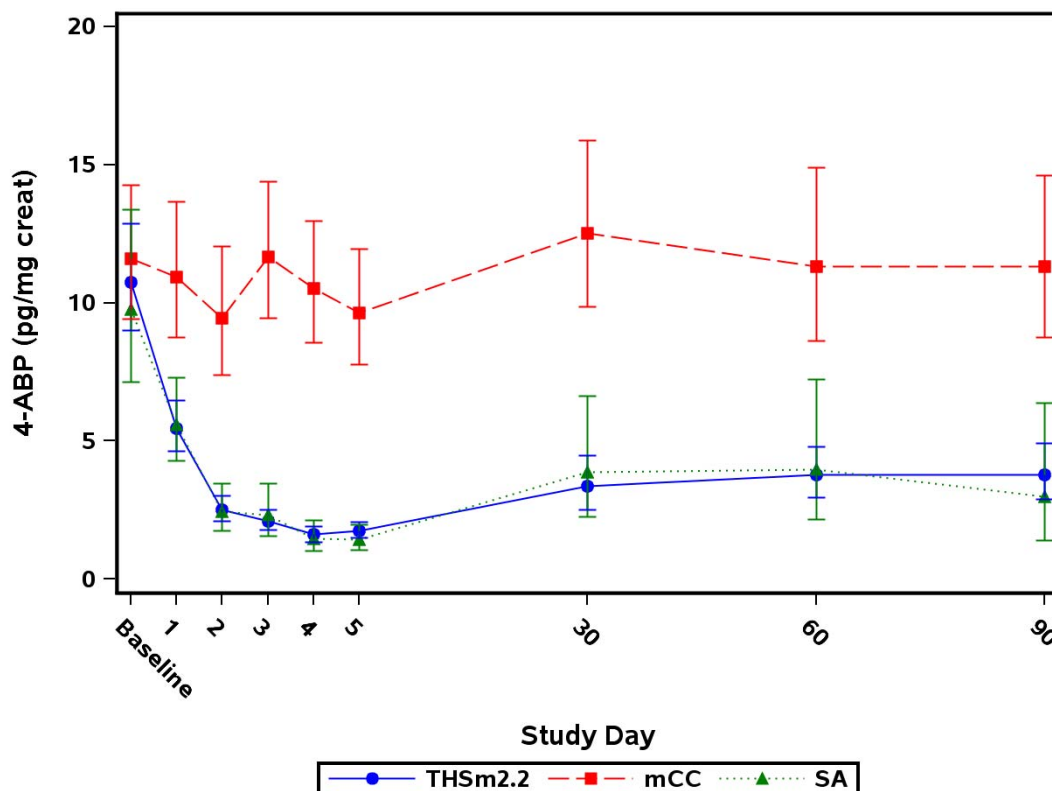
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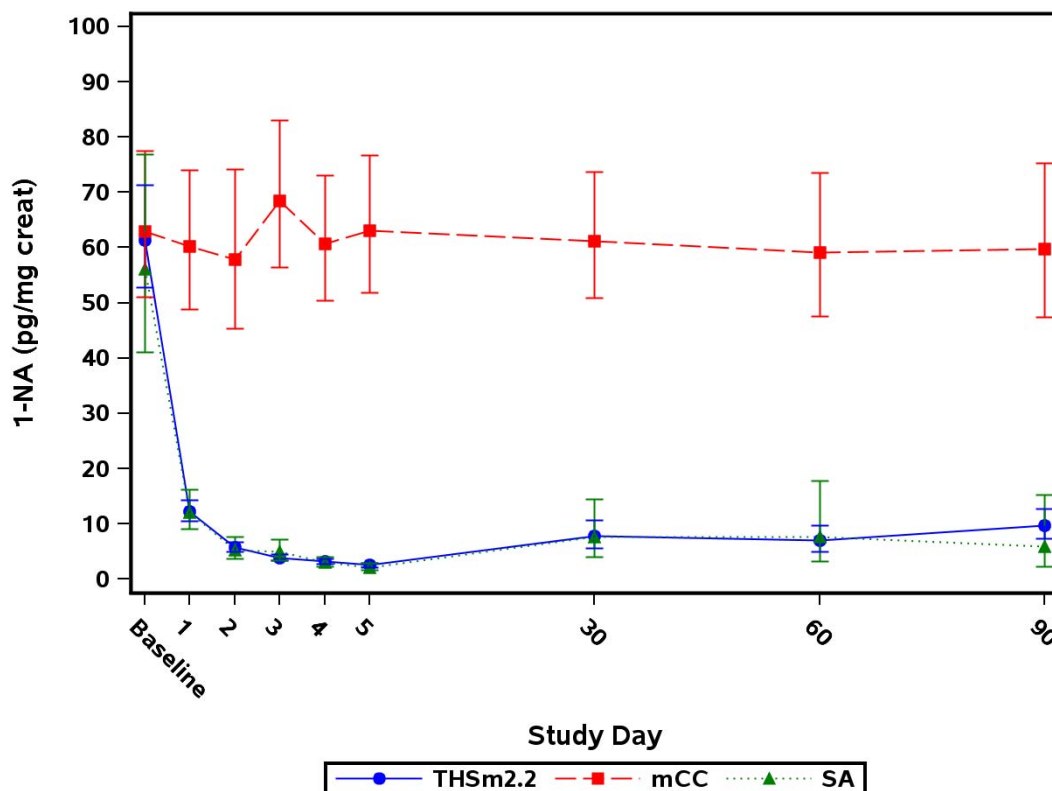
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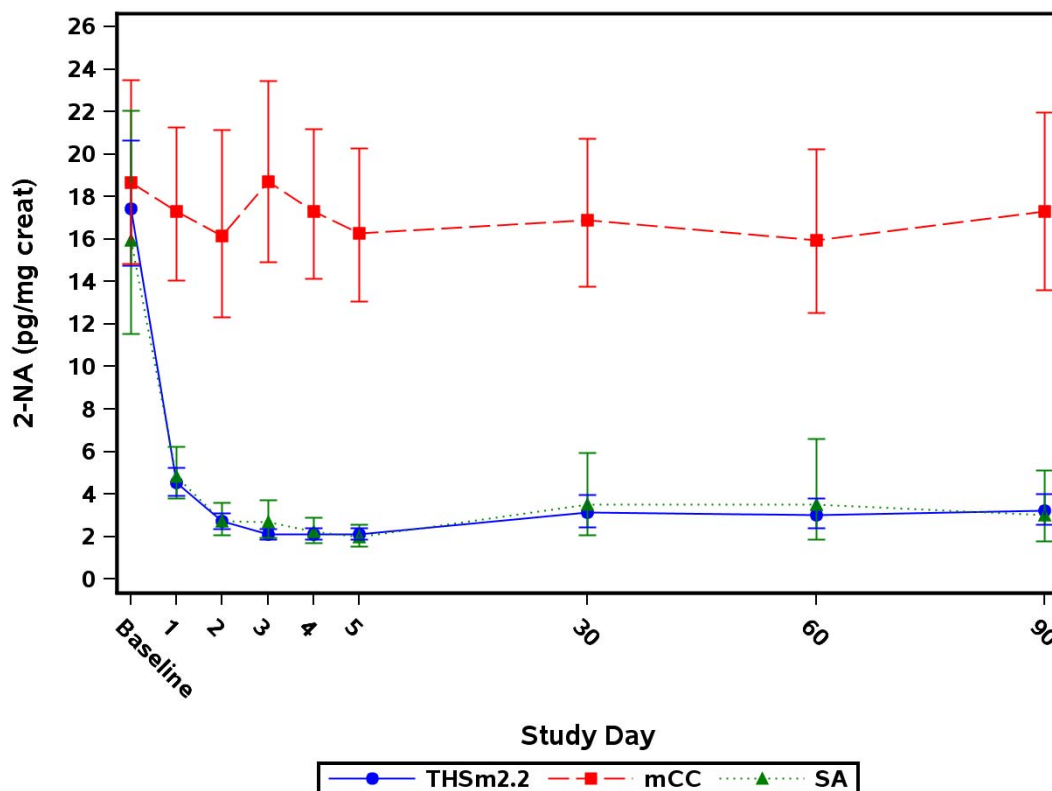
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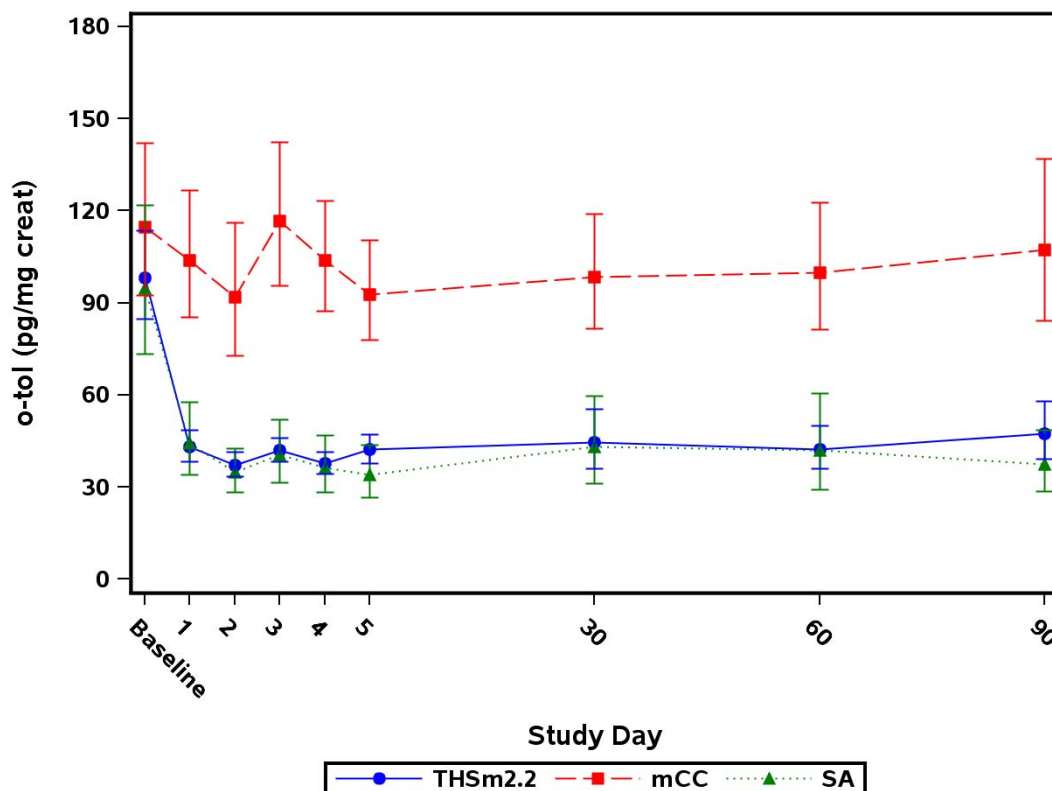
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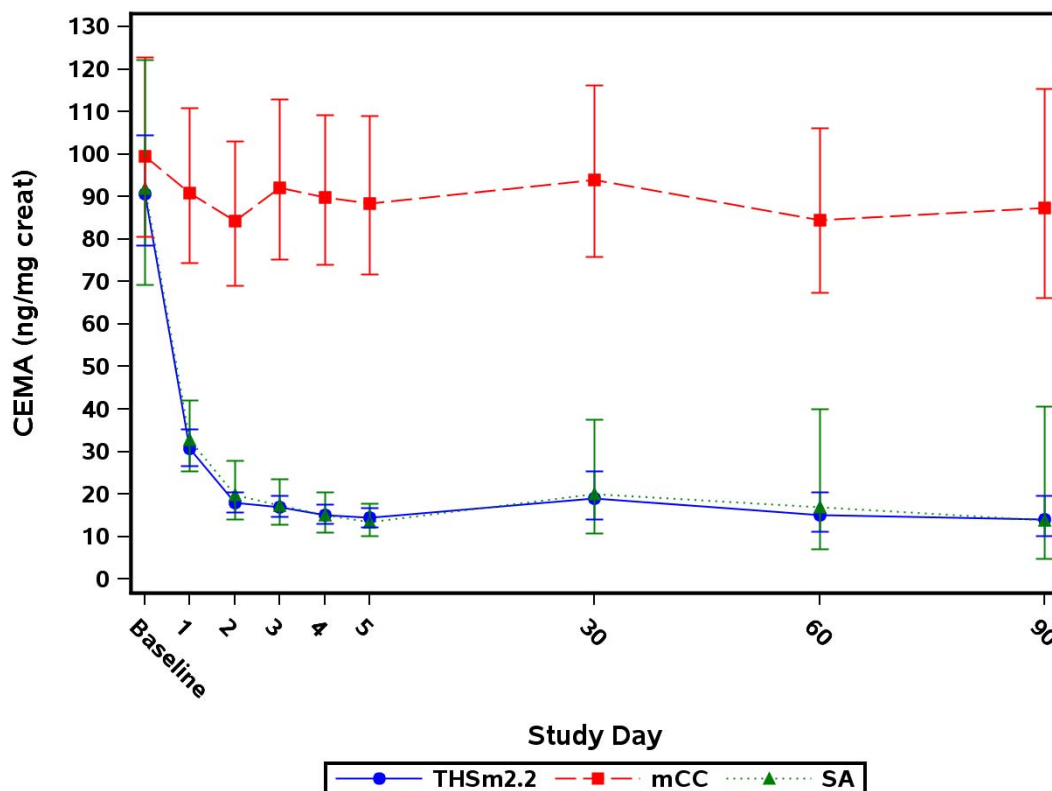
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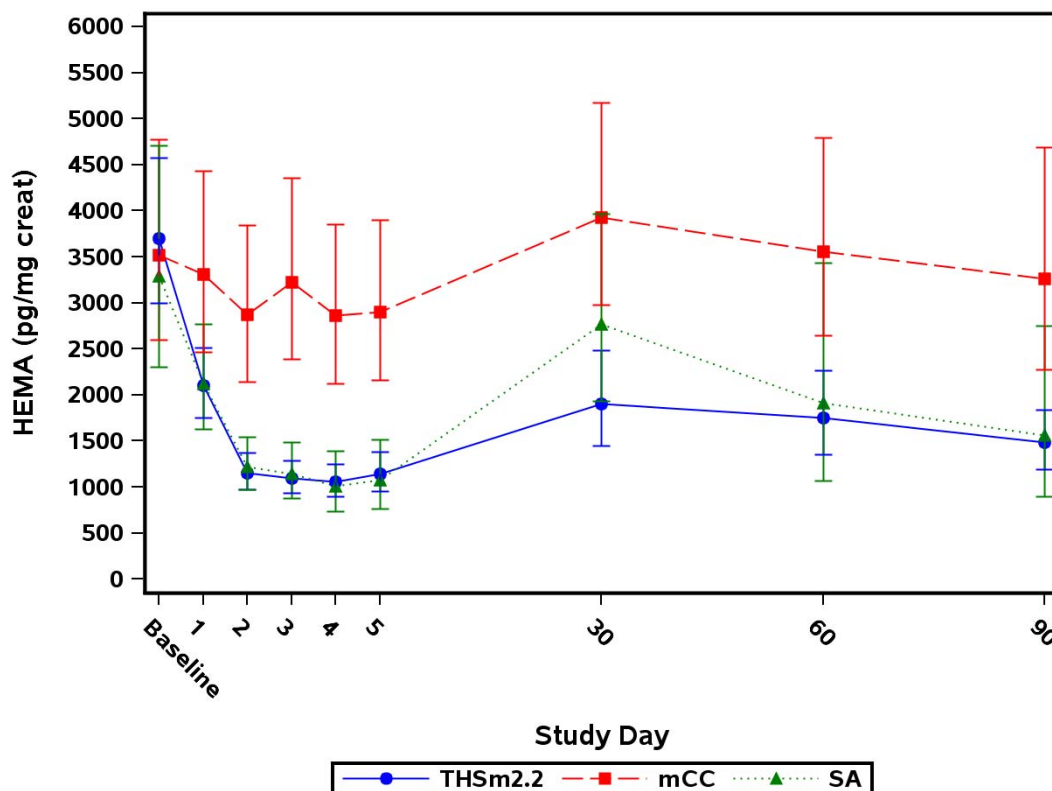
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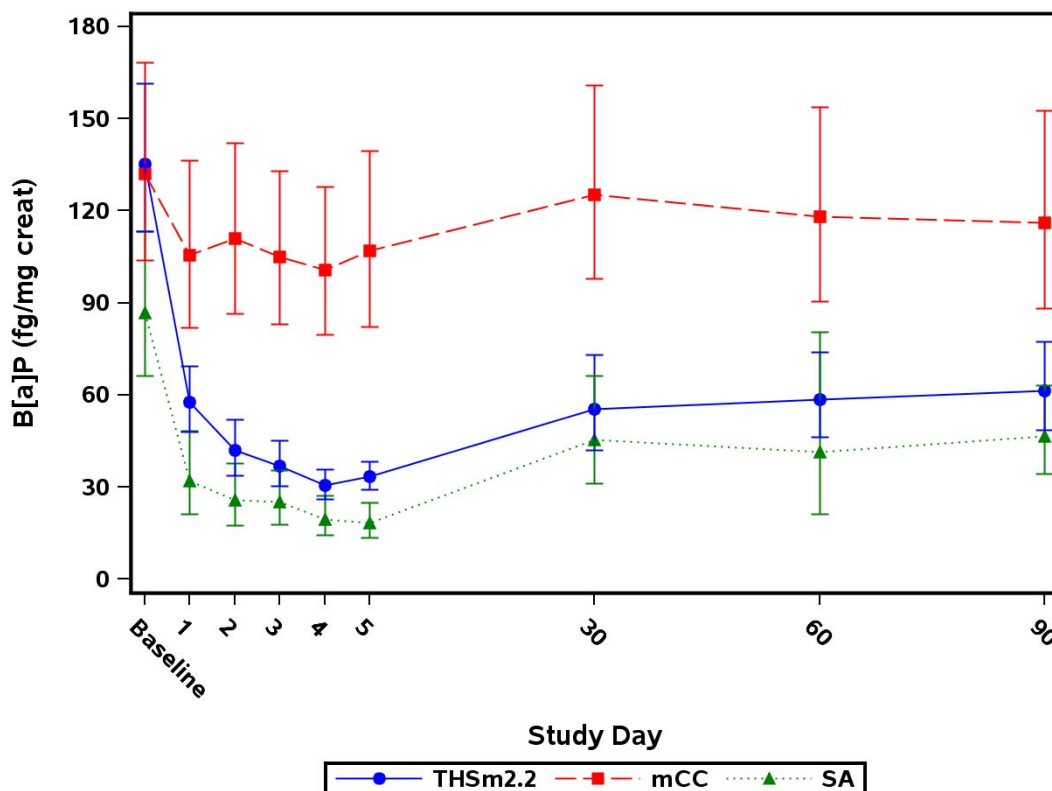
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Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.1, 15.2.4.2.1, 15.2.4.3.1, 15.2.4.4.1, 15.2.4.5.1, 15.2.4.6.1, 15.2.4.7.1, 15.2.4.8.1, 15.2.4.9.1, 15.2.4.10.1, 15.2.4.11.1, 15.2.4.12.1, 15.2.4.13.1, 15.2.4.14.1, 15.2.4.15.1, 15.2.4.16.1, 15.2.4.17.1, 15.2.4.18.1.  
Study ID: ZRHM-REXA-08-US Program: f\_biomark.sas 03DEC15 Status: Final (Page 14 of 18)

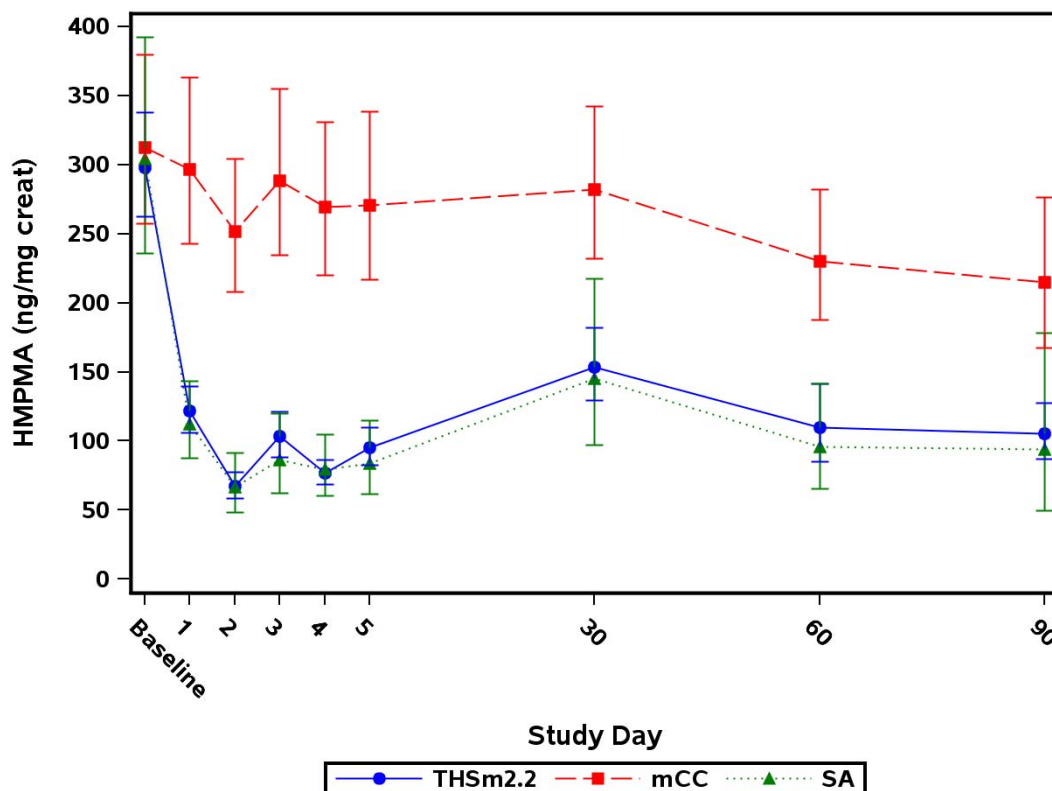
**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.1, 15.2.4.2.1, 15.2.4.3.1, 15.2.4.4.1, 15.2.4.5.1, 15.2.4.6.1, 15.2.4.7.1, 15.2.4.8.1, 15.2.4.9.1, 15.2.4.10.1, 15.2.4.11.1, 15.2.4.12.1, 15.2.4.13.1, 15.2.4.14.1, 15.2.4.15.1, 15.2.4.16.1, 15.2.4.17.1, 15.2.4.18.1.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark.sas 03DEC15 Status: Final (Page 15 of 18)

**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

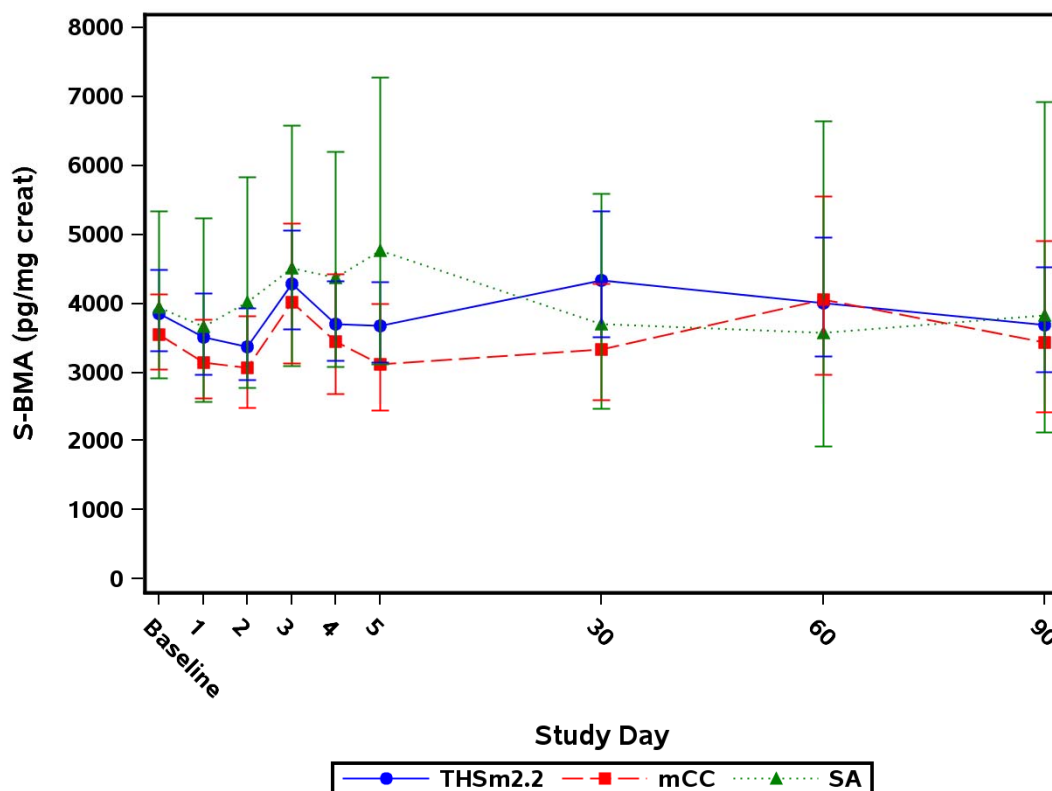
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.1, 15.2.4.2.1, 15.2.4.3.1, 15.2.4.4.1, 15.2.4.5.1, 15.2.4.6.1, 15.2.4.7.1, 15.2.4.8.1, 15.2.4.9.1, 15.2.4.10.1, 15.2.4.11.1, 15.2.4.12.1, 15.2.4.13.1, 15.2.4.14.1, 15.2.4.15.1, 15.2.4.16.1, 15.2.4.17.1, 15.2.4.18.1.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark.sas 03DEC15 Status: Final (Page 16 of 18)



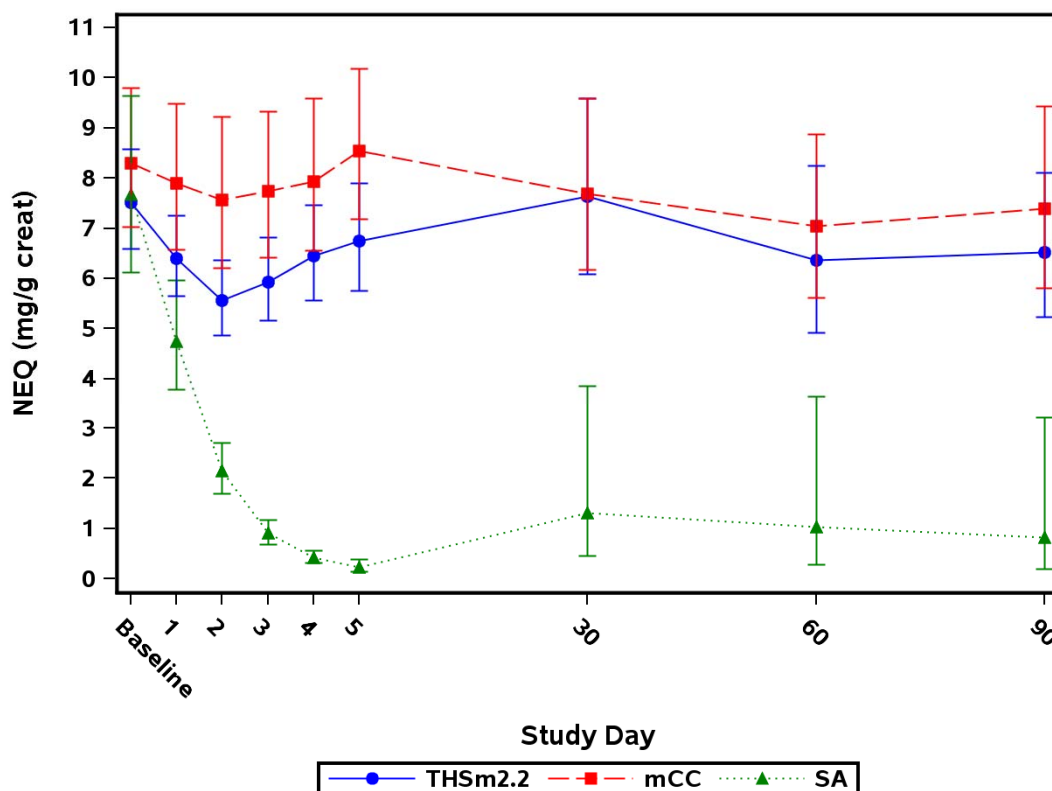
**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.1, 15.2.4.2.1, 15.2.4.3.1, 15.2.4.4.1, 15.2.4.5.1, 15.2.4.6.1, 15.2.4.7.1, 15.2.4.8.1, 15.2.4.9.1, 15.2.4.10.1, 15.2.4.11.1, 15.2.4.12.1, 15.2.4.13.1, 15.2.4.14.1, 15.2.4.15.1, 15.2.4.16.1, 15.2.4.17.1, 15.2.4.18.1.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark.sas 03DEC15 Status: Final (Page 17 of 18)

**Figure 15.1.1.2 Biomarkers of Exposure Geometric Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

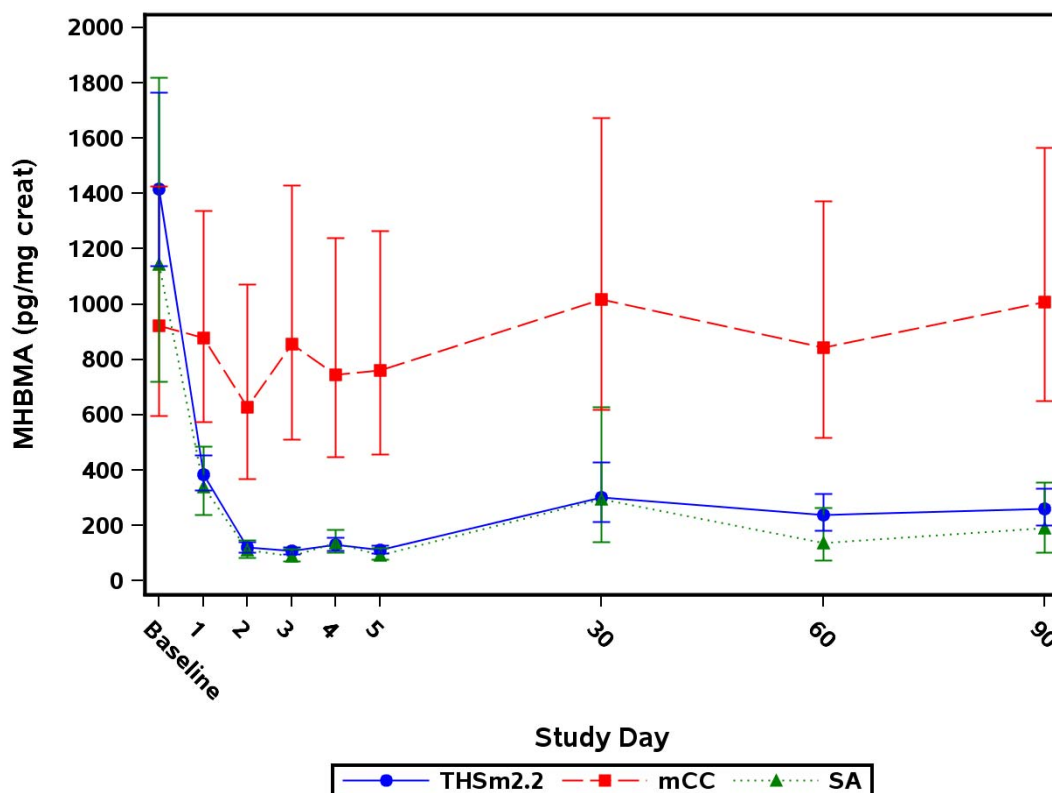
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.1, 15.2.4.2.1, 15.2.4.3.1, 15.2.4.4.1, 15.2.4.5.1, 15.2.4.6.1, 15.2.4.7.1, 15.2.4.8.1, 15.2.4.9.1, 15.2.4.10.1, 15.2.4.11.1, 15.2.4.12.1, 15.2.4.13.1, 15.2.4.14.1, 15.2.4.15.1, 15.2.4.16.1, 15.2.4.17.1, 15.2.4.18.1.  
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**Figure 15.1.1.3 Biomarkers of Exposure Geometric Mean and 95% CI for the Primary Objective – Compliant Population**



Note: Baseline is summarized using the baseline data from the Compliant Population for Period 1.  
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

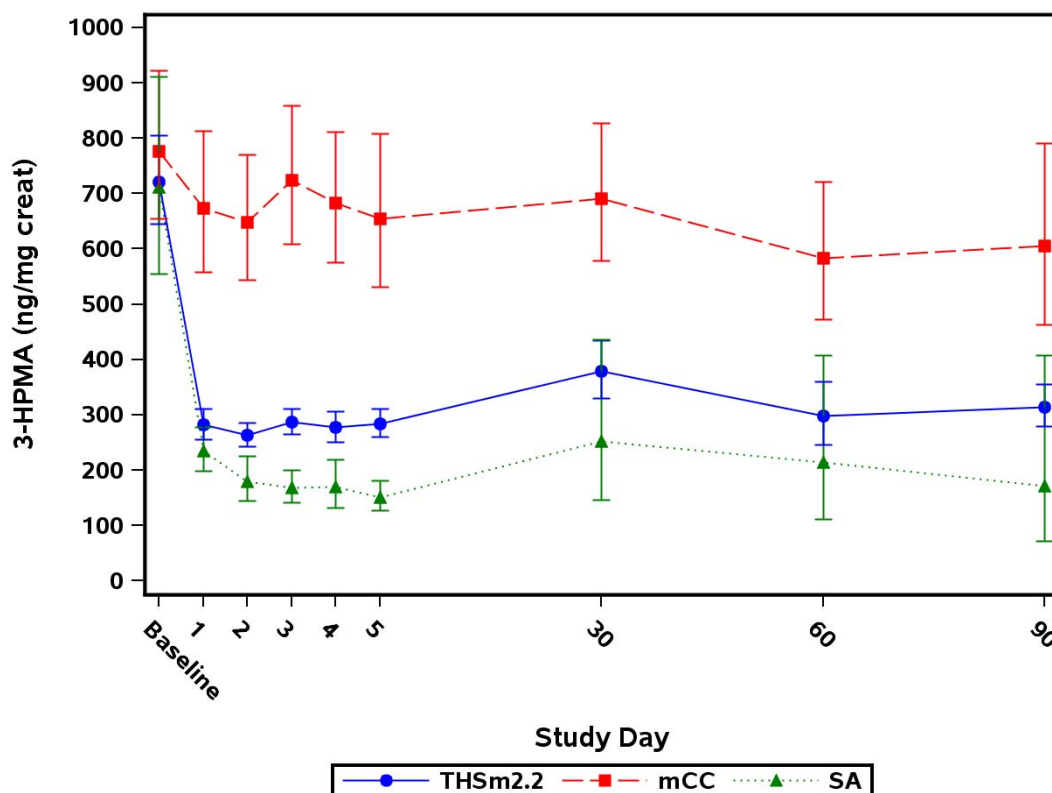
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.3, 15.2.4.2.3, 15.2.4.3.3, 15.2.4.4.3, 15.2.4.5.3.

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**Figure 15.1.1.3 Biomarkers of Exposure Geometric Mean and 95% CI for the Primary Objective – Compliant Population**



Note: Baseline is summarized using the baseline data from the Compliant Population for Period 1.  
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

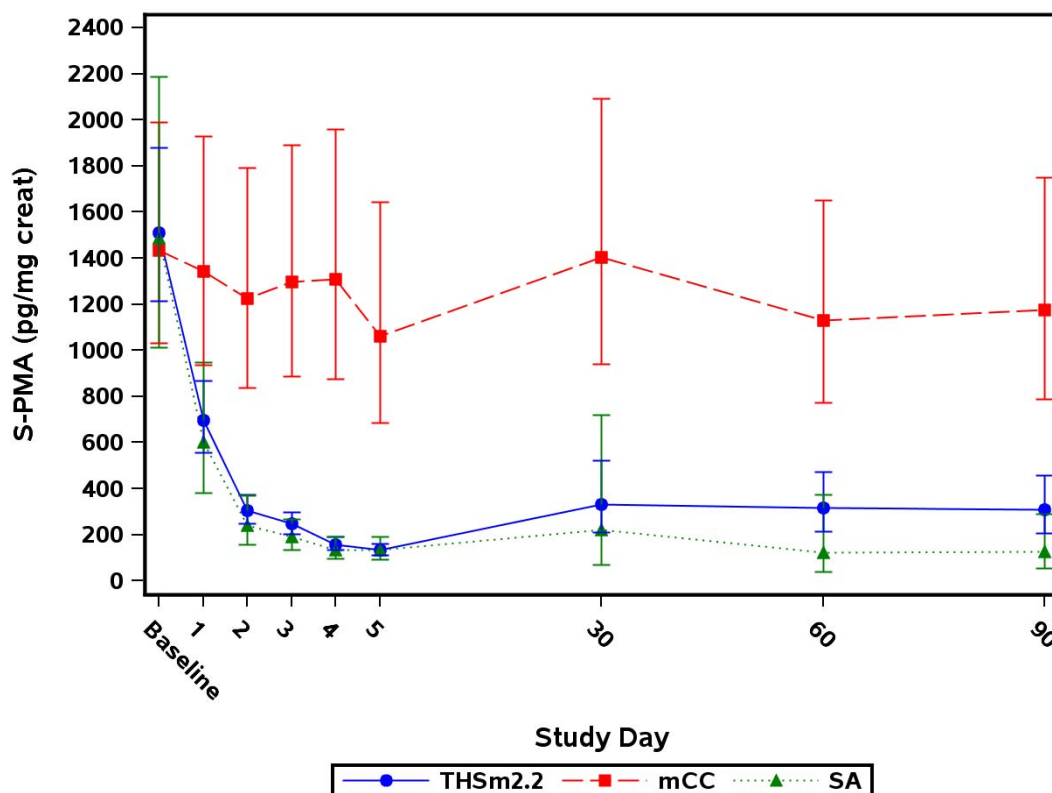
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.3, 15.2.4.2.3, 15.2.4.3.3, 15.2.4.4.3, 15.2.4.5.3.

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**Figure 15.1.1.3 Biomarkers of Exposure Geometric Mean and 95% CI for the Primary Objective – Compliant Population**



Note: Baseline is summarized using the baseline data from the Compliant Population for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

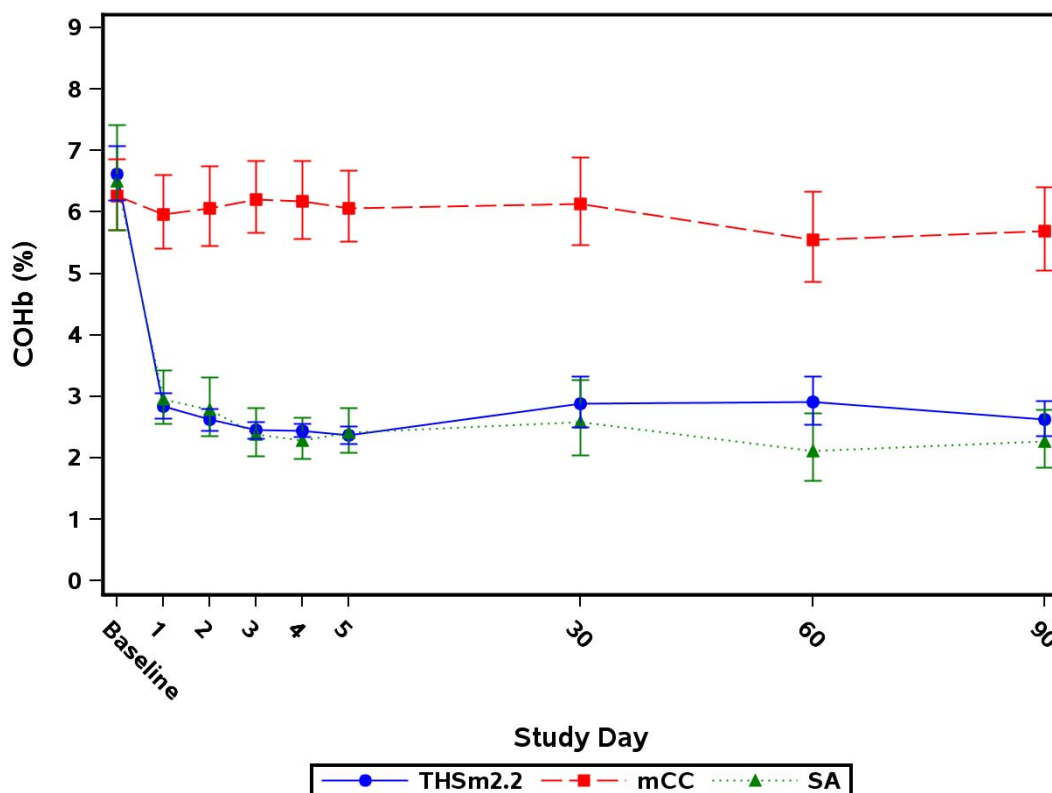
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.3, 15.2.4.2.3, 15.2.4.3.3, 15.2.4.4.3, 15.2.4.5.3.

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**Figure 15.1.1.3 Biomarkers of Exposure Geometric Mean and 95% CI for the Primary Objective – Compliant Population**



Note: COHb on Day 5 represents the evening sample collected.

Note: Baseline is summarized using the baseline data from the Compliant Population for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

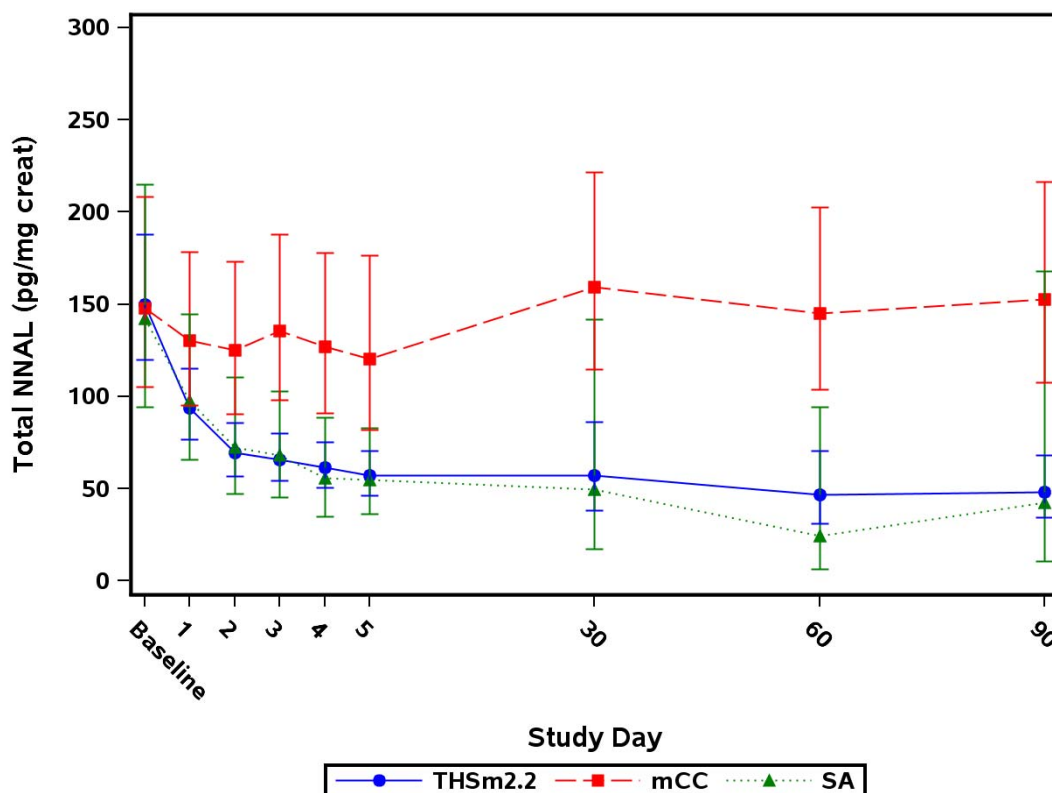
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.3, 15.2.4.2.3, 15.2.4.3.3, 15.2.4.4.3, 15.2.4.5.3.

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**Figure 15.1.1.3 Biomarkers of Exposure Geometric Mean and 95% CI for the Primary Objective – Compliant Population**

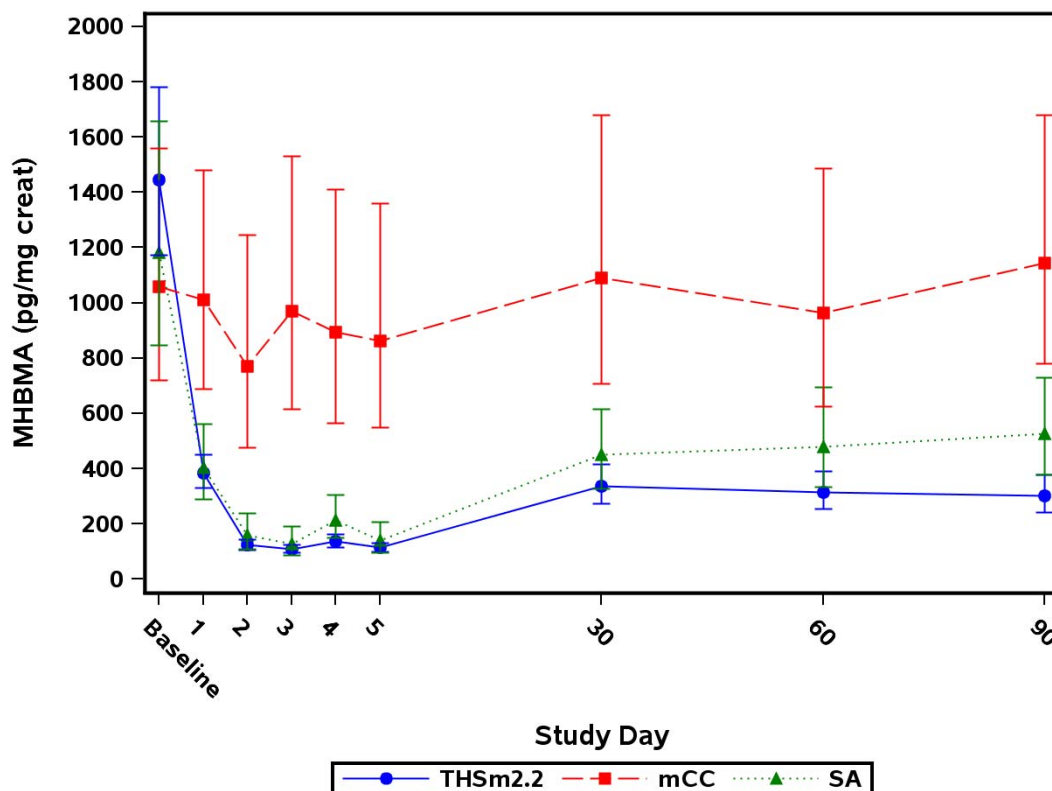


Note: Baseline is summarized using the baseline data from the Compliant Population for Period 1.  
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.3, 15.2.4.2.3, 15.2.4.3.3, 15.2.4.4.3, 15.2.4.5.3.

Study ID: ZRHM-REXA-08-US Program: f\_biomark\_cp.sas 21SEP15 Status: Final (Page 5 of 5)

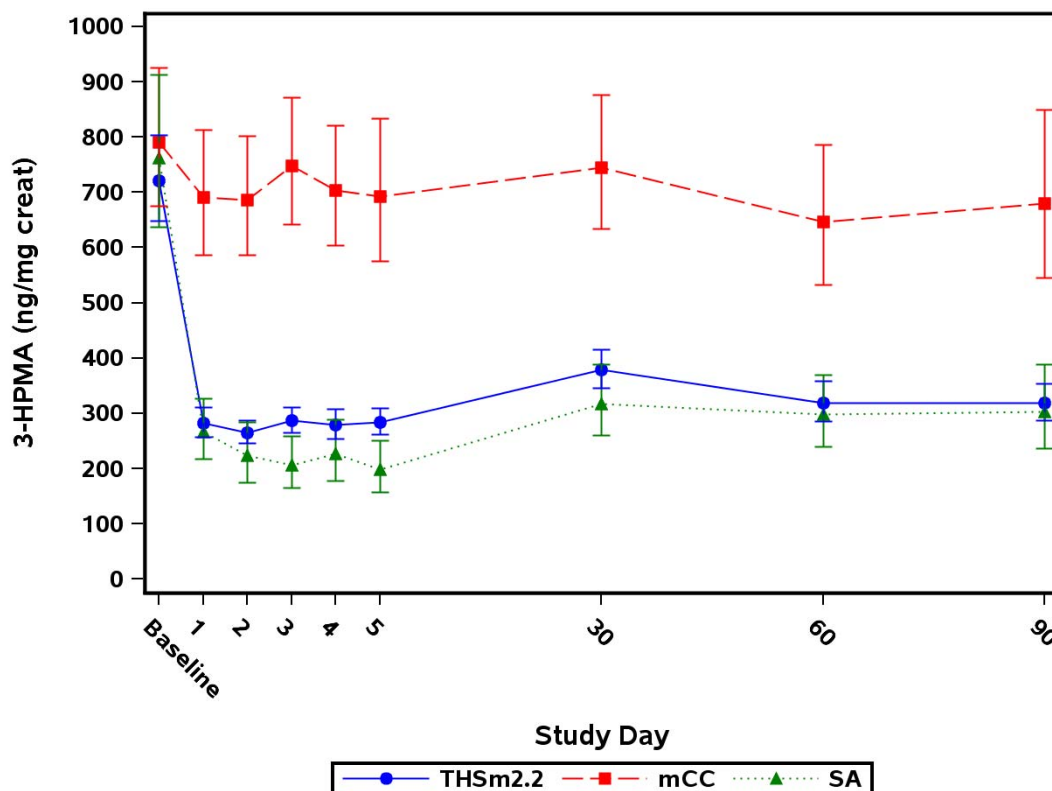
**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 1 of 18)

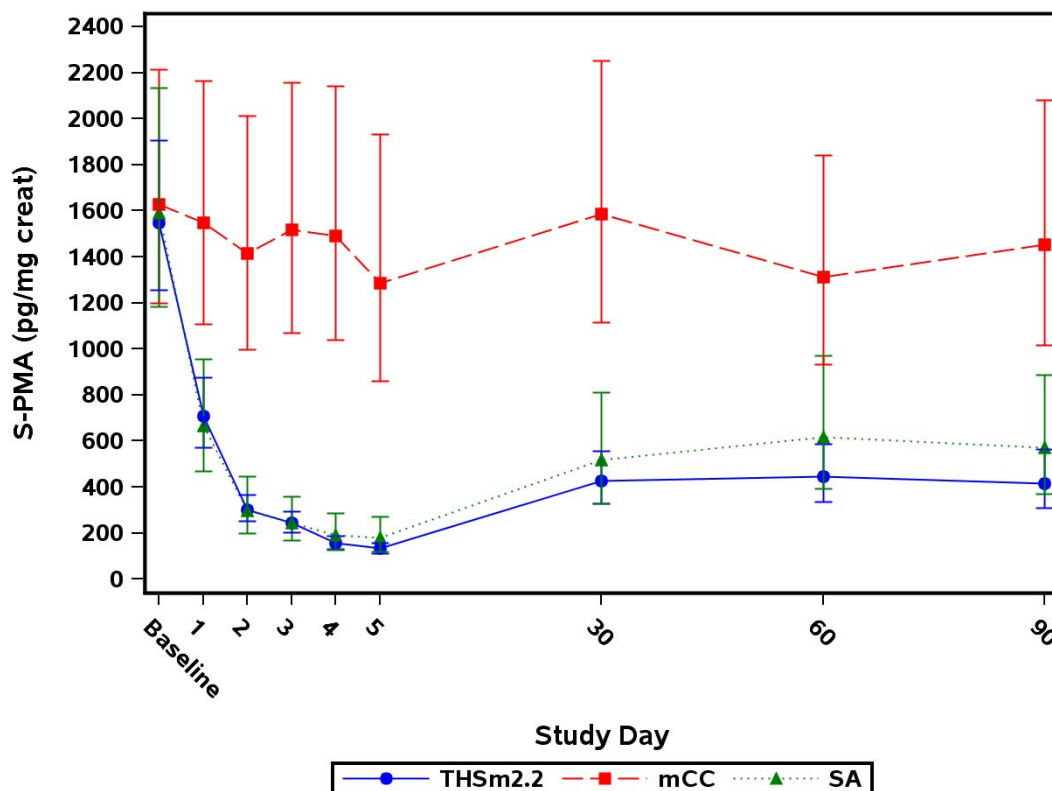


**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

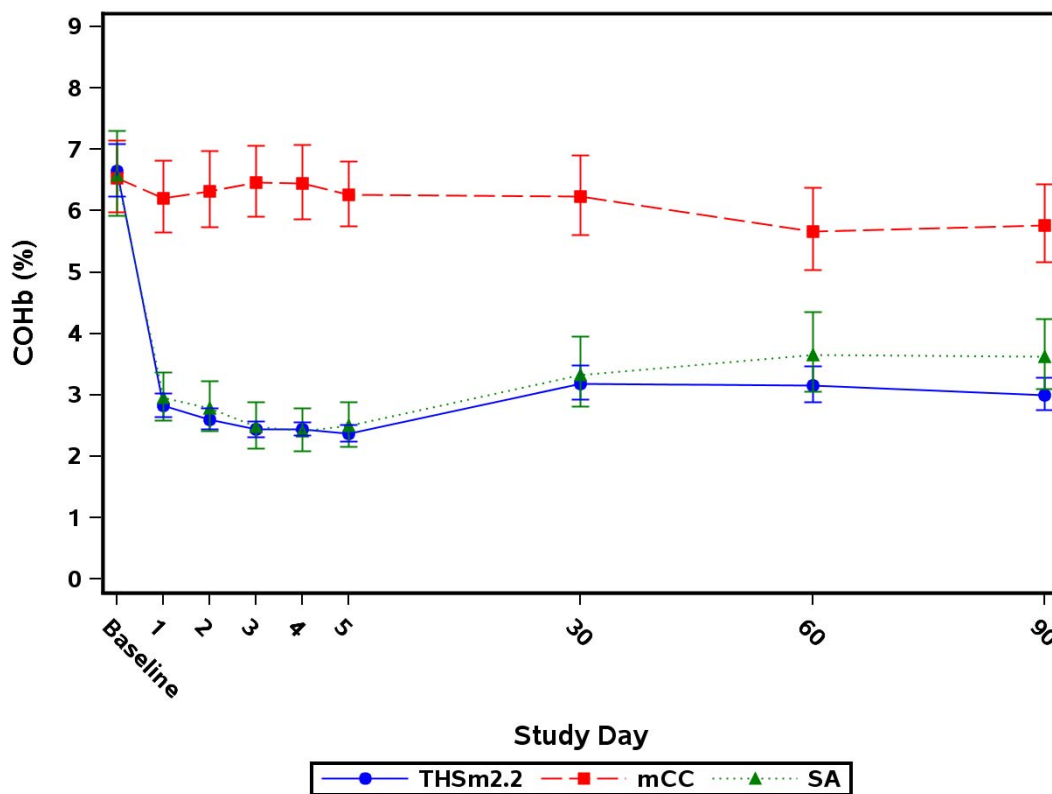
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**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 3 of 18)

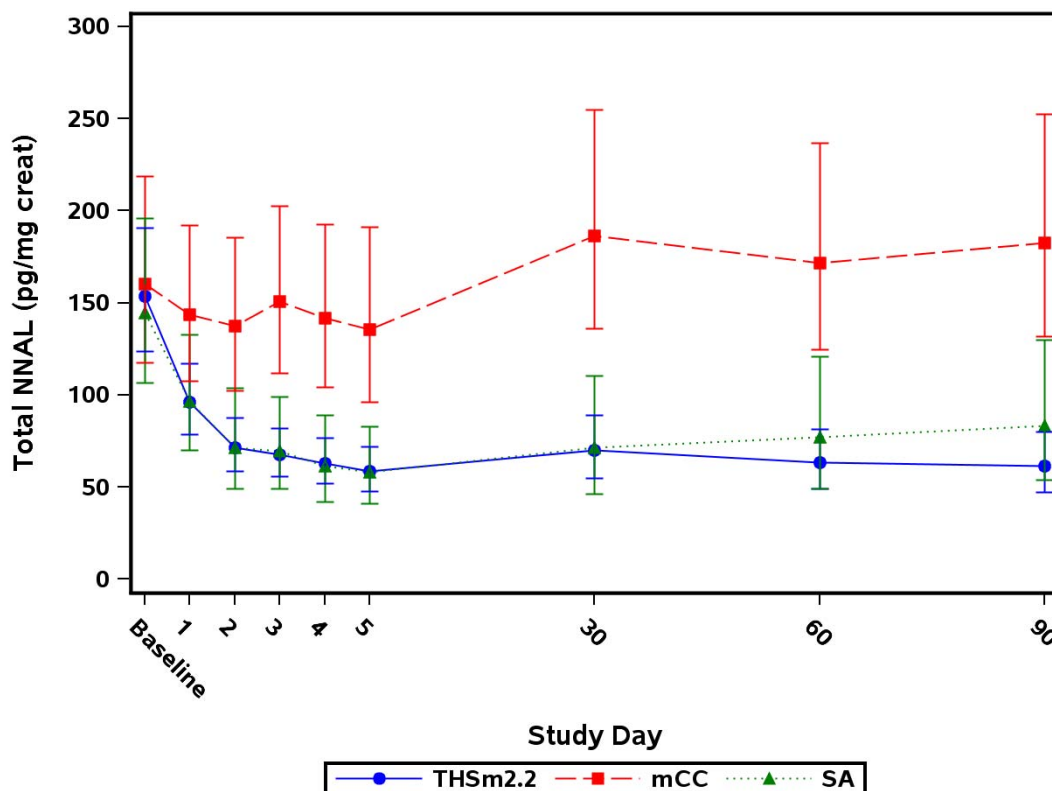
**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: COHb on Day 5 represents the evening sample collected.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

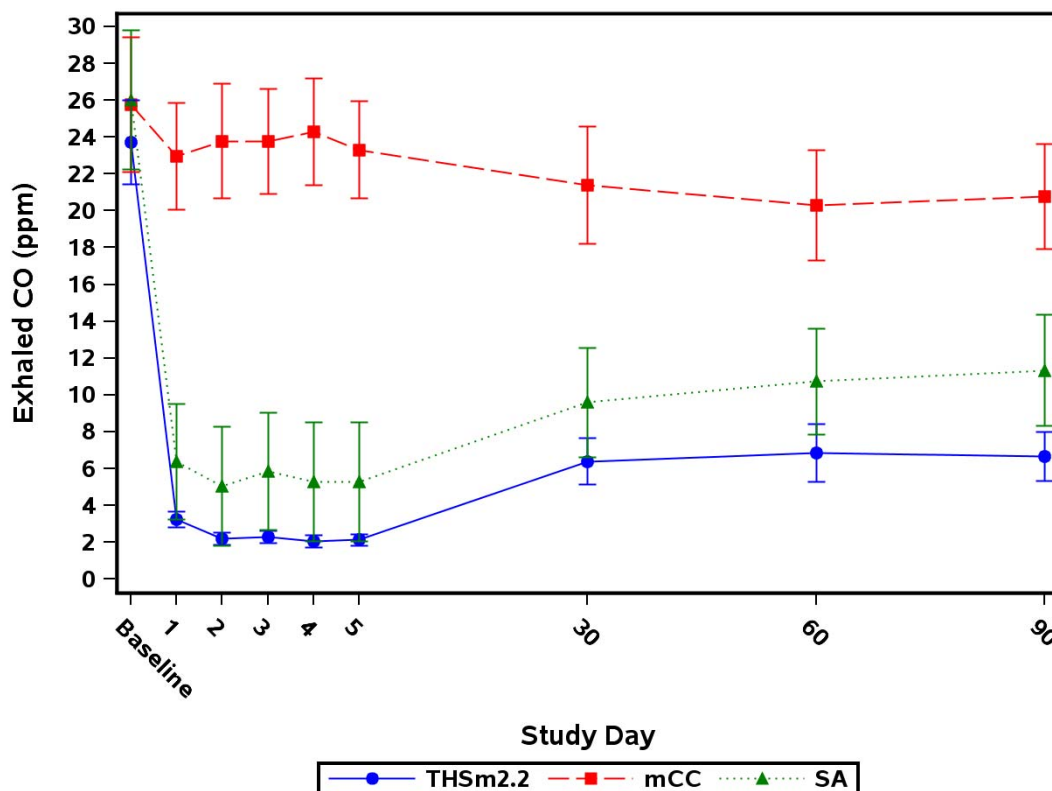
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**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 5 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

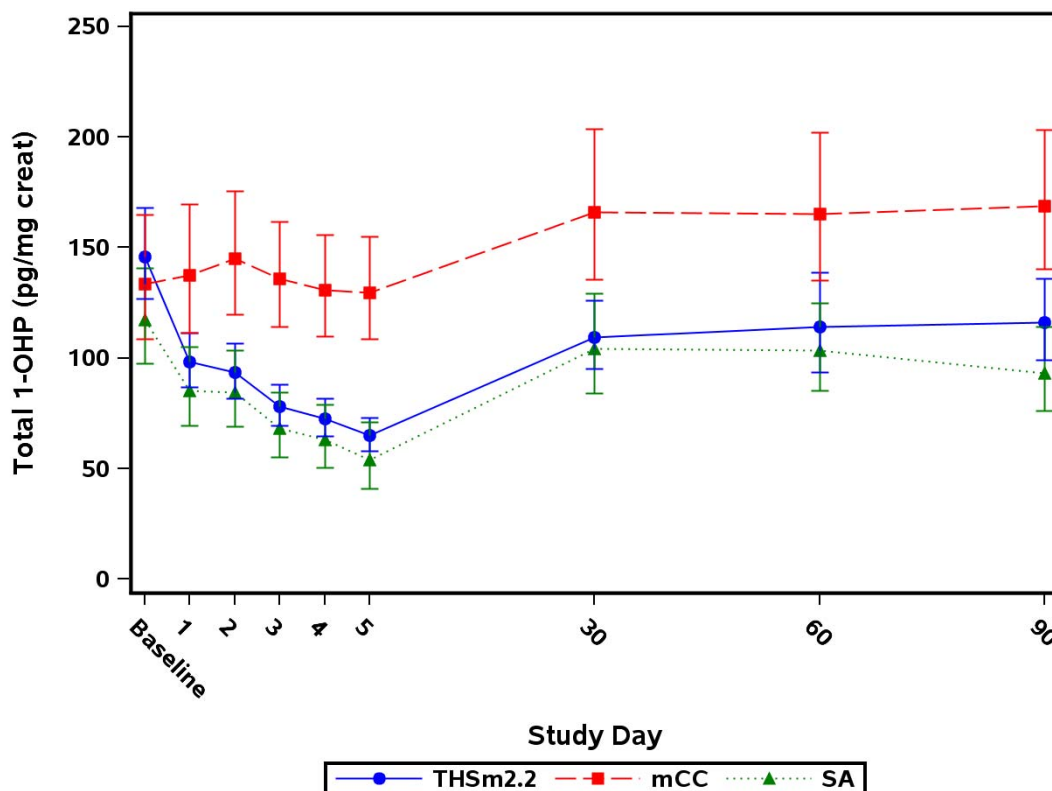
Note: CO on Baseline and Days 1- 5 represent the evening sample collected.

Note: Arithmetic mean and 95% CI are plotted for Exhaled CO (ppm).

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

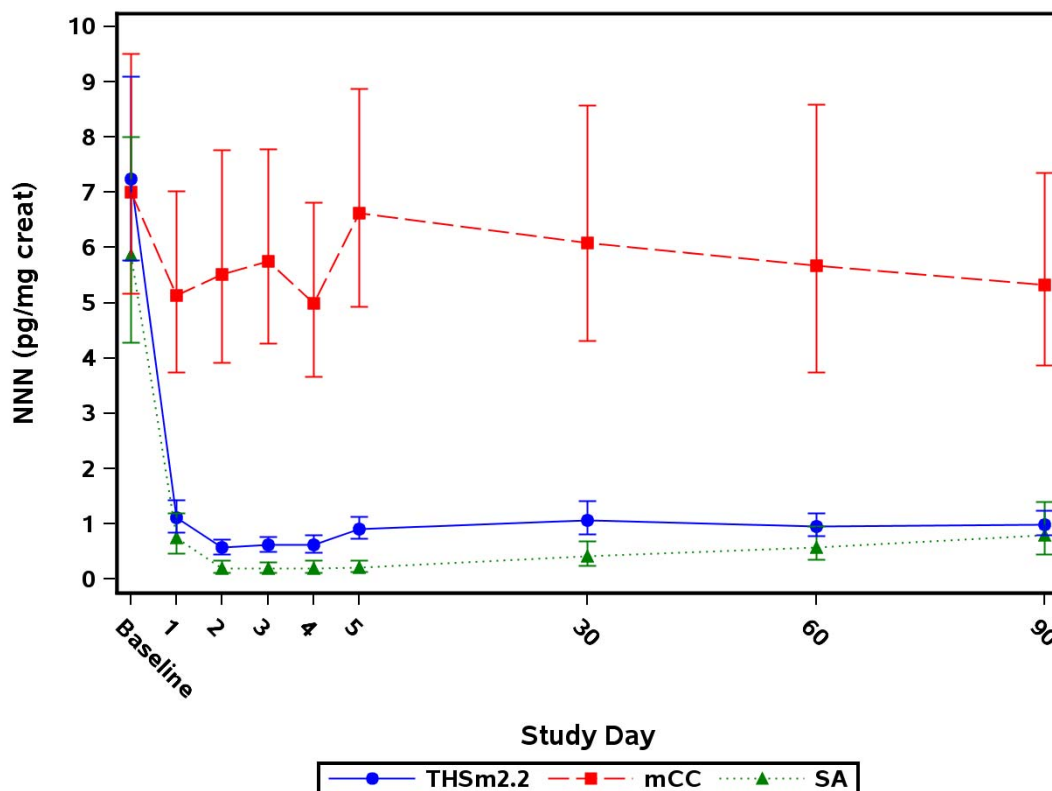
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Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 6 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

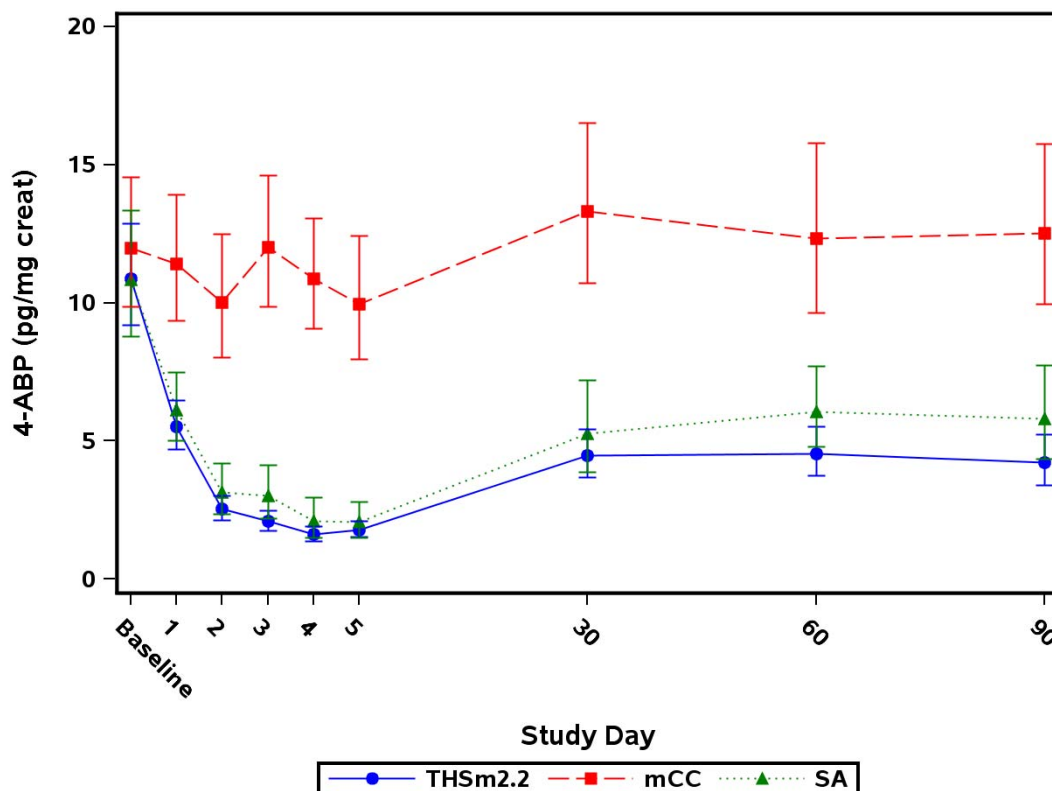
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**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 8 of 18)

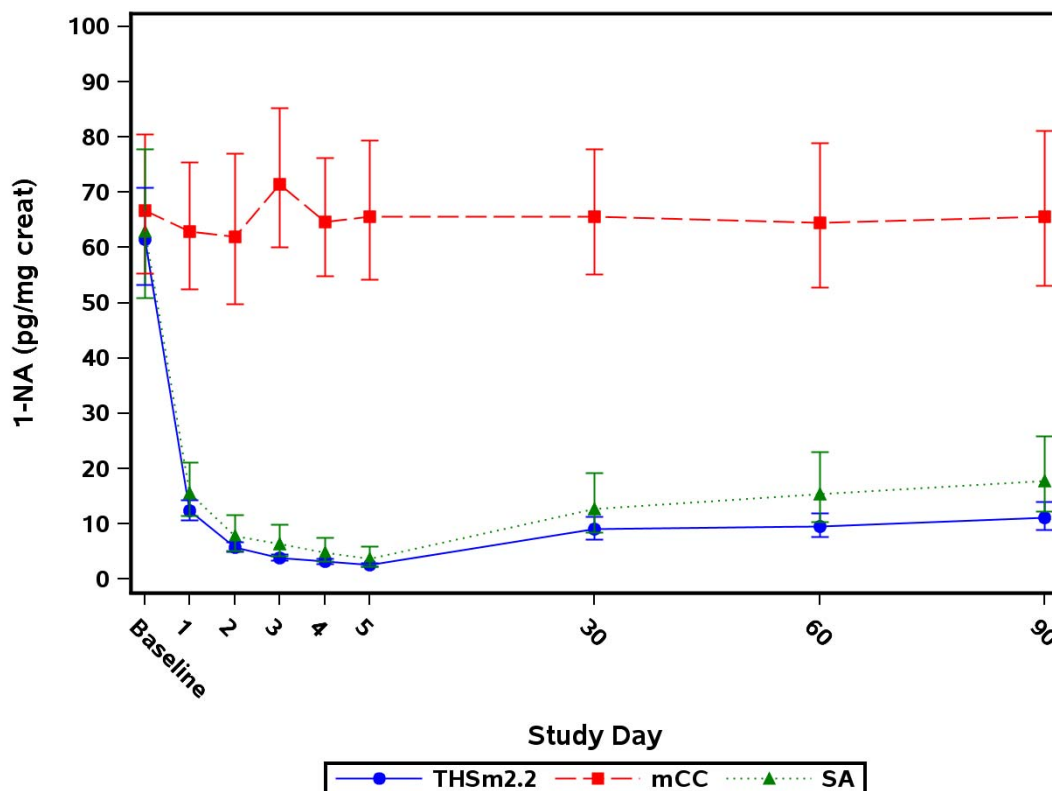
**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
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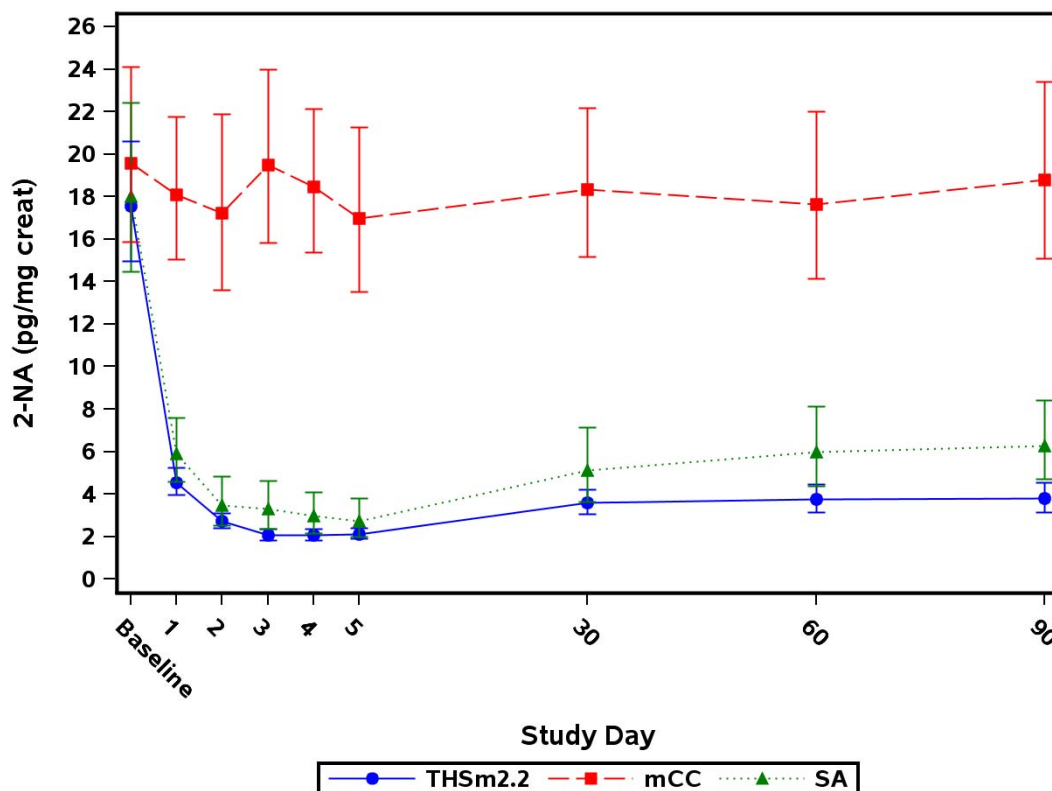


**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

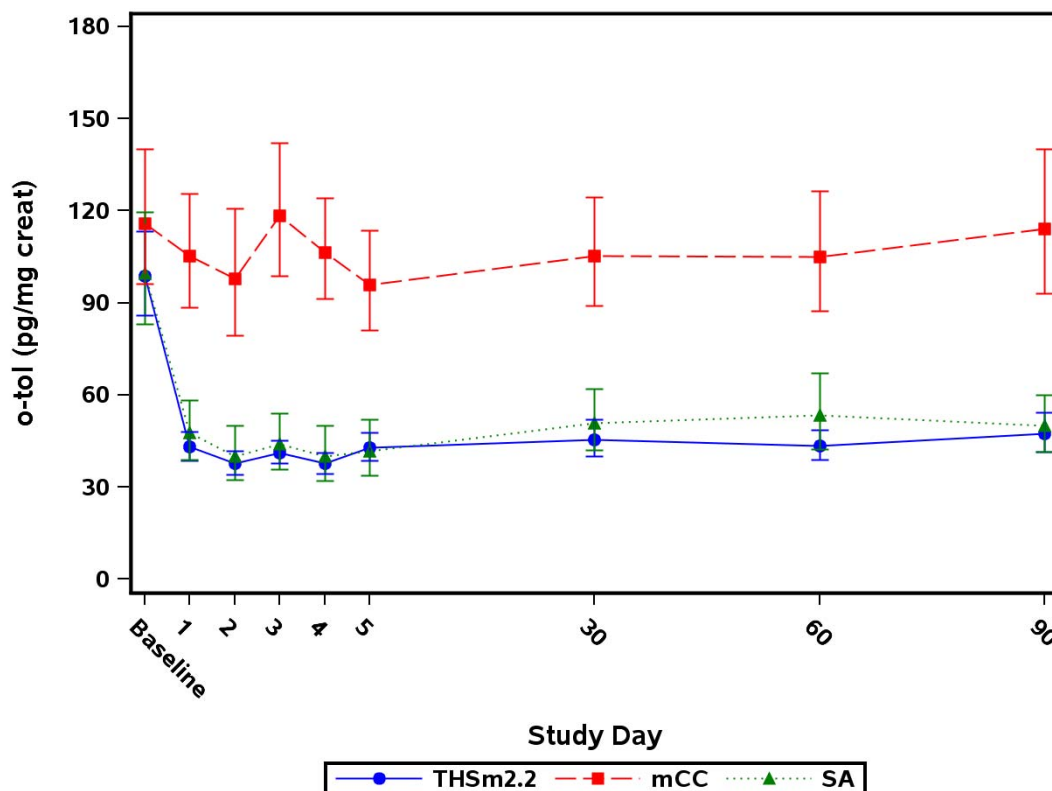
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Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 10 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

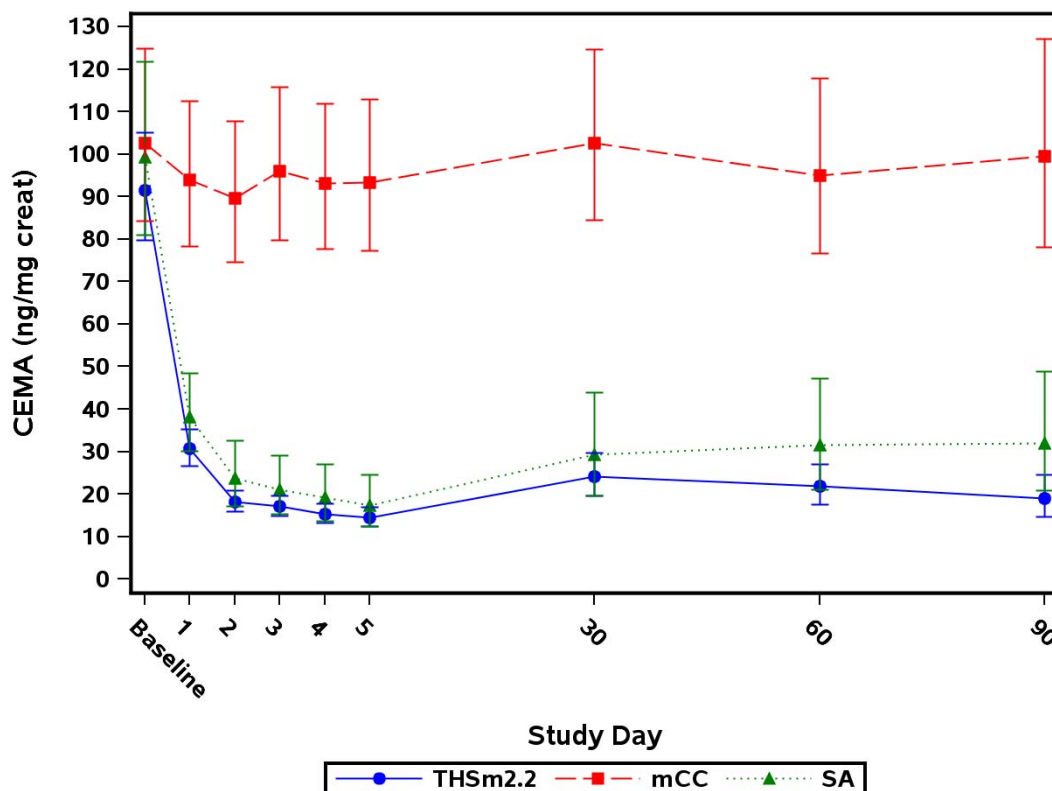
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Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 11 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

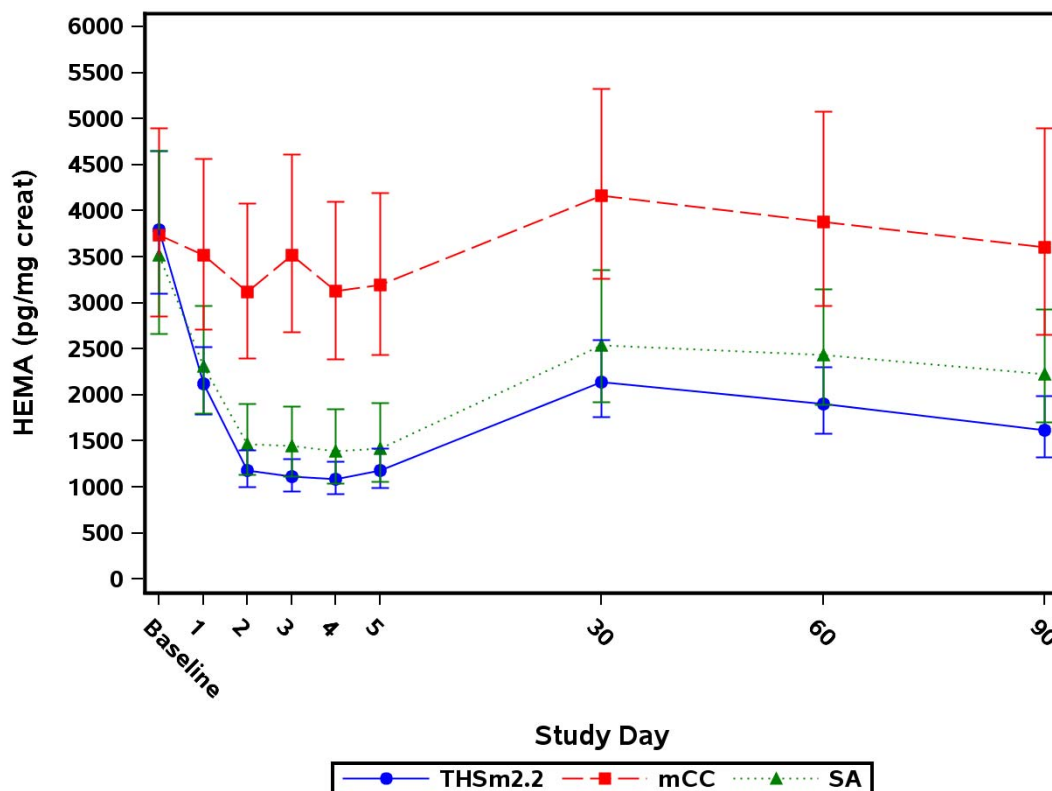
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Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 12 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

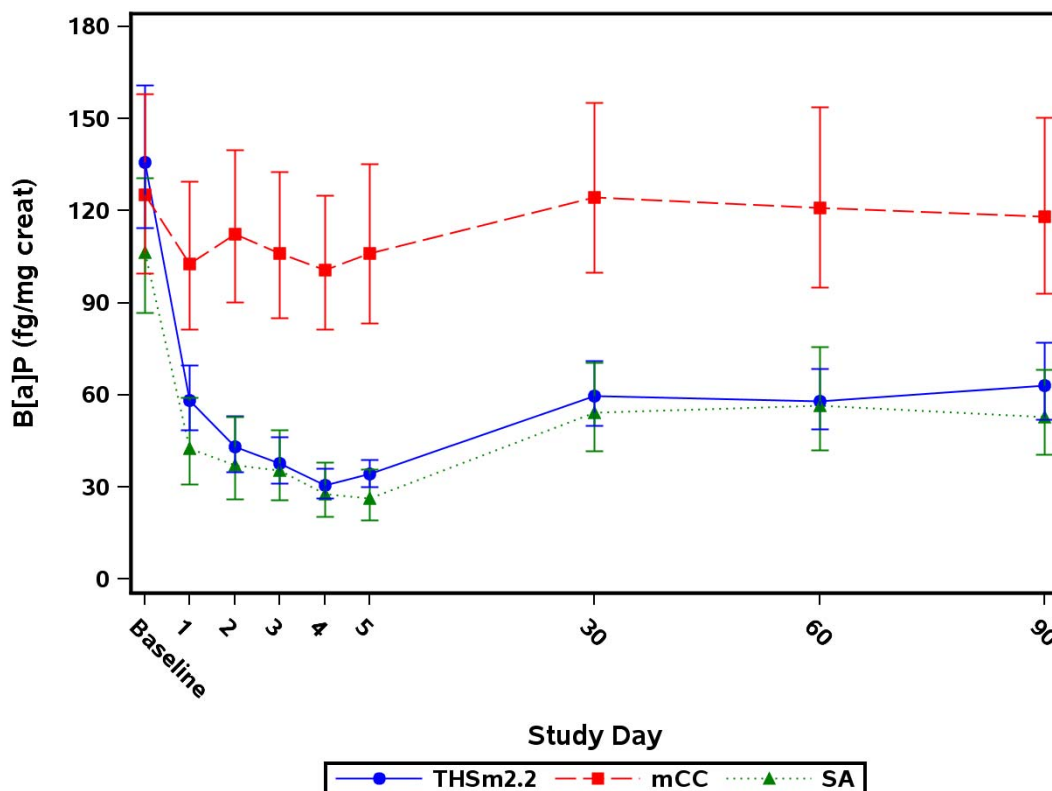
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Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 13 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

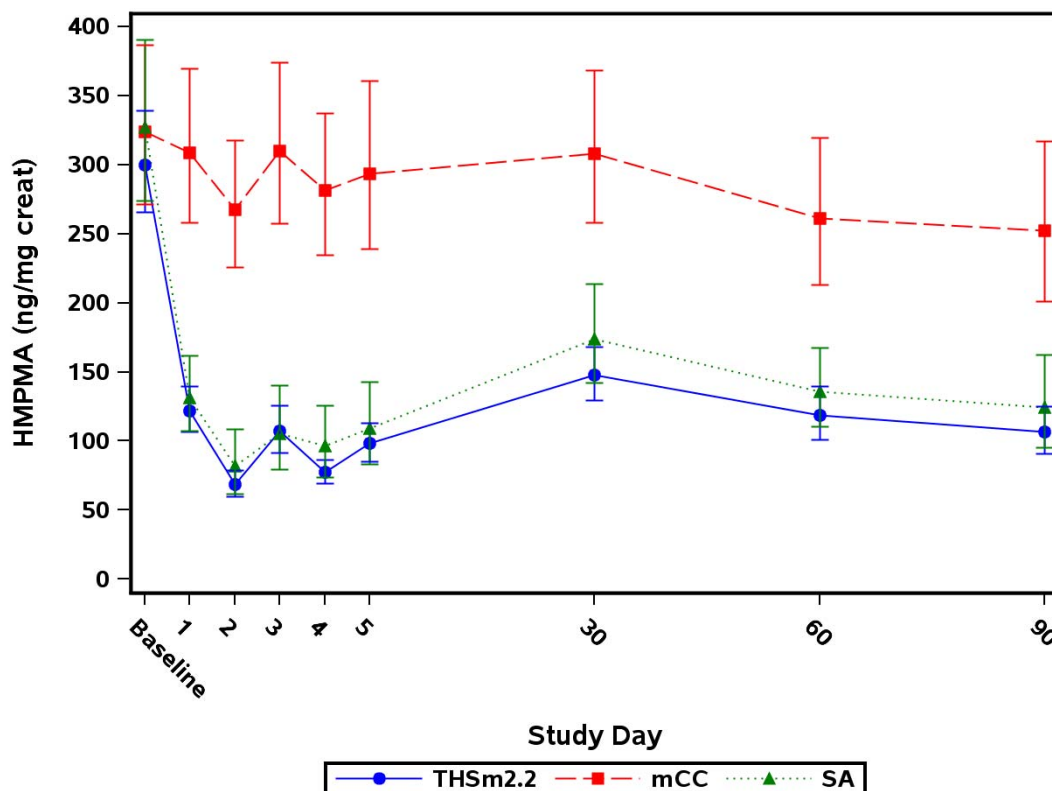
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Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 14 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

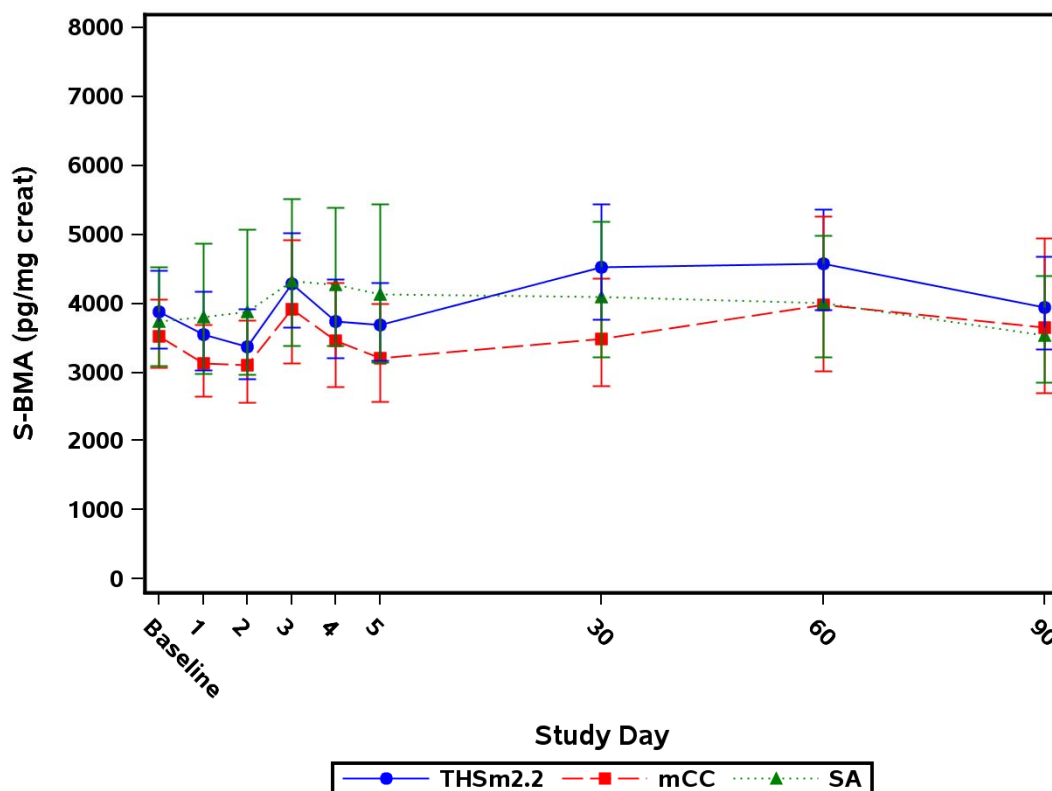
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Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 15 of 18)

**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 16 of 18)

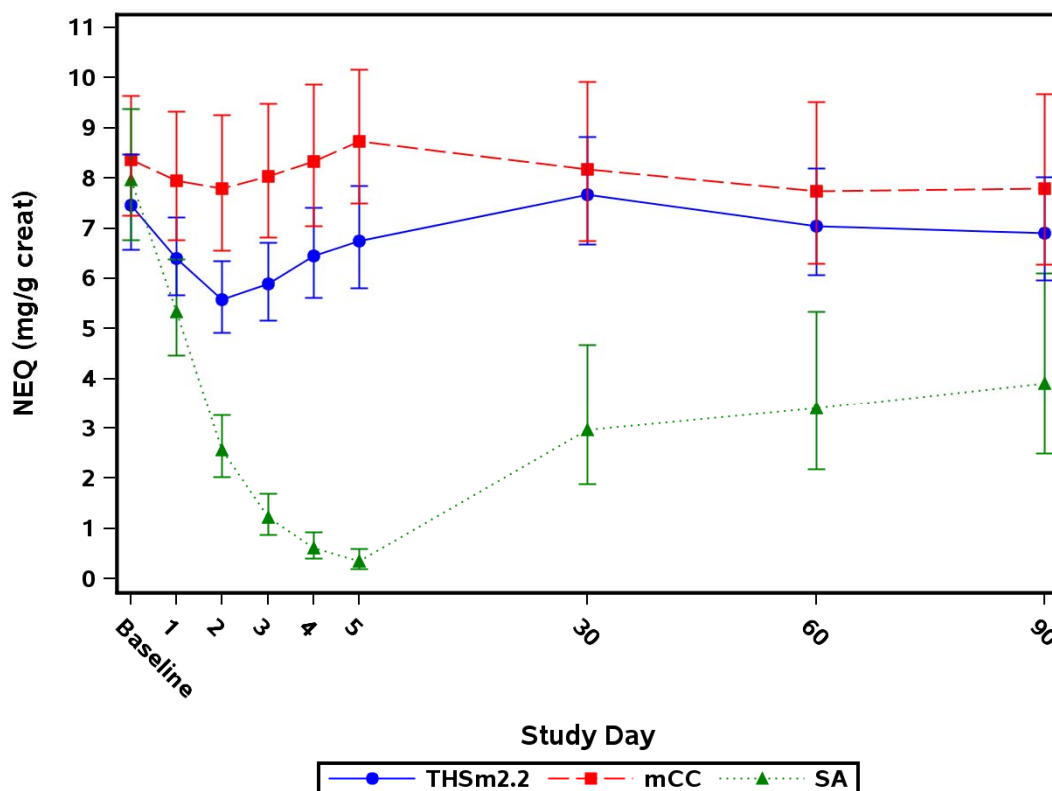
**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID:ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 17 of 18)



**Figure 15.1.1.4 Biomarkers of Exposure Geometric Mean and 95% CI – FAS**

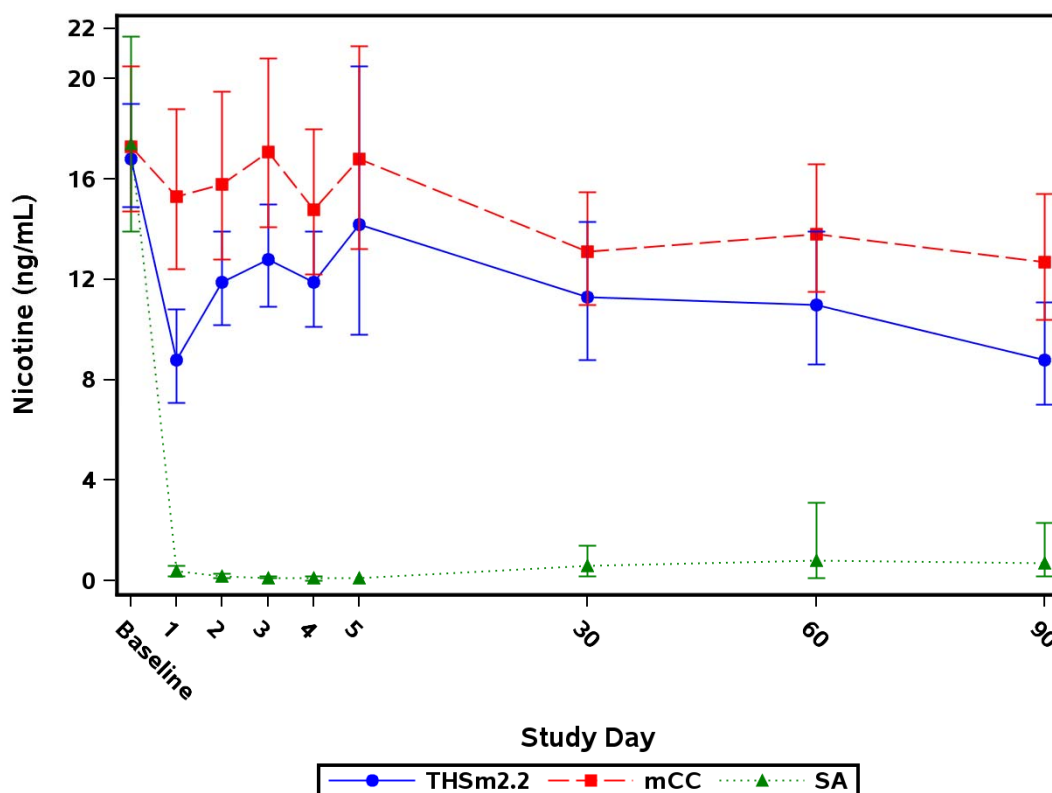
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.1.2, 15.2.4.2.2, 15.2.4.3.2, 15.2.4.4.2, 15.2.4.5.2, 15.2.4.6.2, 15.2.4.7.2, 15.2.4.8.2, 15.2.4.9.2, 15.2.4.10.2, 15.2.4.11.2, 15.2.4.12.2, 15.2.4.13.2, 15.2.4.14.2, 15.2.4.15.2, 15.2.4.16.2, 15.2.4.17.2, 15.2.4.18.2.  
Study ID: ZRHM-REXA-08-US Program: f\_biomark\_fas.sas 04DEC15 Status: Final (Page 18 of 18)



## **15.1.2 Secondary Endpoints**

**Figure 15.1.2.1.1 Plasma Nicotine and Cotinine Profile (ng/mL) Geometric Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.  
Note: Evening result is presented for Day 5.  
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

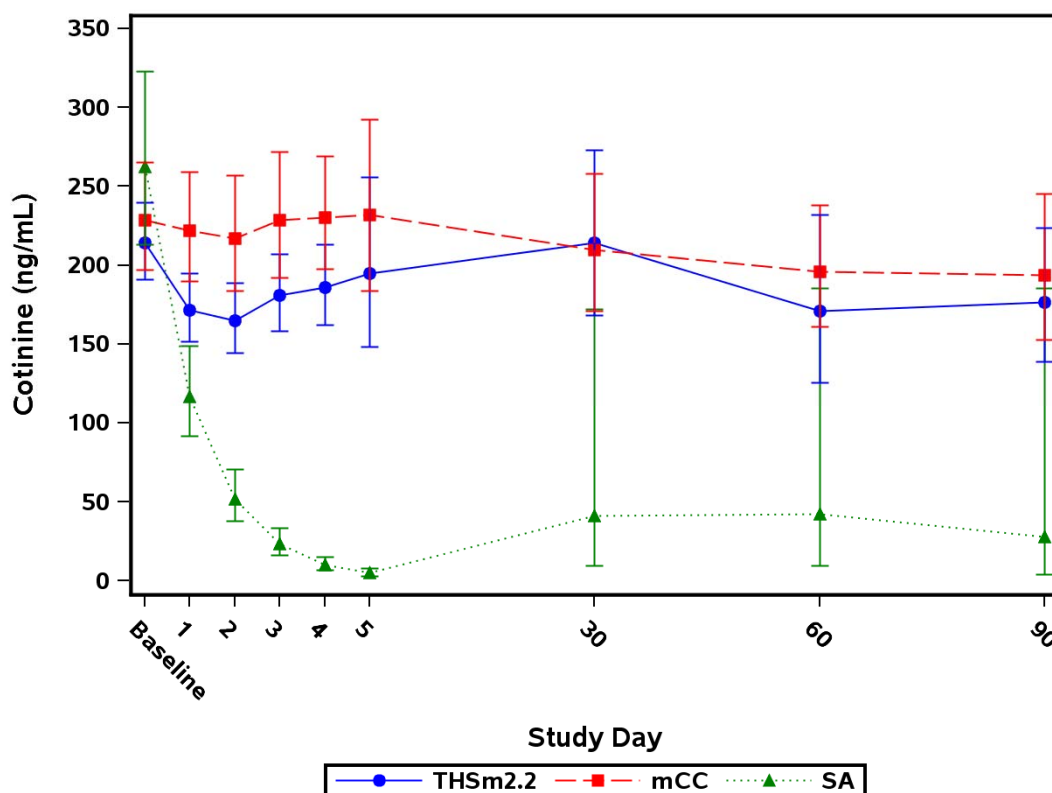
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.19.1

Study ID: ZRHM-REXA-08-US Program: f\_pnic\_pp.sas 21SEP15 Status: Final (Page 1 of 2)



**Figure 15.1.2.1.1 Plasma Nicotine and Cotinine Profile (ng/mL) Geometric Mean and 95% CI – PP Set**



Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

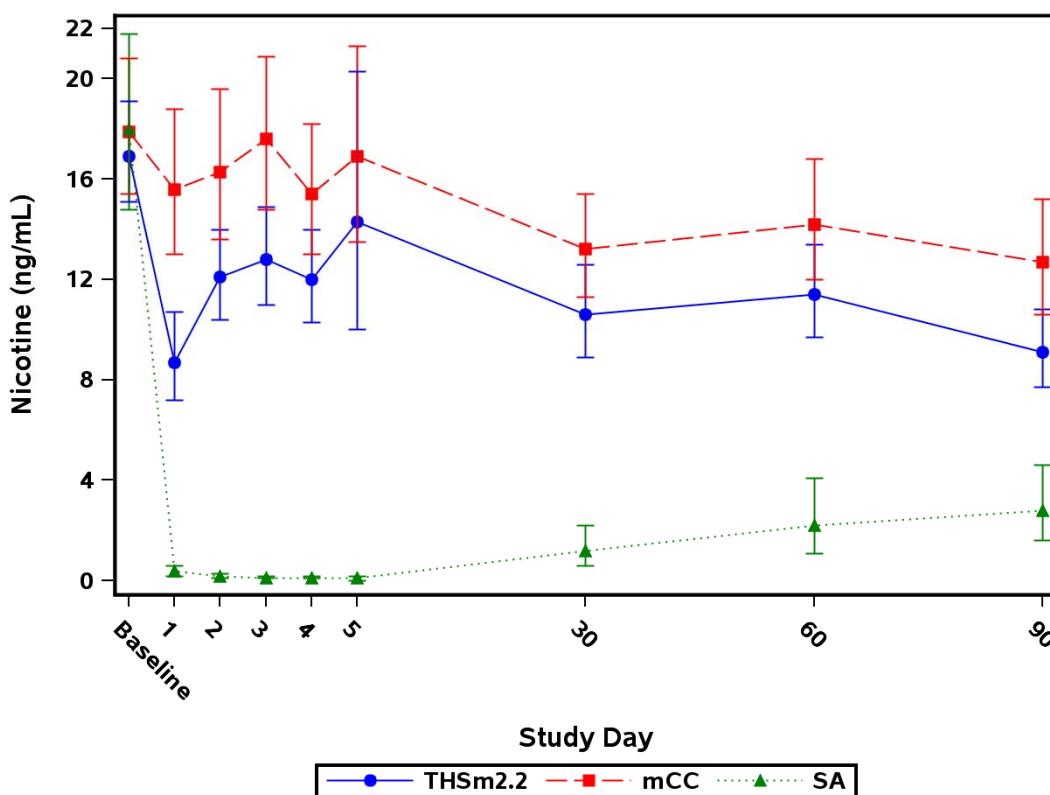
Note: Evening result is presented for Day 5.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.19.1

Study ID: ZRHM-REXA-08-US Program: f\_pnic\_pp.sas 21SEP15 Status: Final (Page 2 of 2)

**Figure 15.1.2.1.2 Plasma Nicotine and Cotinine Profile (ng/mL) Geometric Mean and 95% CI – FAS**

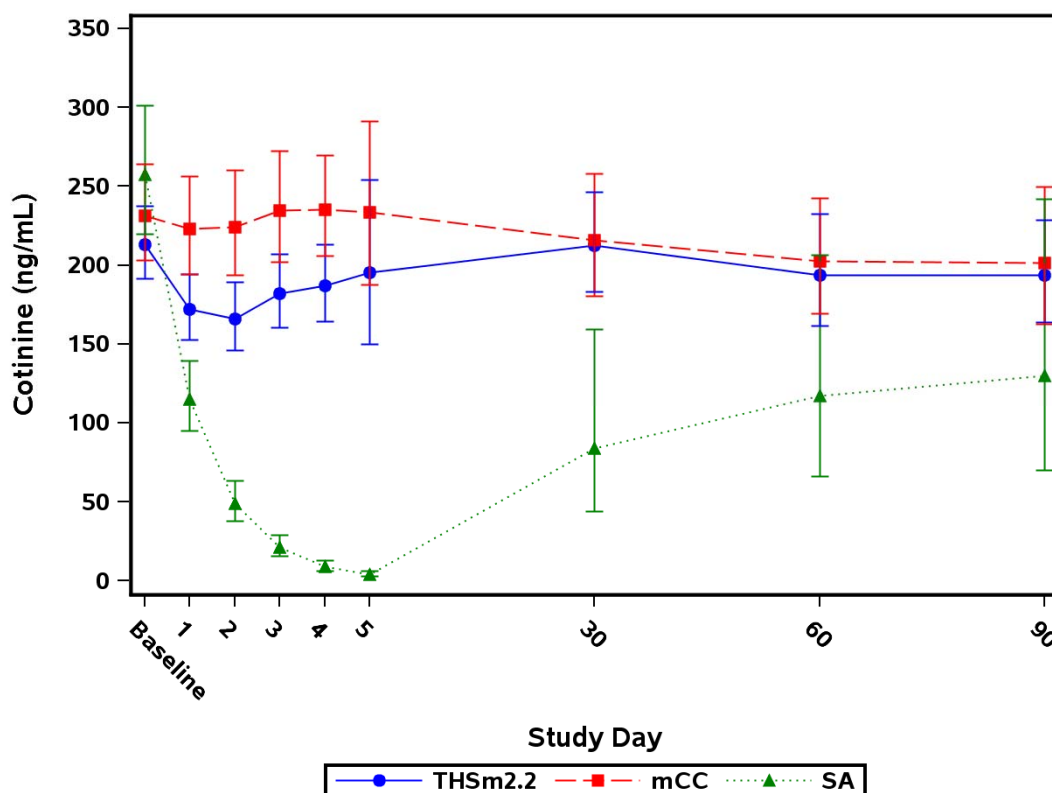
Note: Evening result is presented for Day 5.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.19.2

Study ID: ZRHM-REXA-08-US Program: f\_pnic\_fas.sas 21SEP15 Status: Final (Page 1 of 2)

**Figure 15.1.2.1.2 Plasma Nicotine and Cotinine Profile (ng/mL) Geometric Mean and 95% CI – FAS**

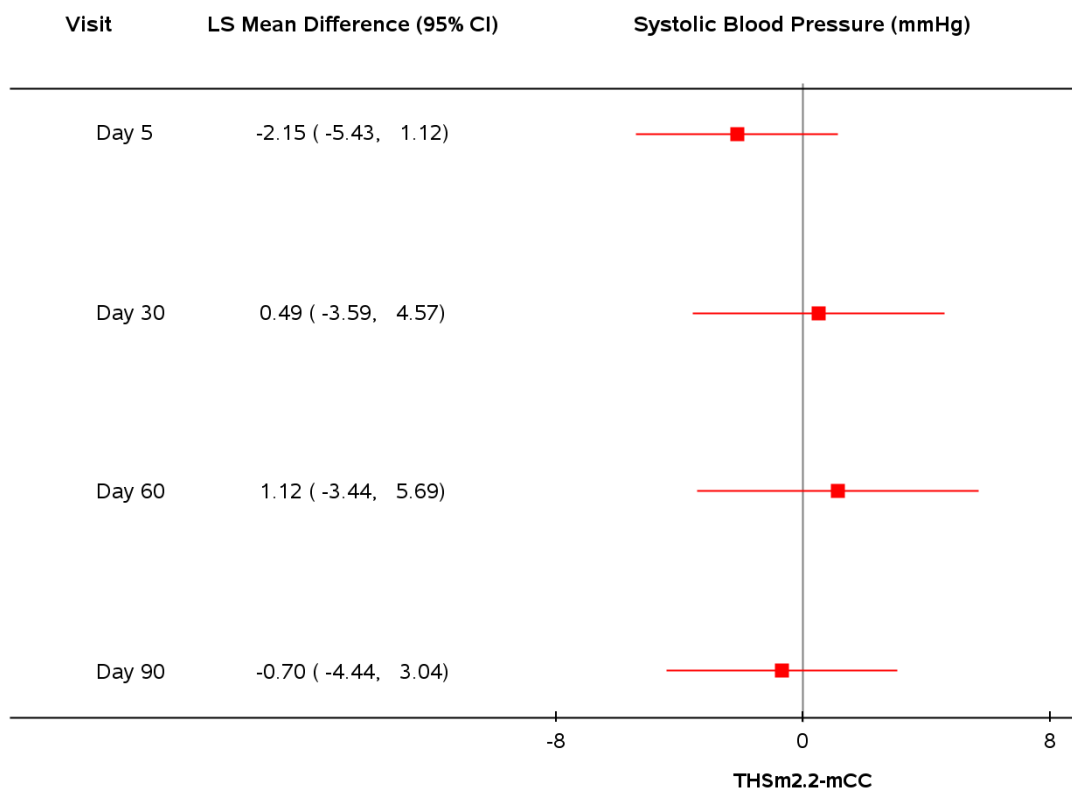
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Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Appendix 15.2.4.19.2

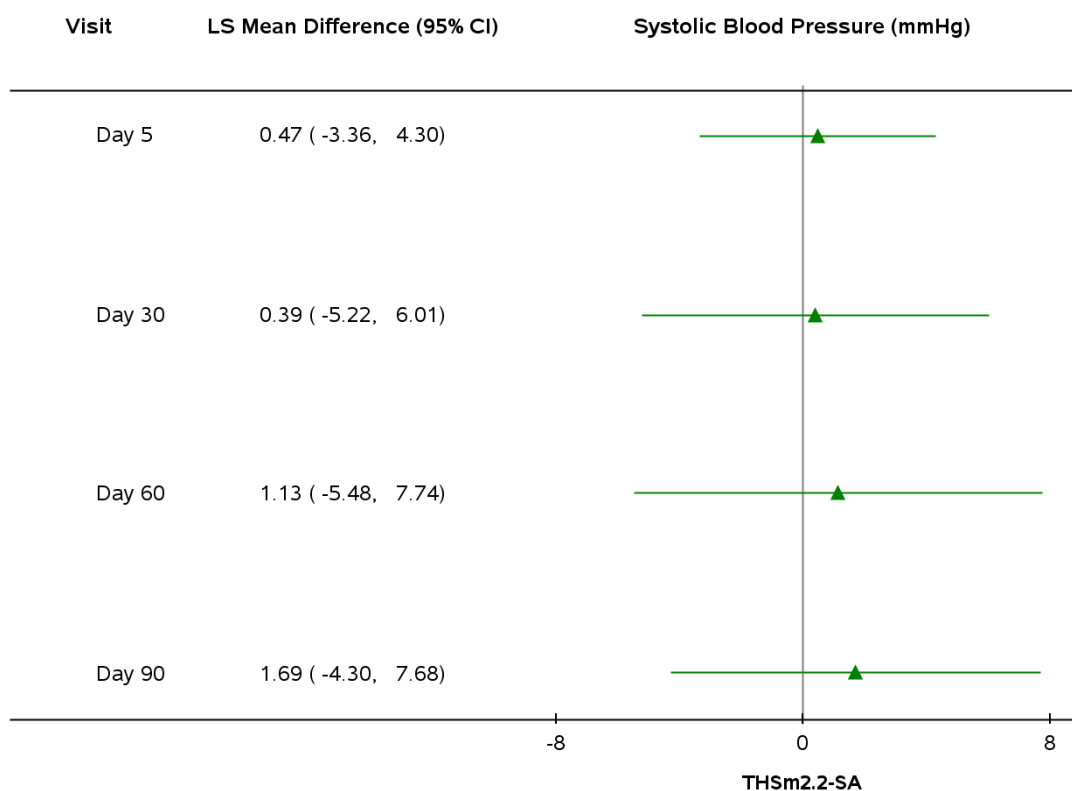
Study ID: ZRHM-REXA-08-US Program: f\_pnic\_fas.sas 21SEP15 Status: Final (Page 2 of 2)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 1 of 50)

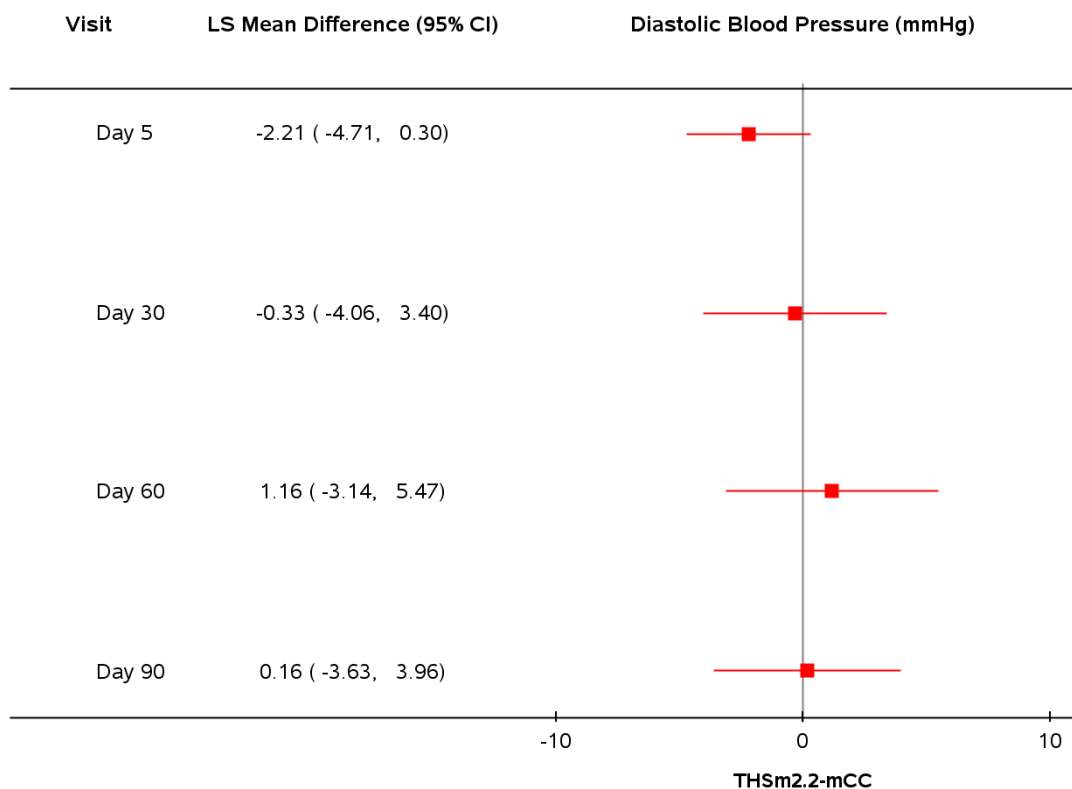
**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 2 of 50)

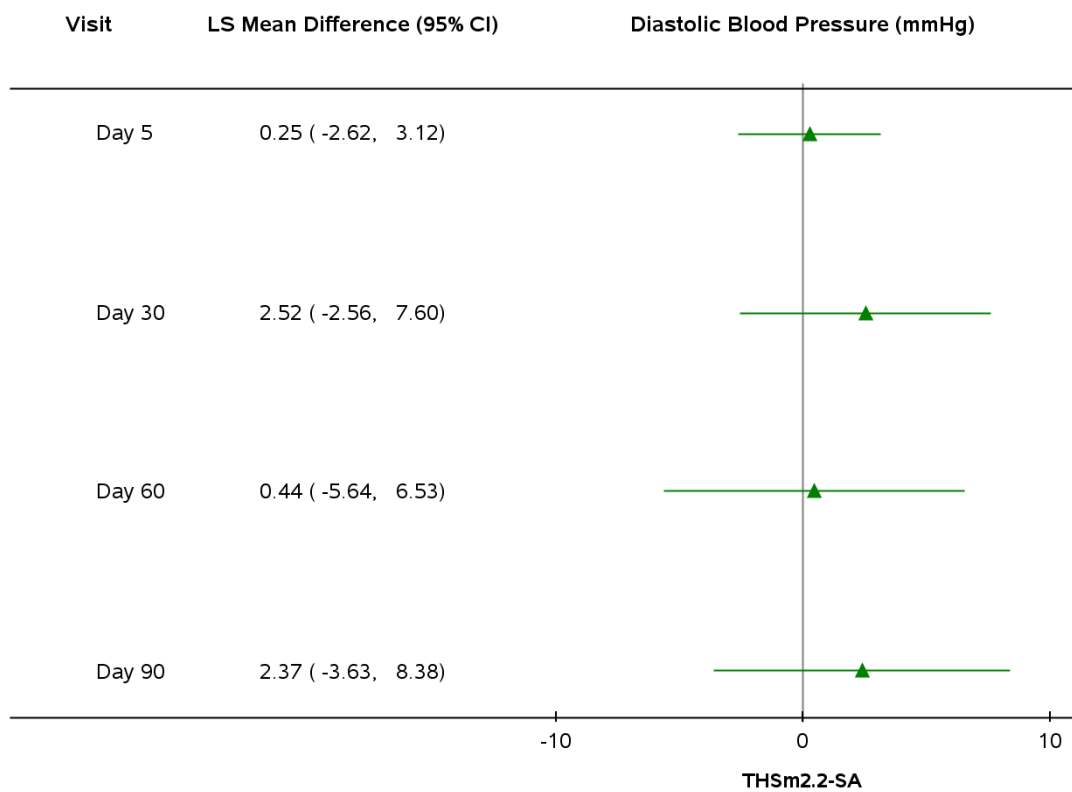


**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

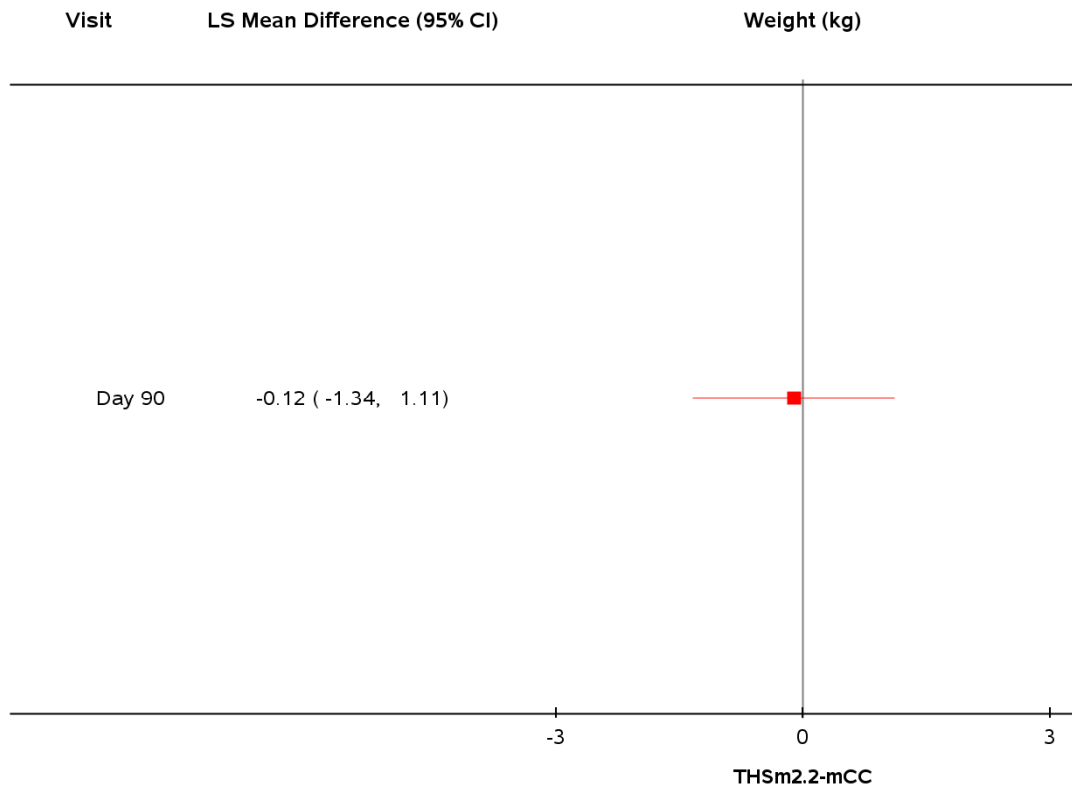
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 3 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

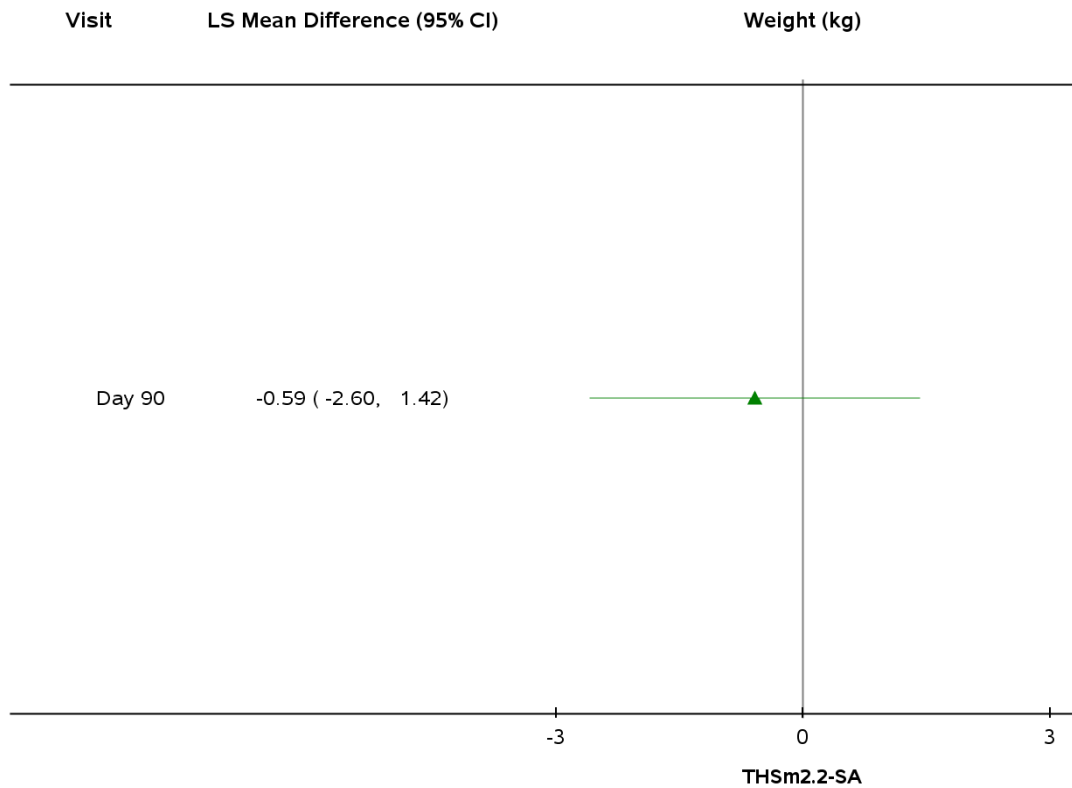
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 4 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

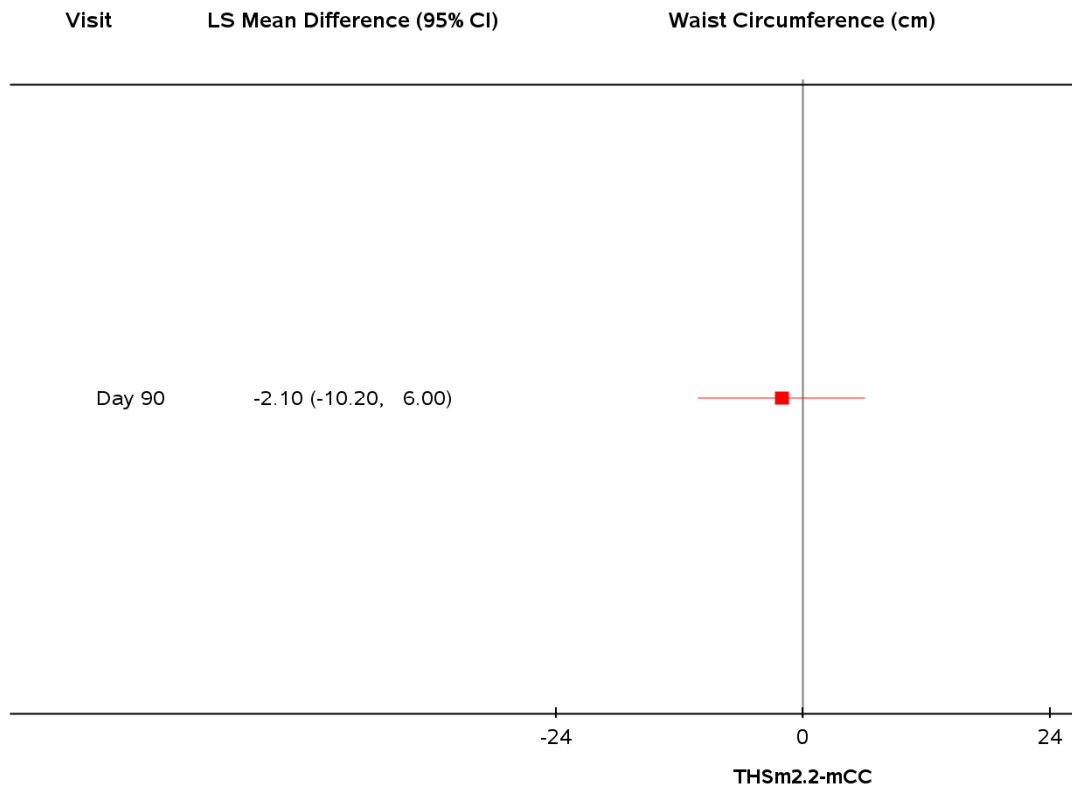
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 5 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

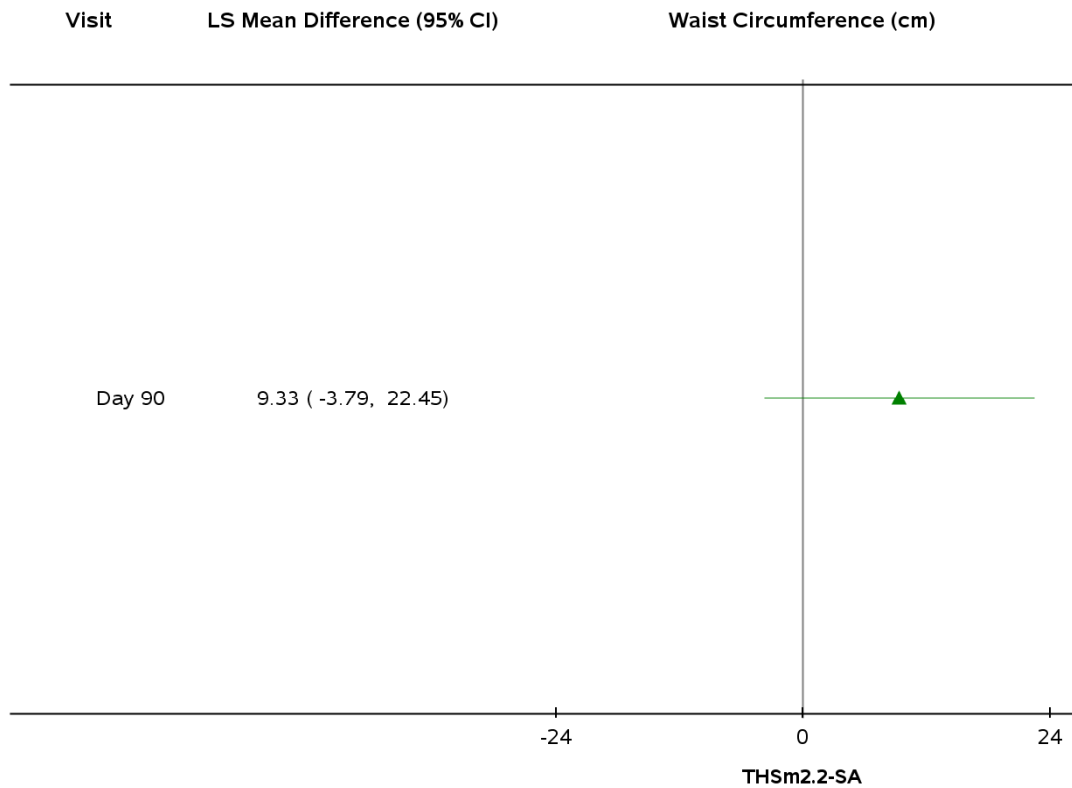
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 6 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

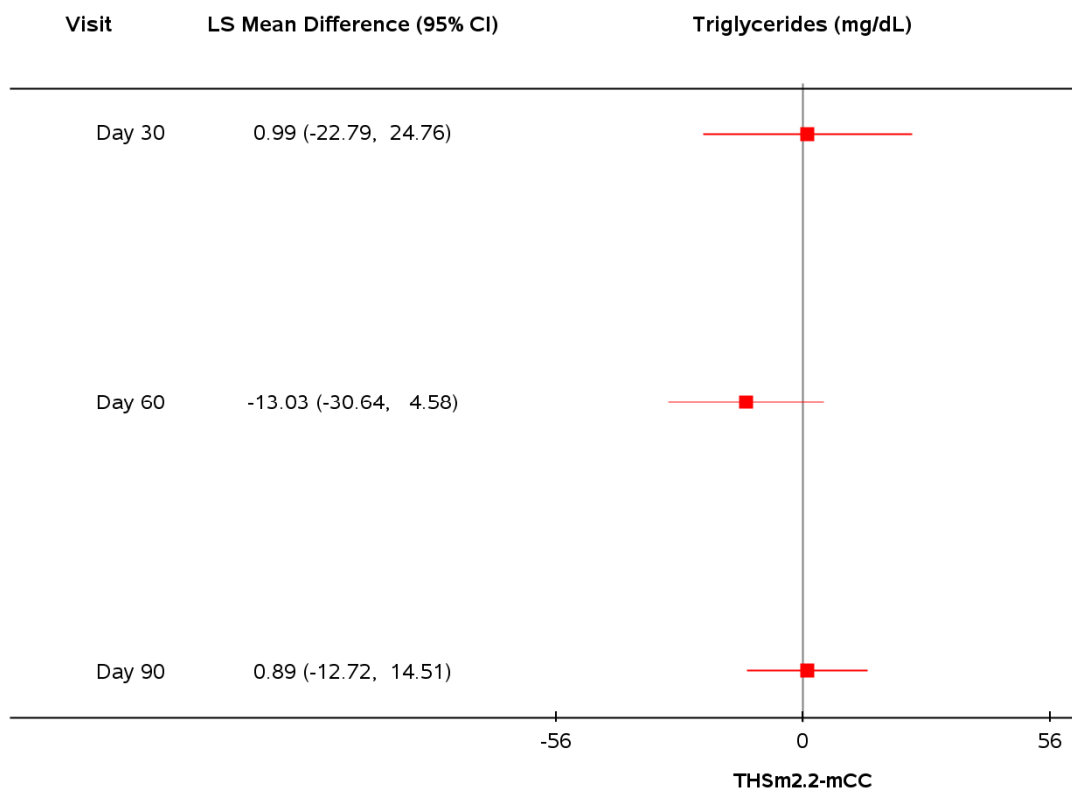
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 7 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

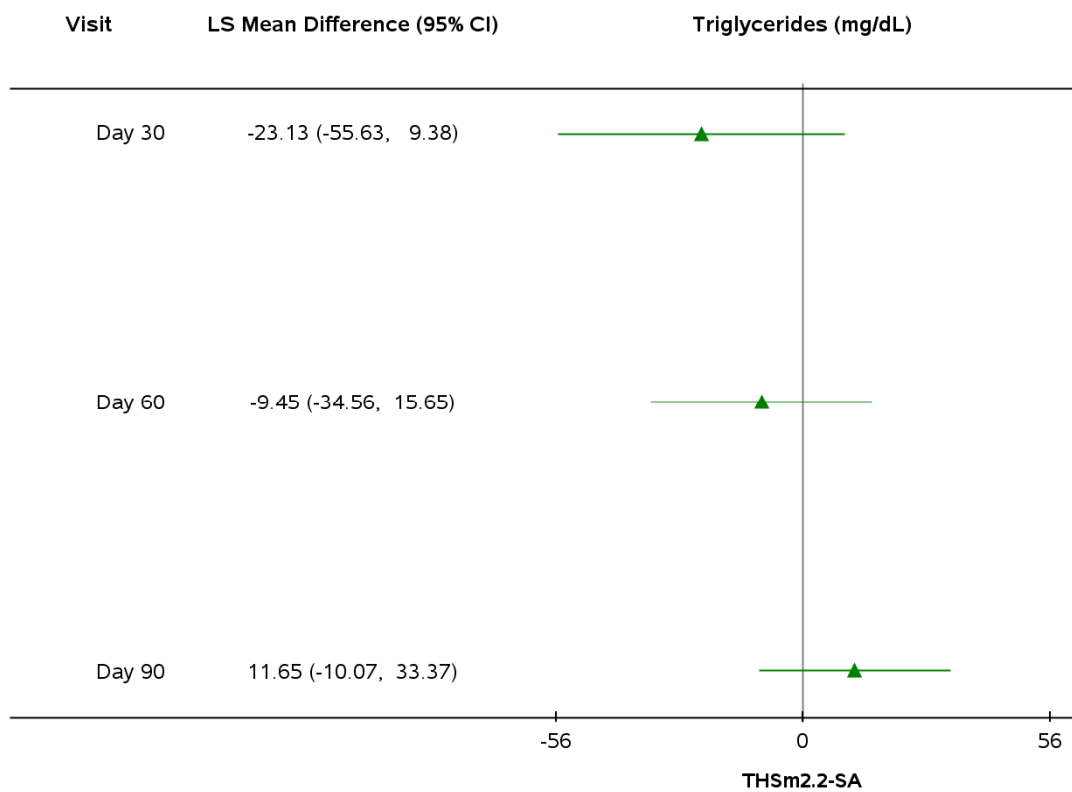
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 8 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 9 of 50)

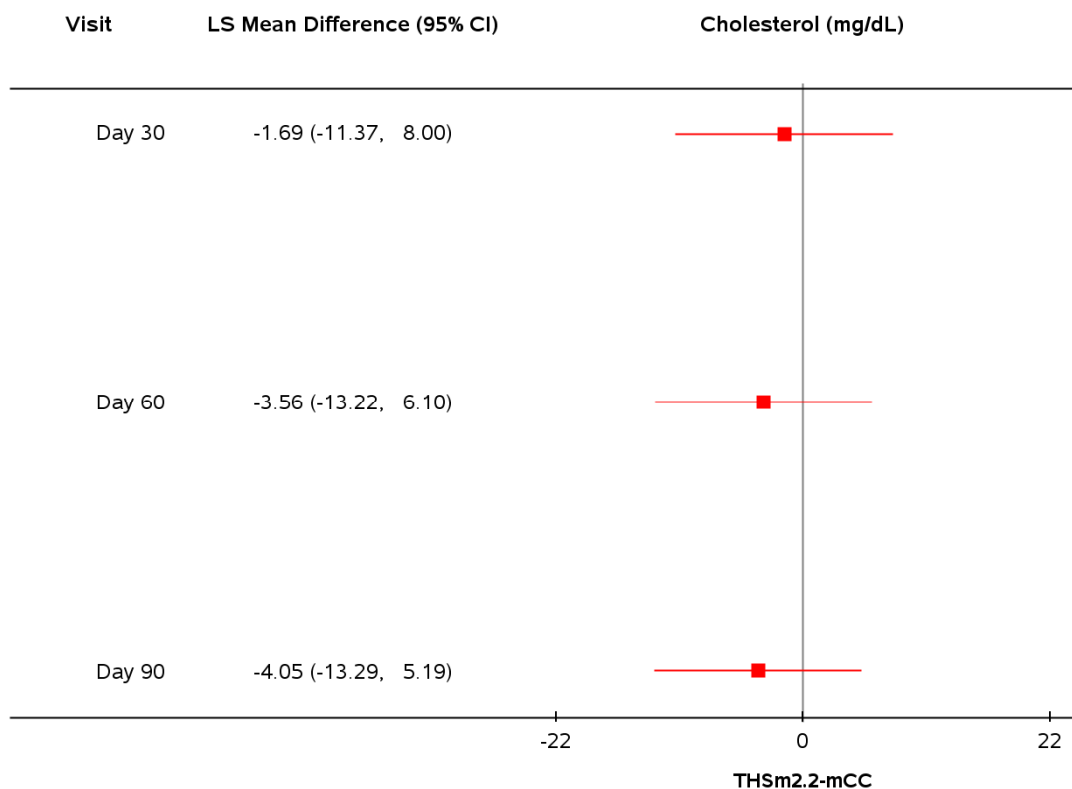
**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 10 of 50)

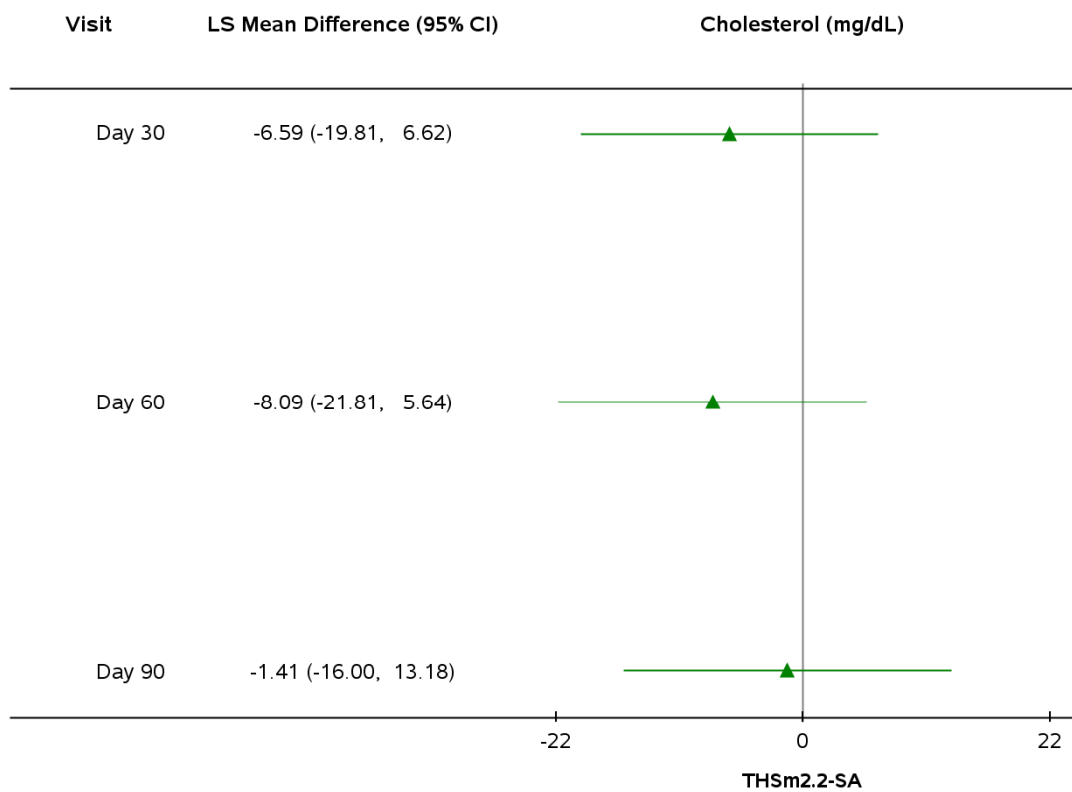


**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

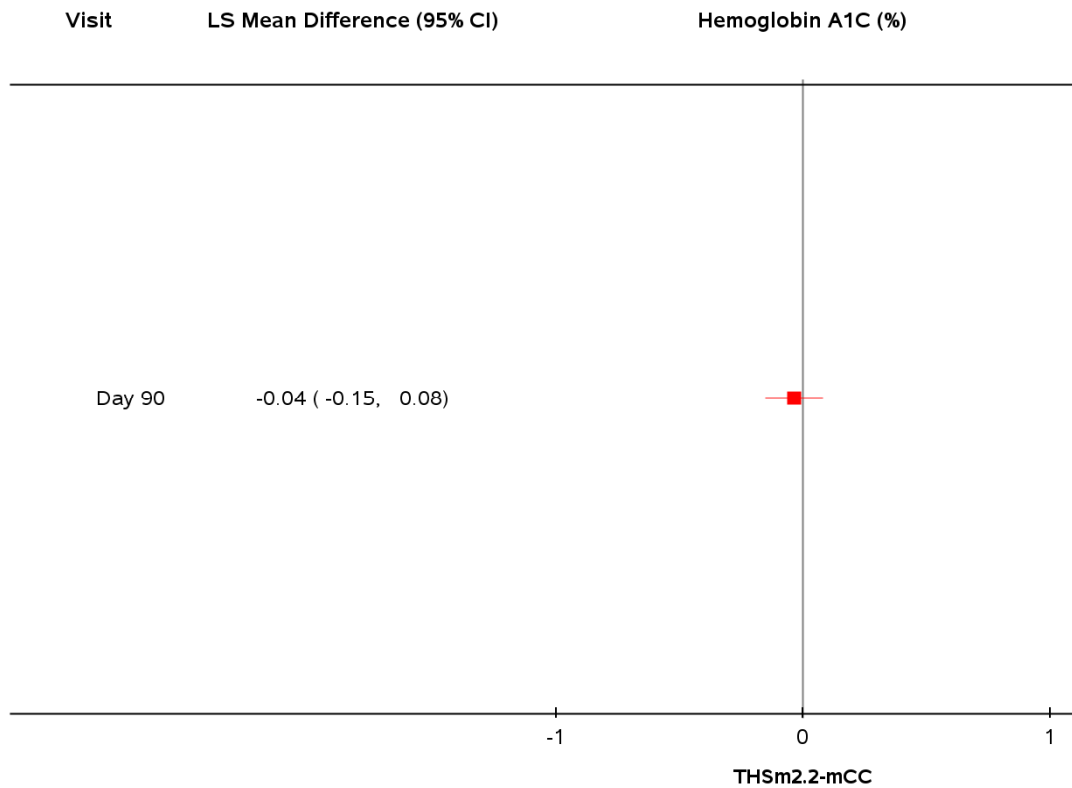
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 11 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

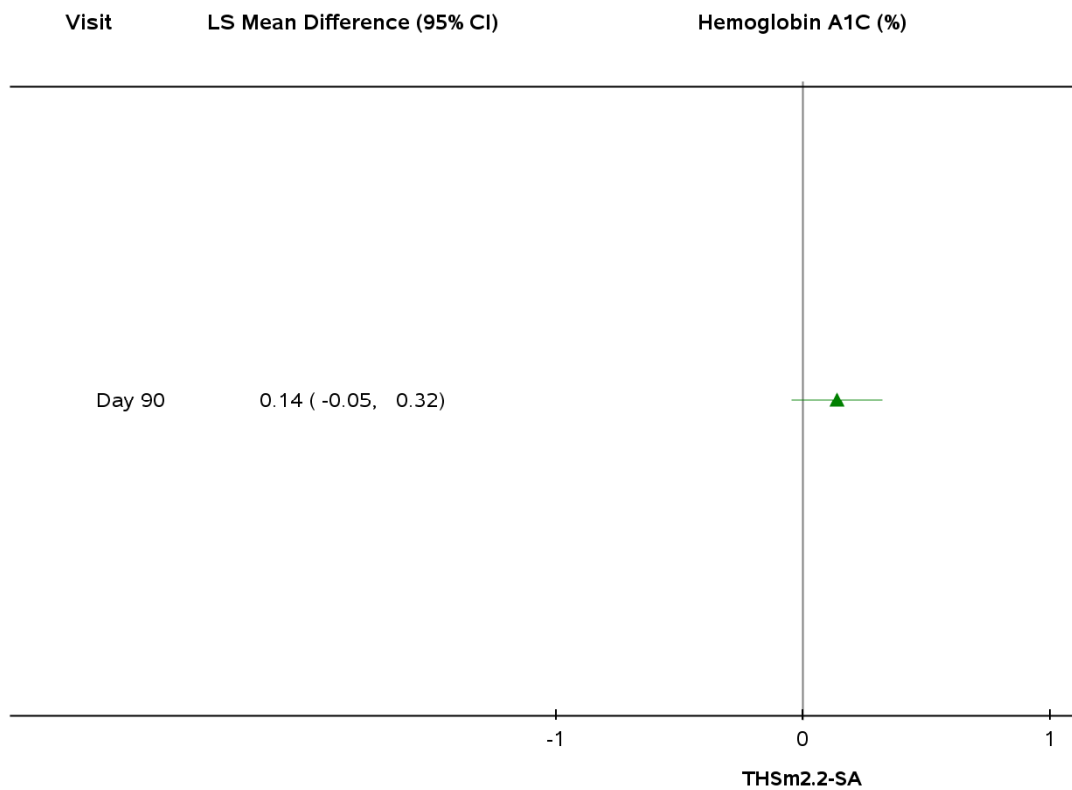
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 12 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

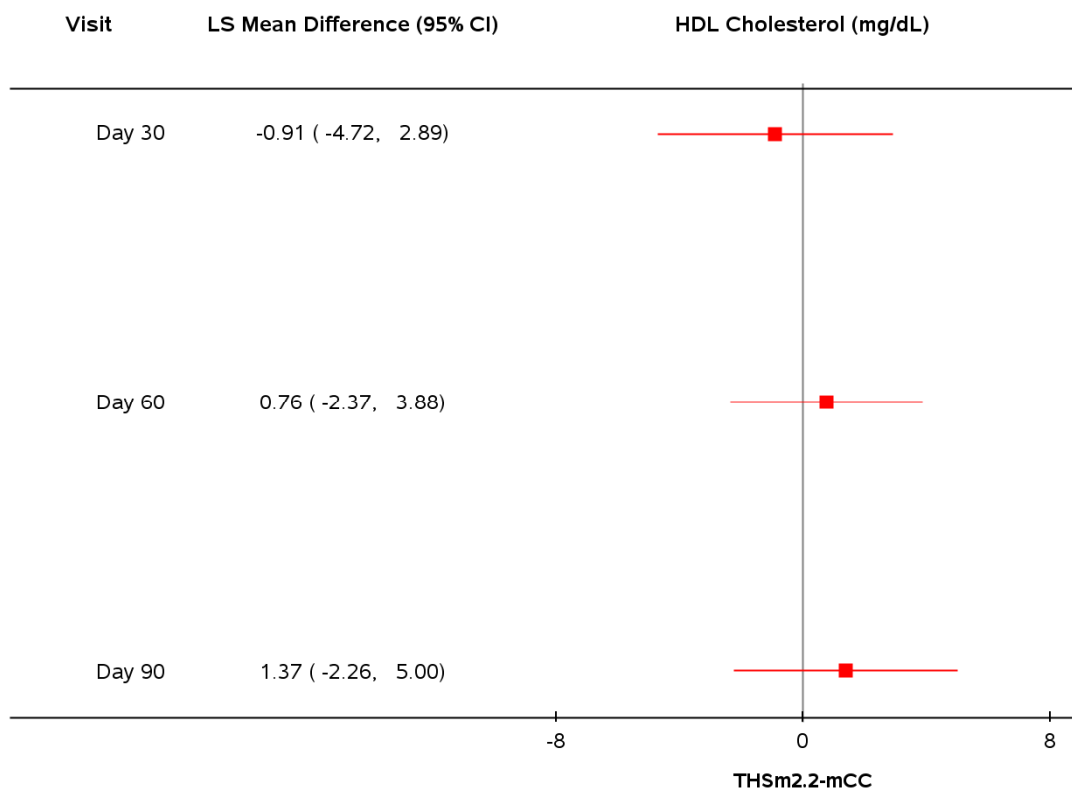
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 13 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

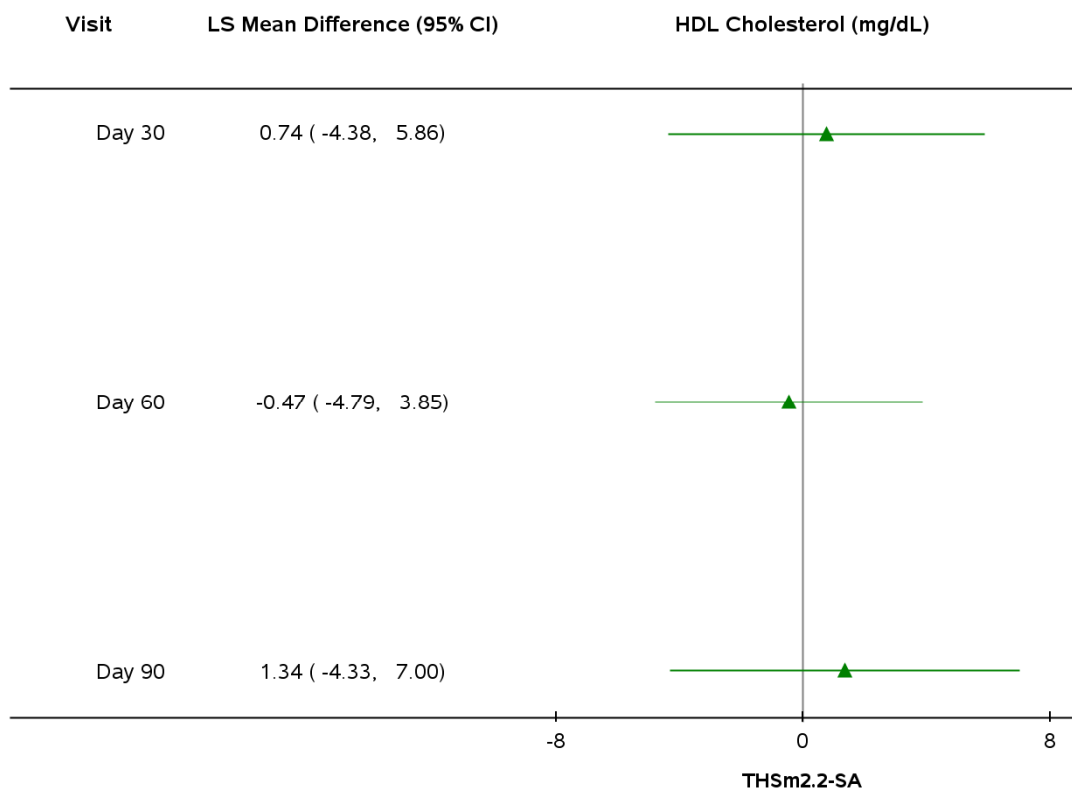
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 14 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

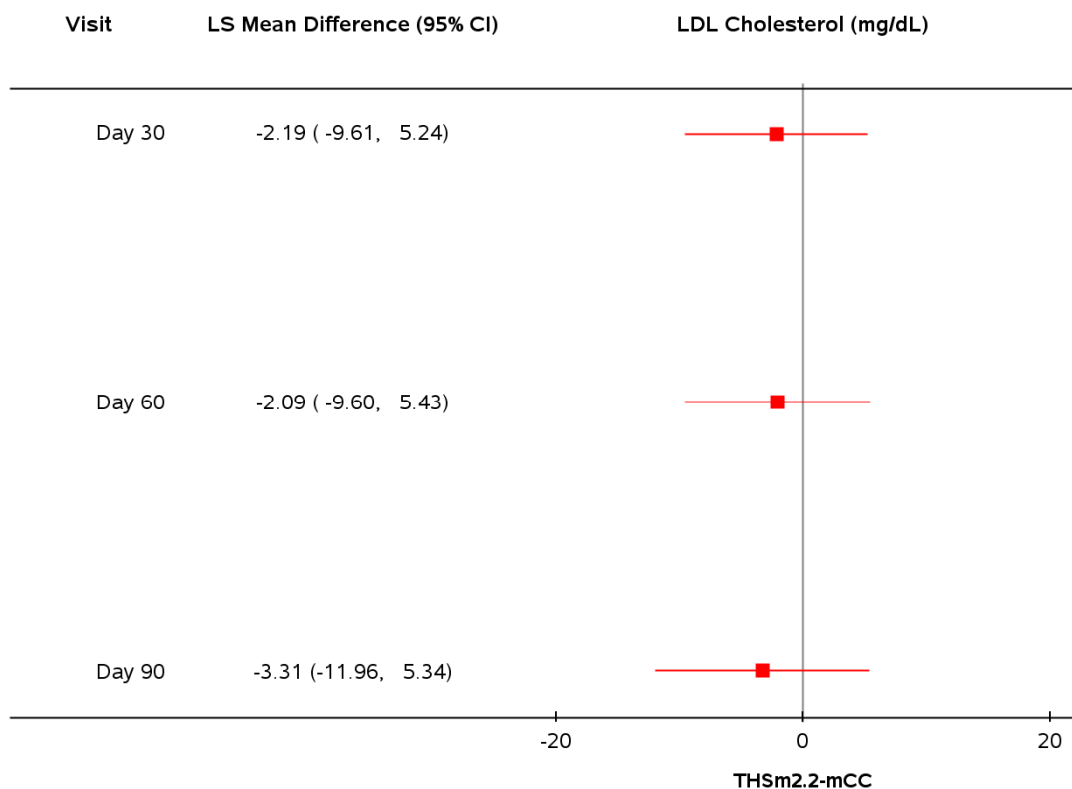
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 15 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

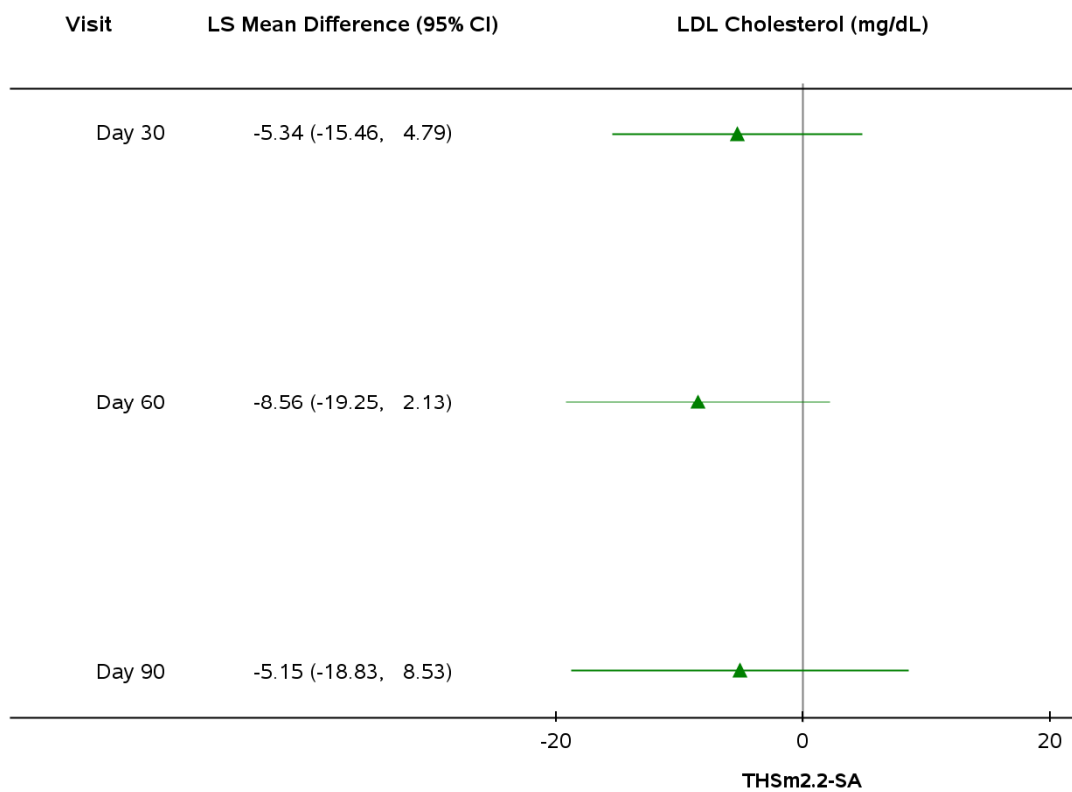
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 16 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 17 of 50)

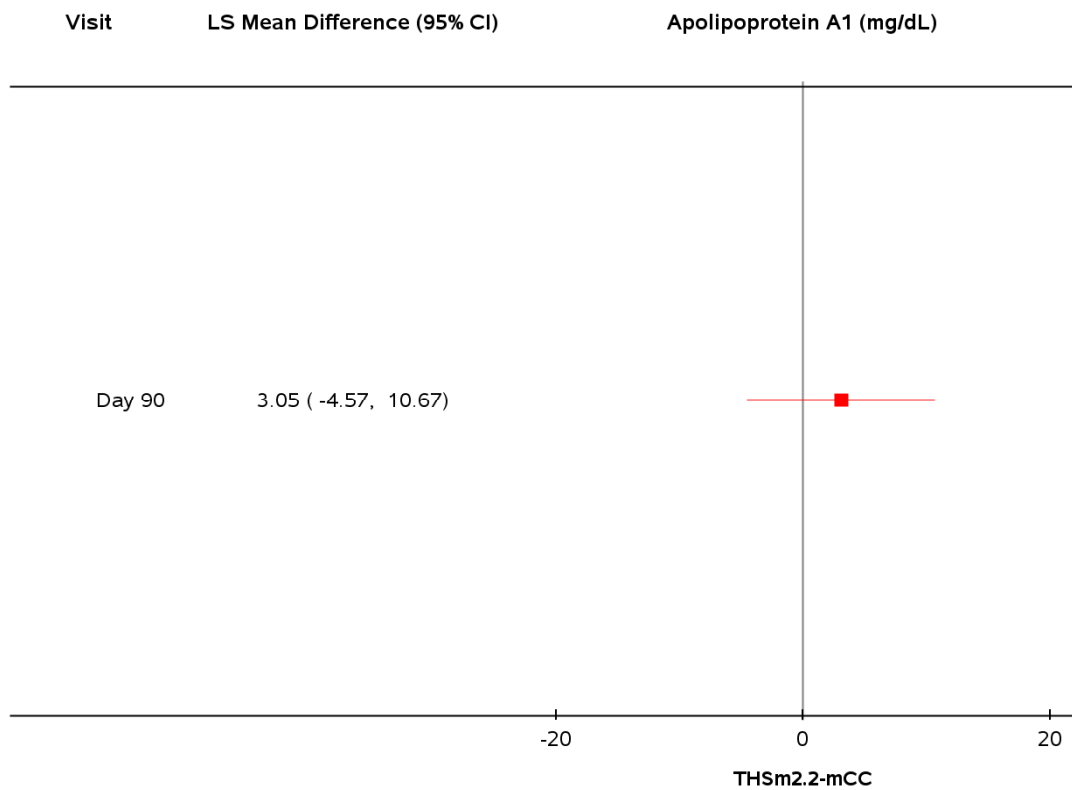
**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 18 of 50)

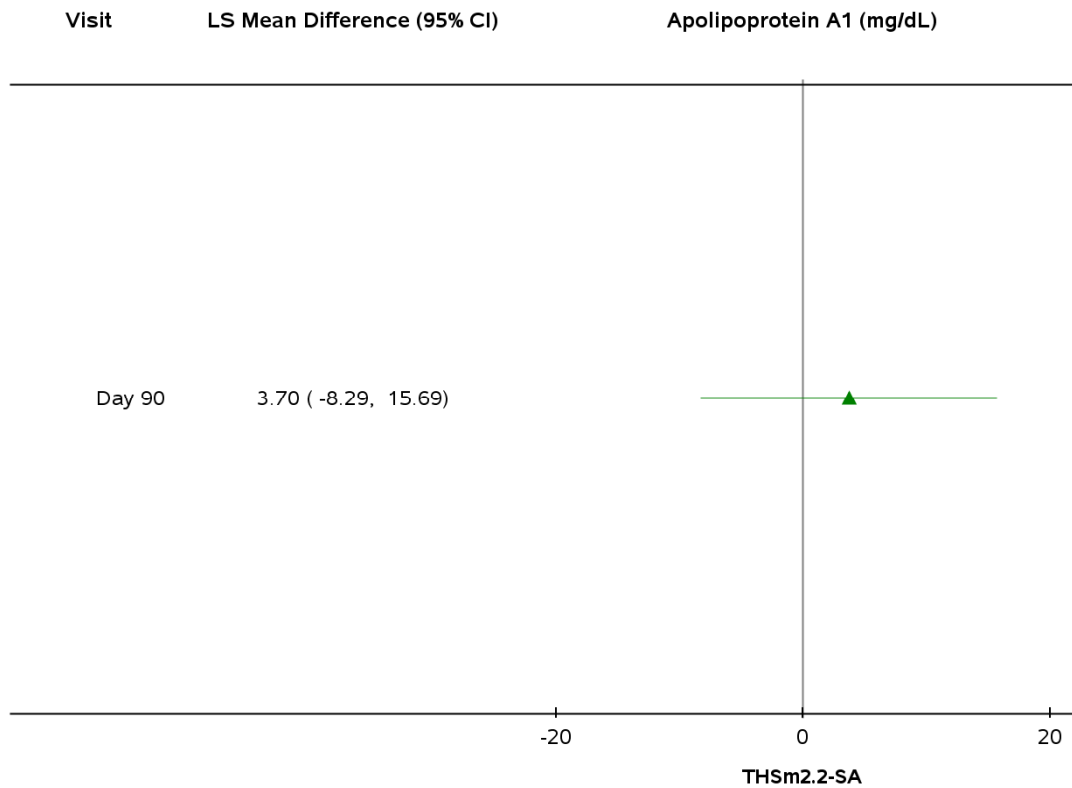


**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

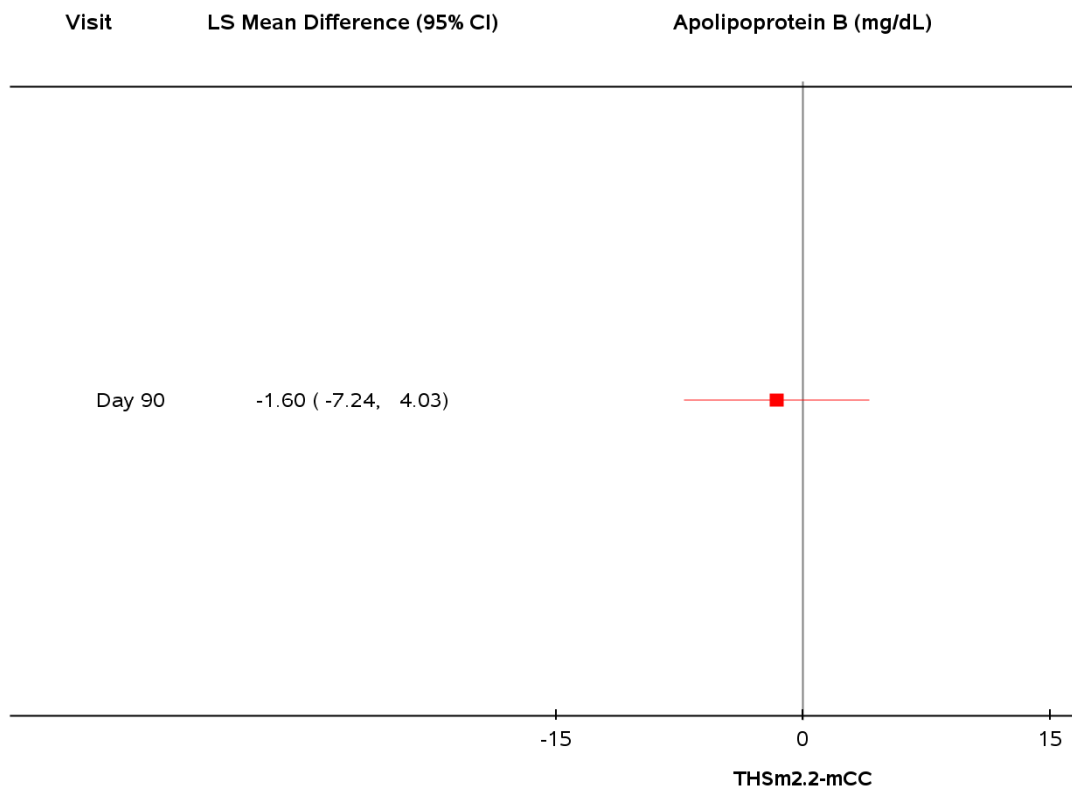
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 19 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

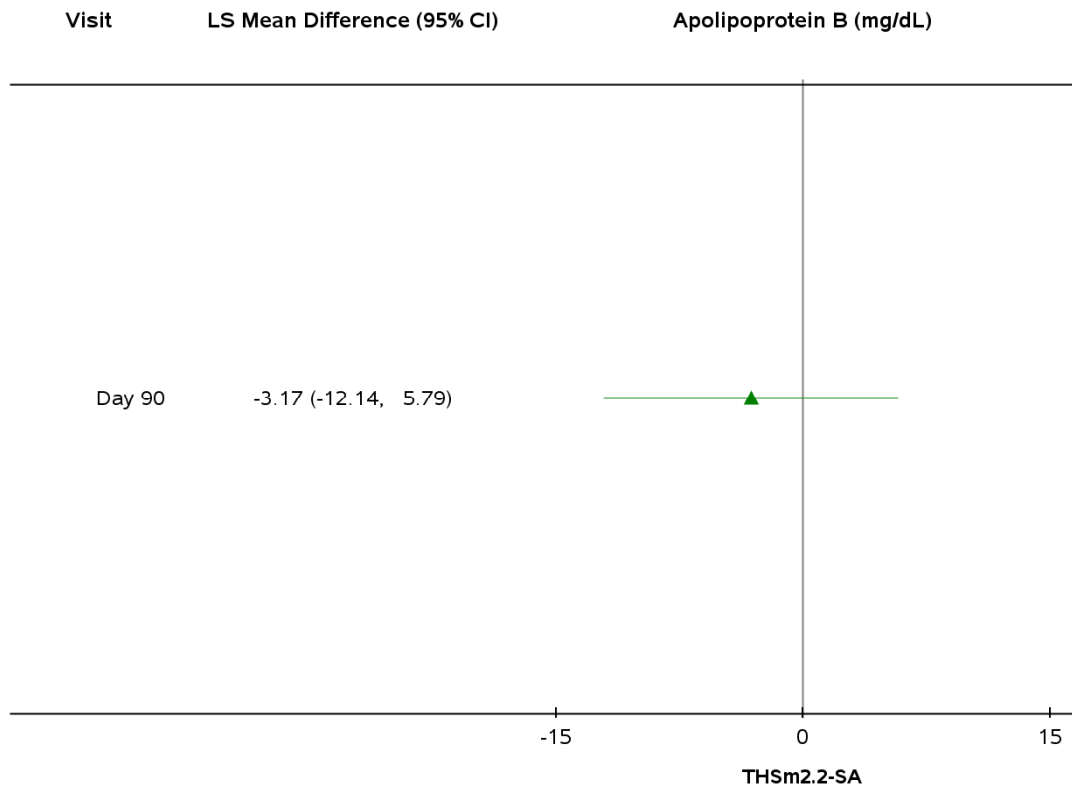
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 20 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

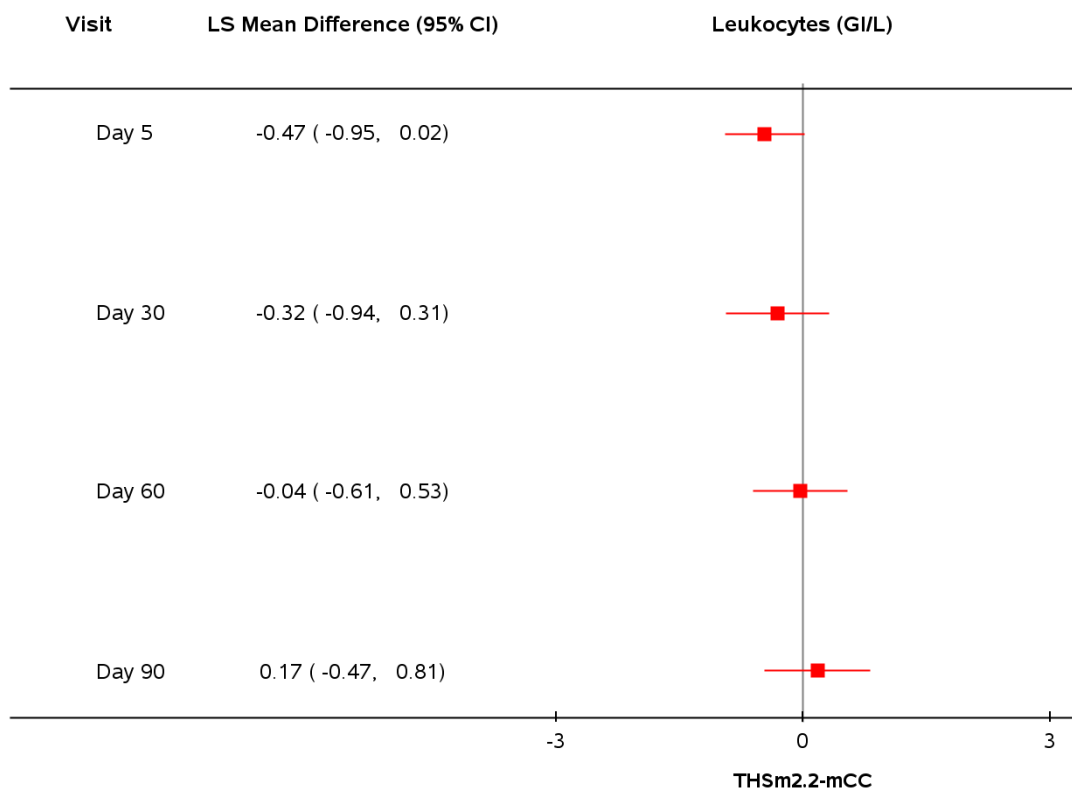
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 21 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

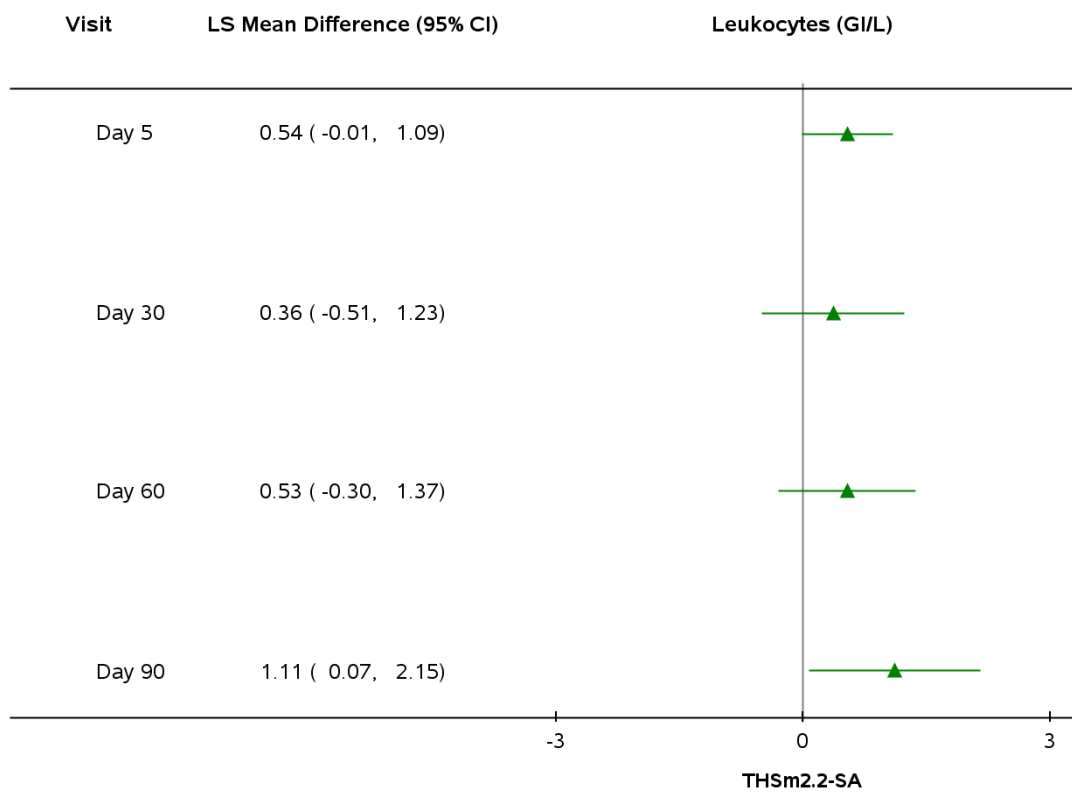
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 22 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

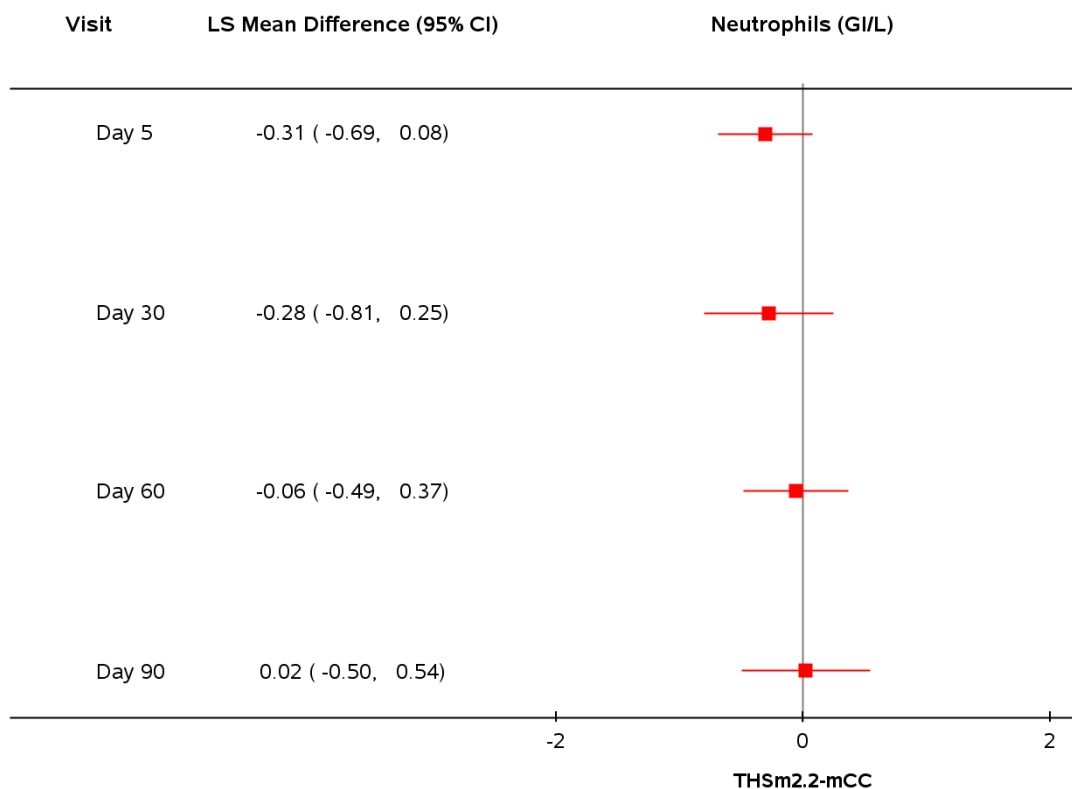
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 23 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

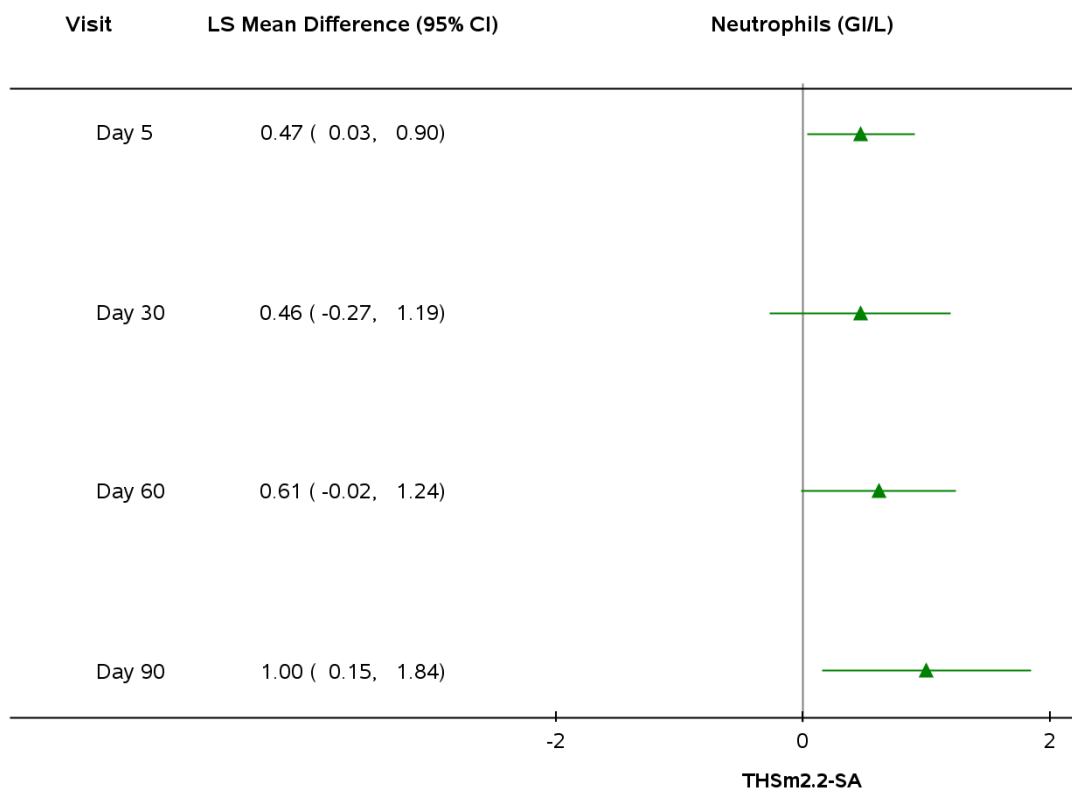
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 24 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 25 of 50)

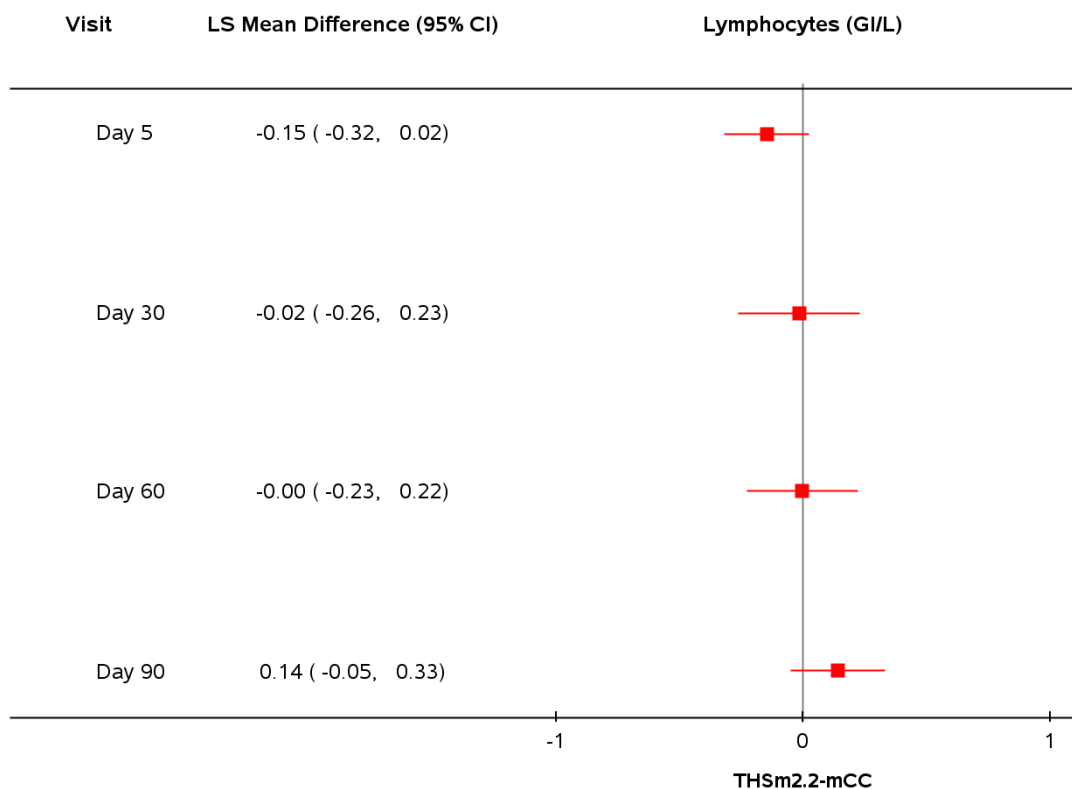
**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 26 of 50)

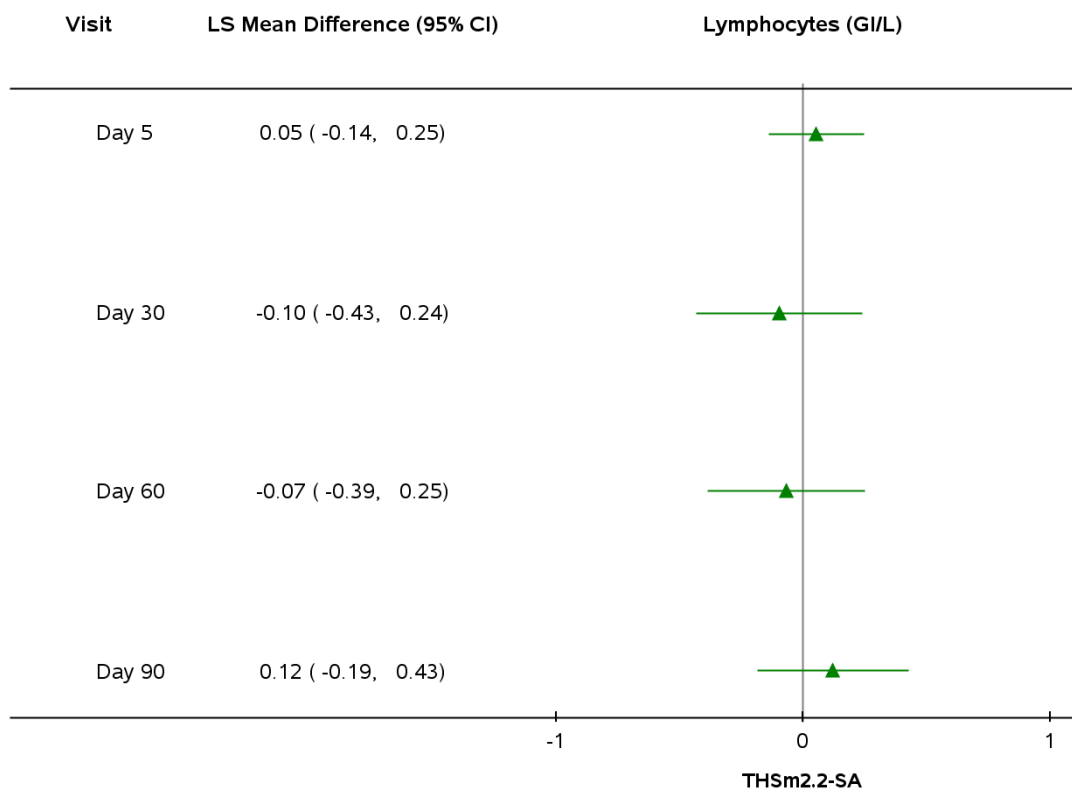


**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

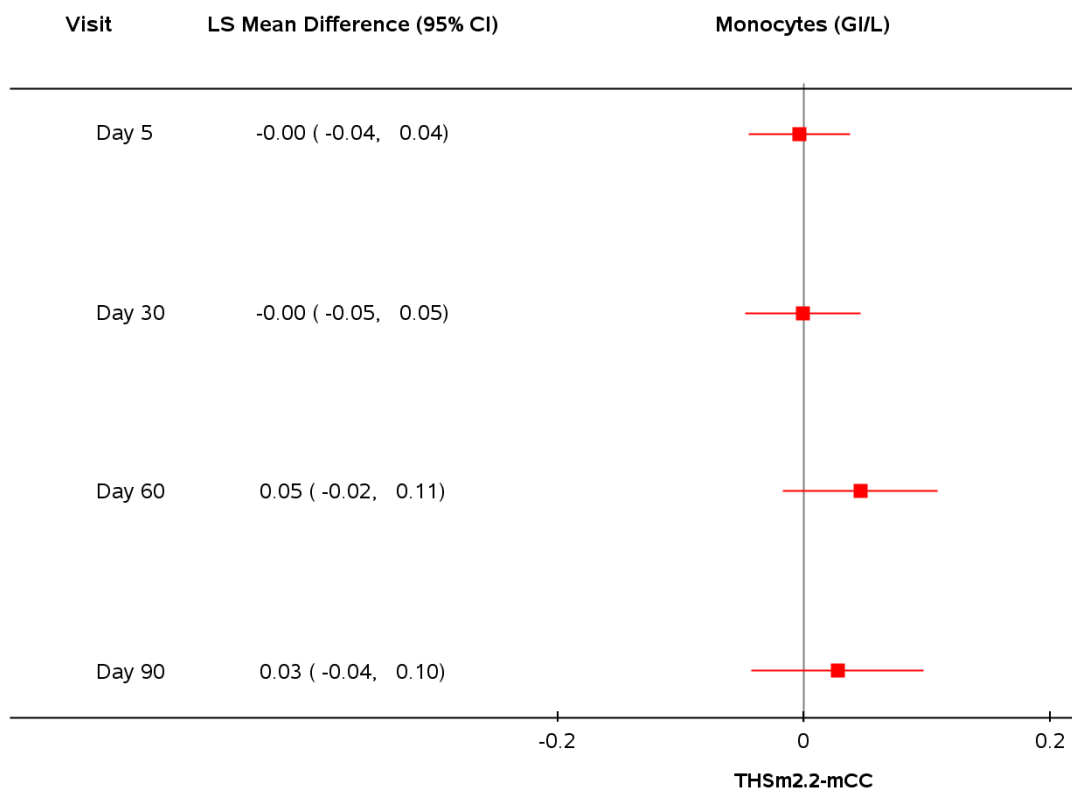
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 27 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

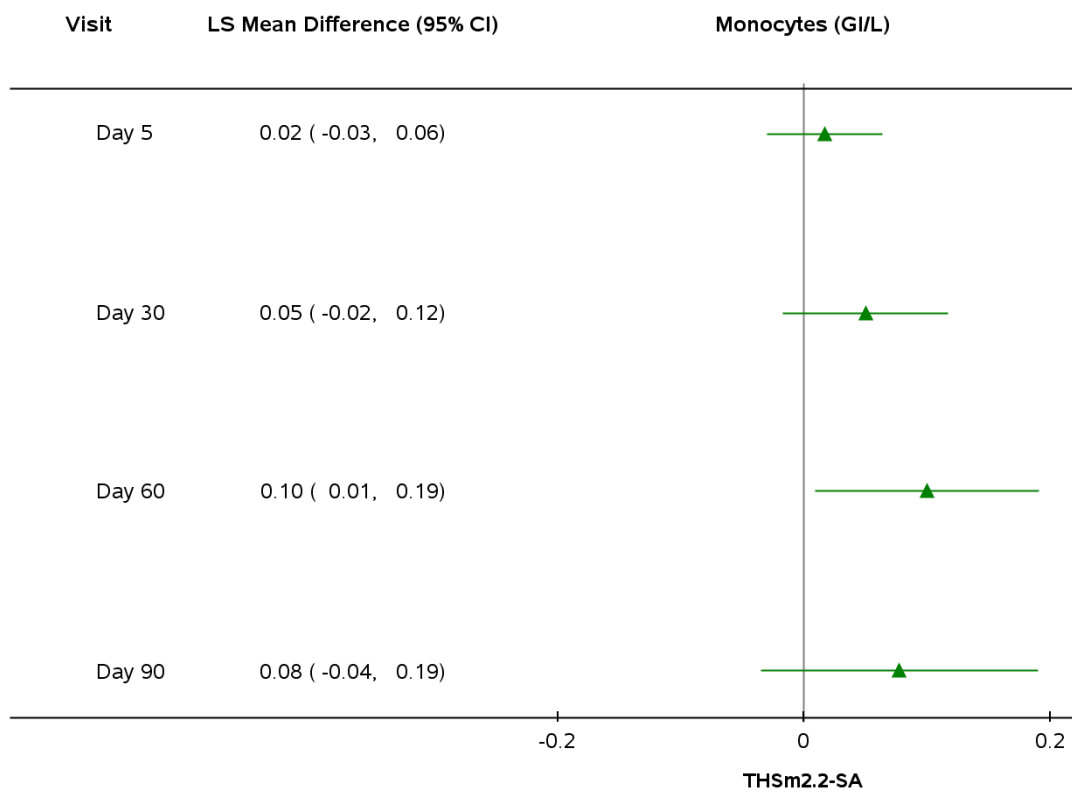
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 28 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

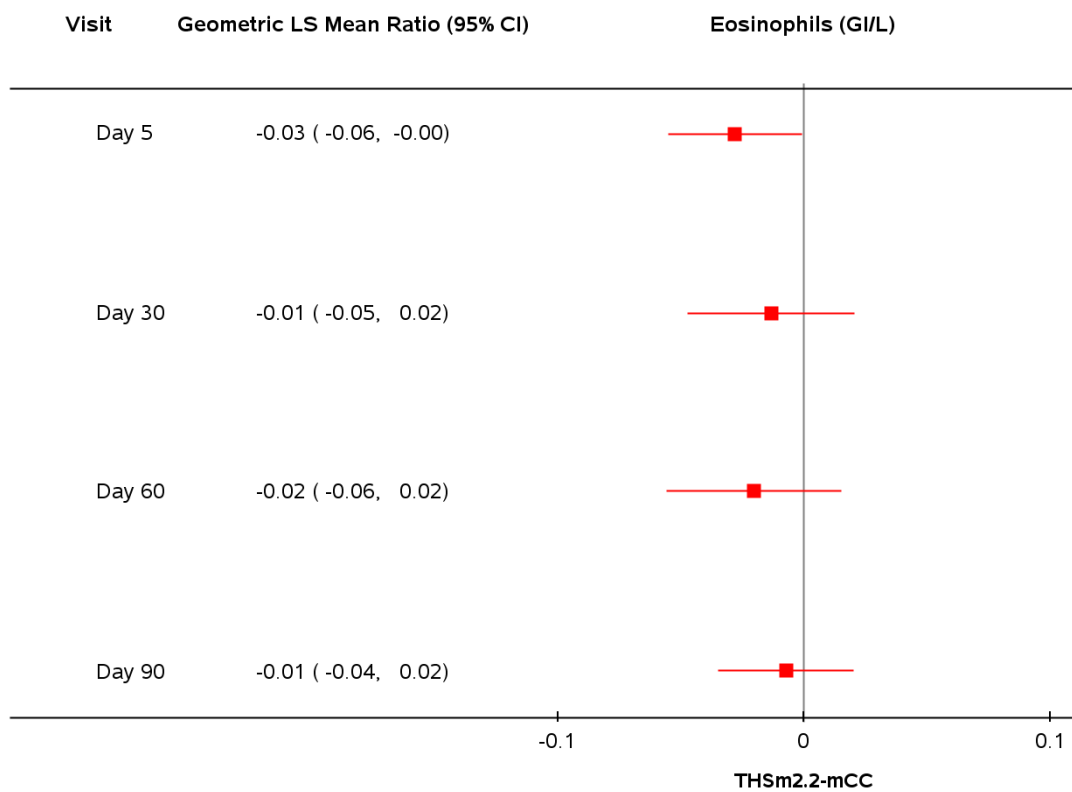
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 29 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

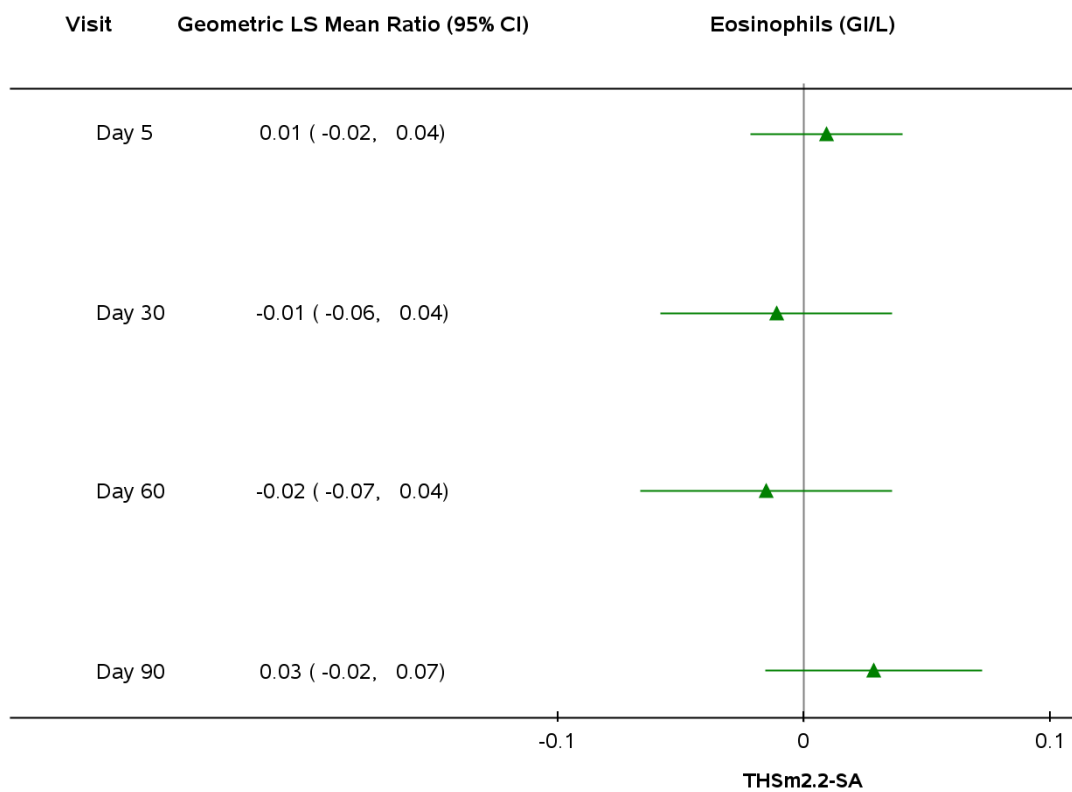
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 30 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

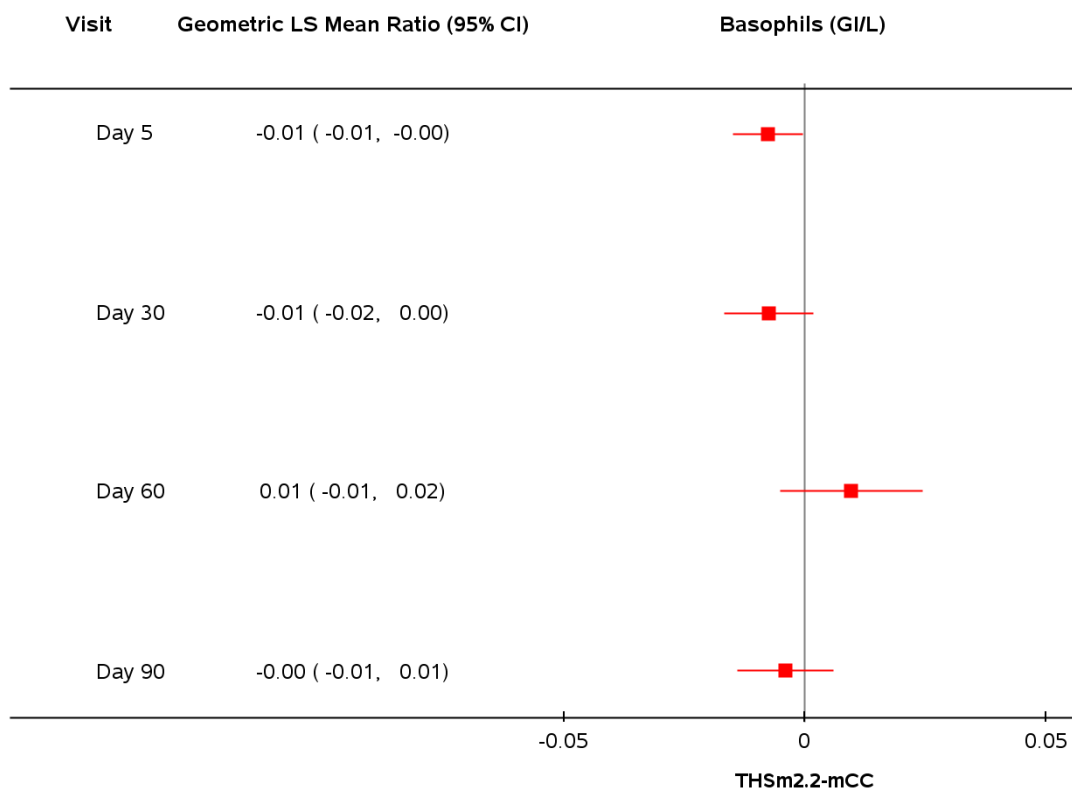
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 31 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

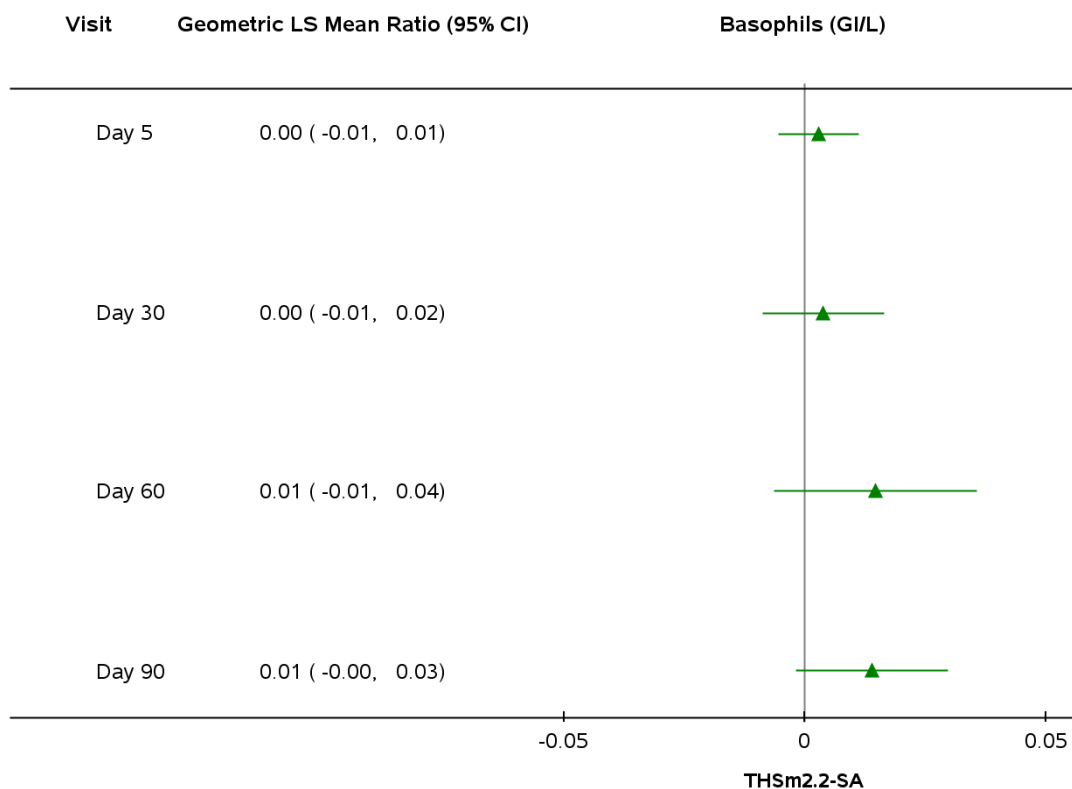
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 32 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 33 of 50)

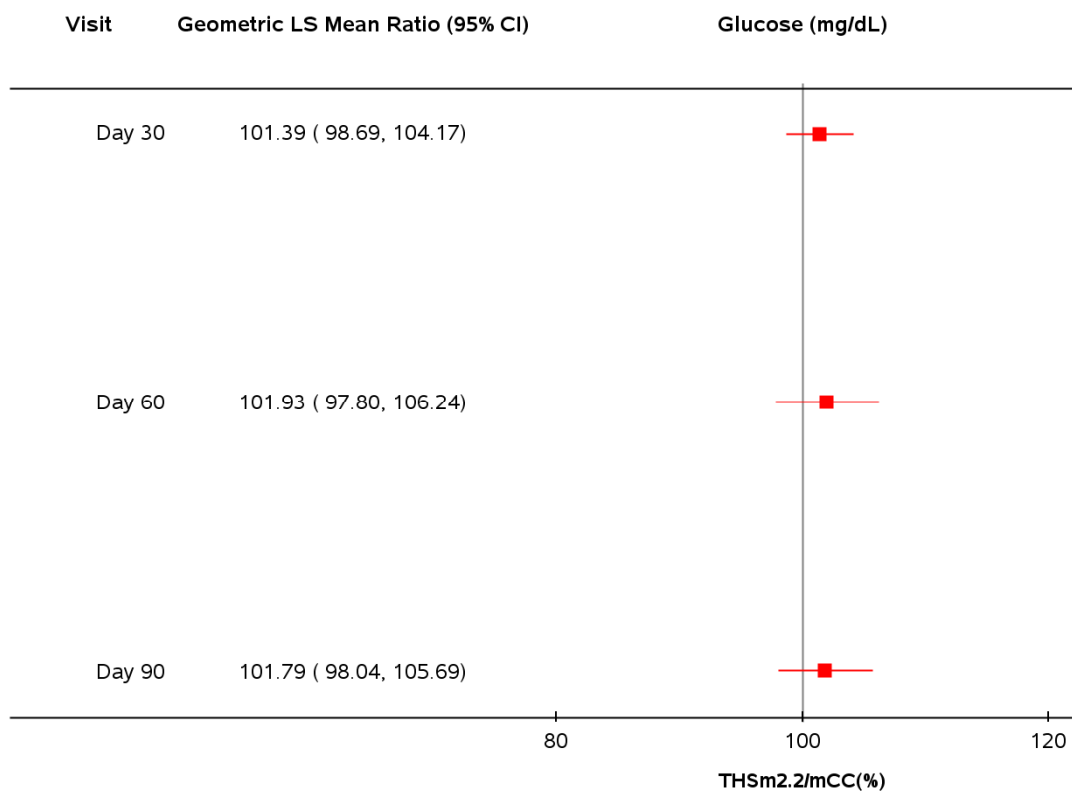
**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 34 of 50)

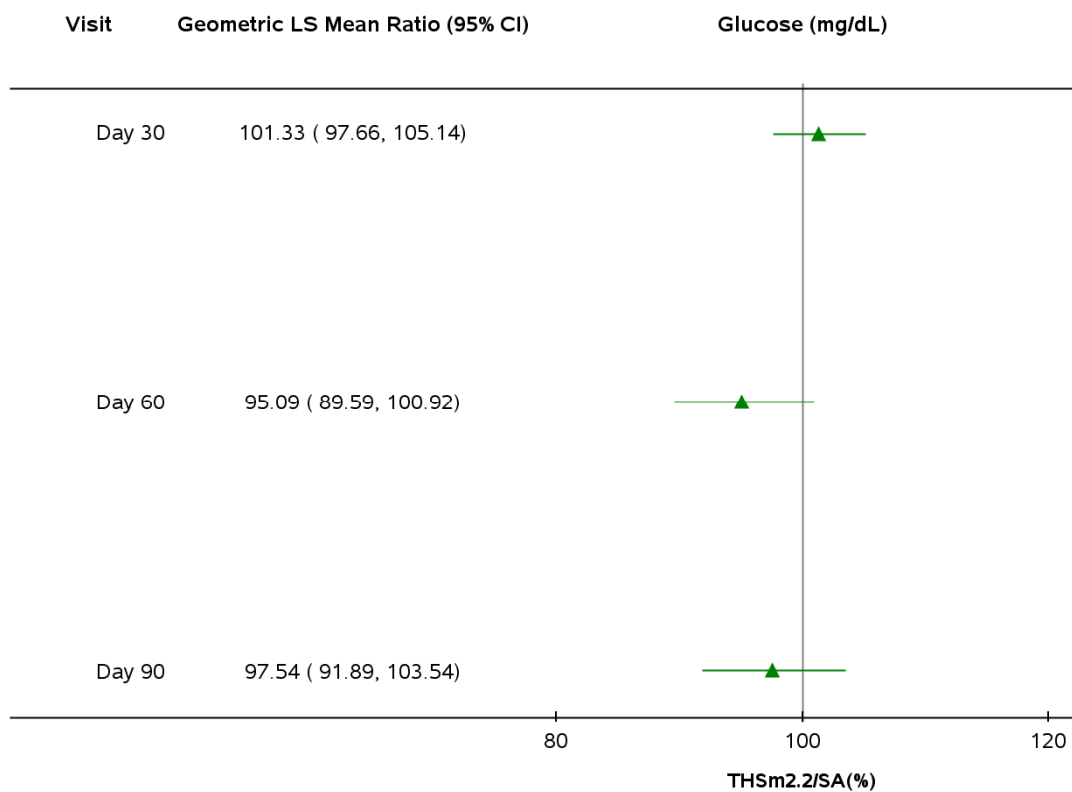


**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

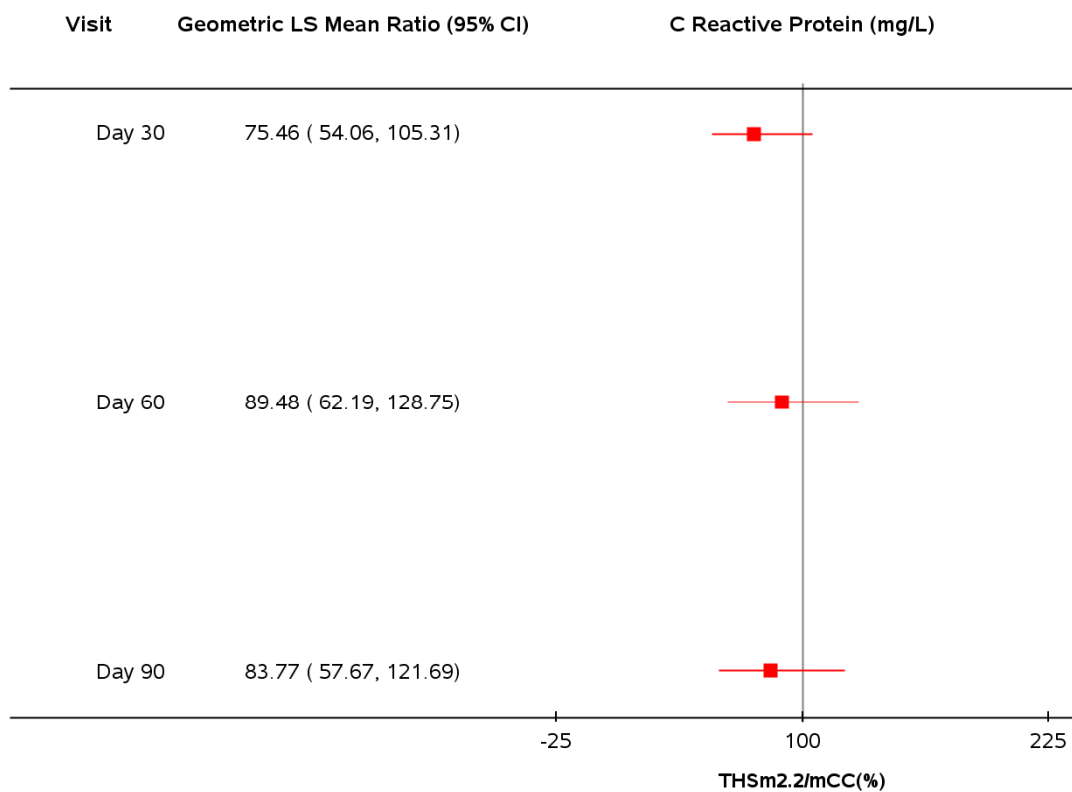
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 35 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

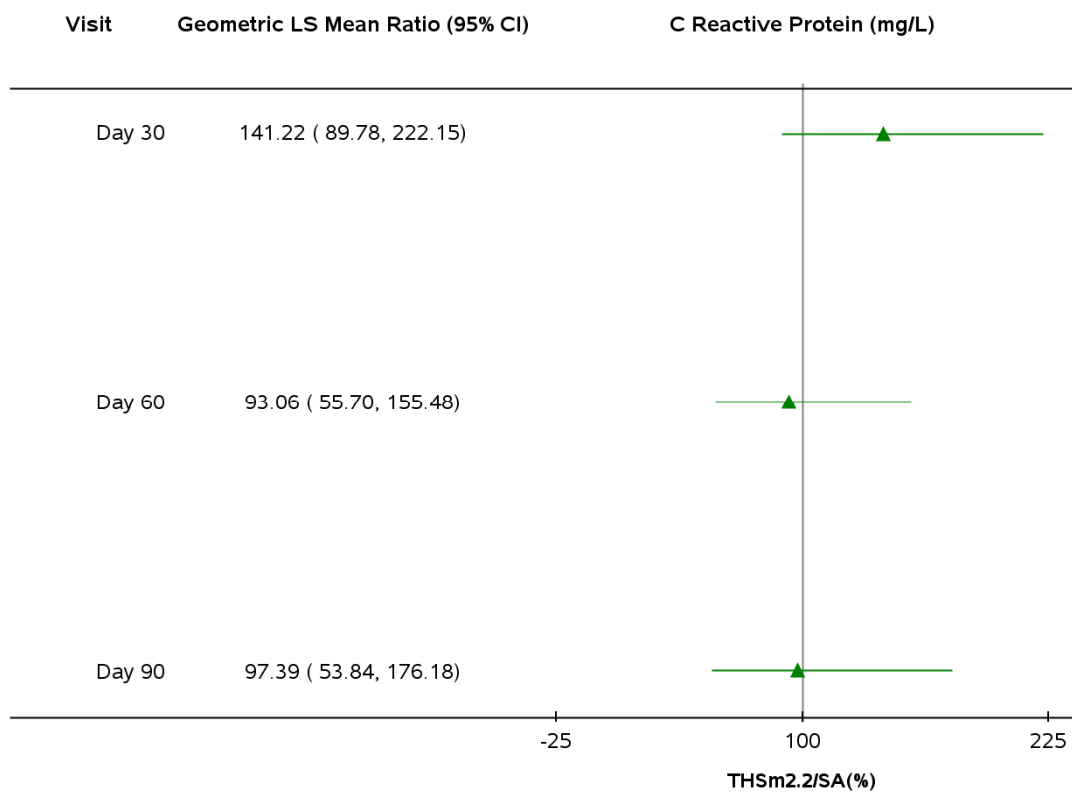
Study ID:ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 36 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

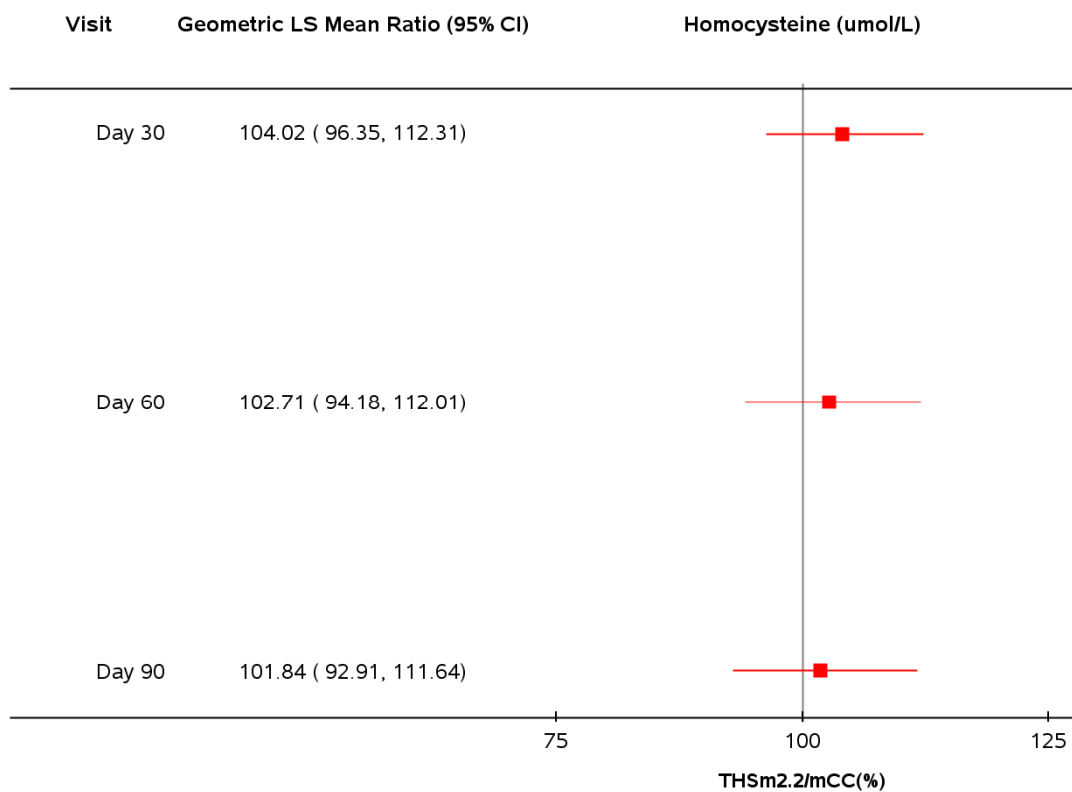
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 37 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

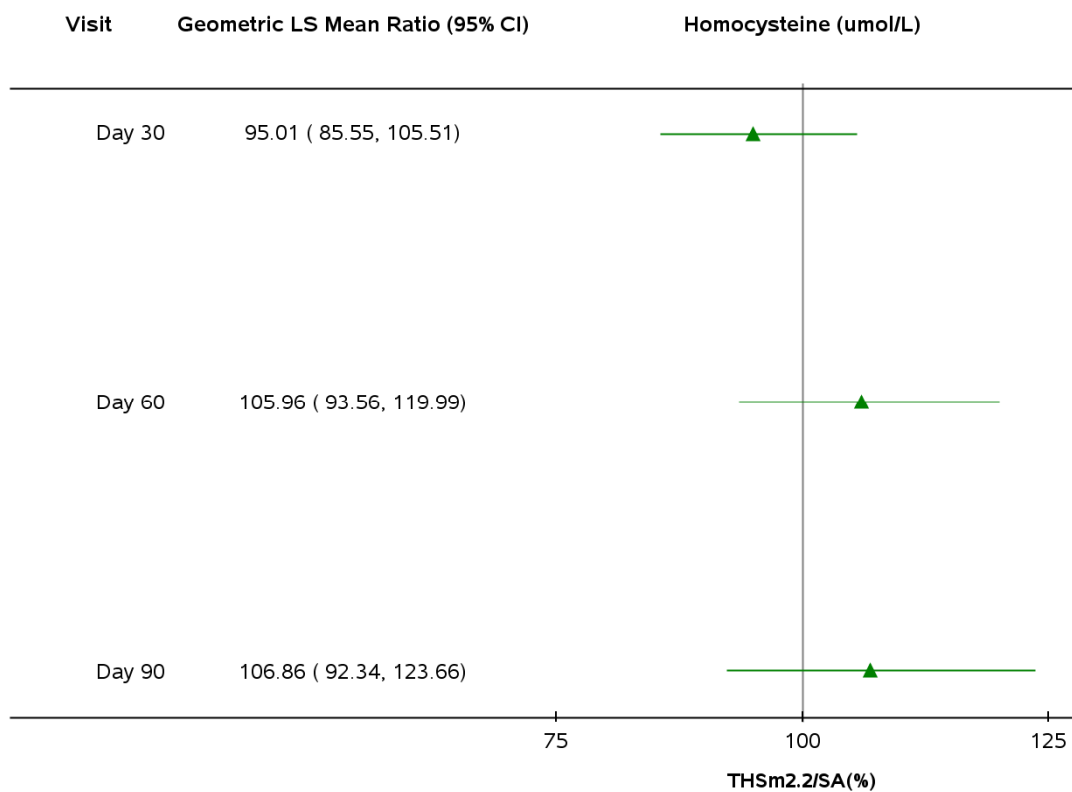
Study ID: ZRHM-REXA-08-US    Program: f\_forest\_rm.sas    16MAR16    Status: Final    (Page 38 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

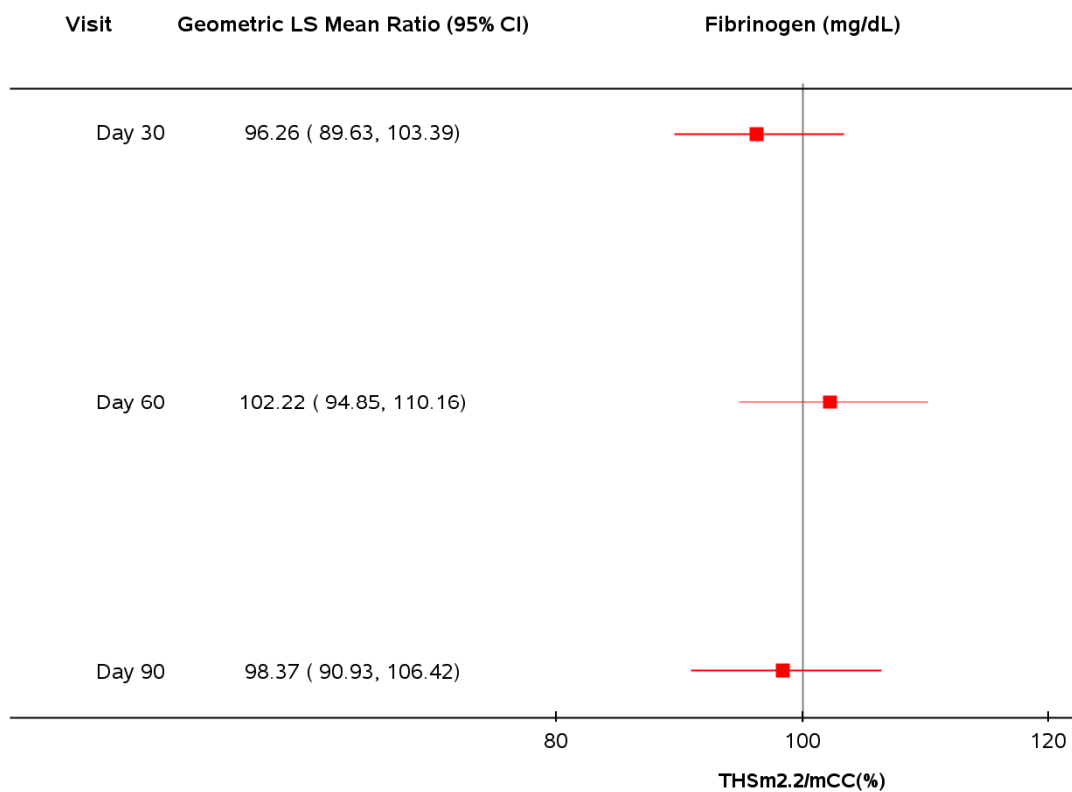
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 39 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

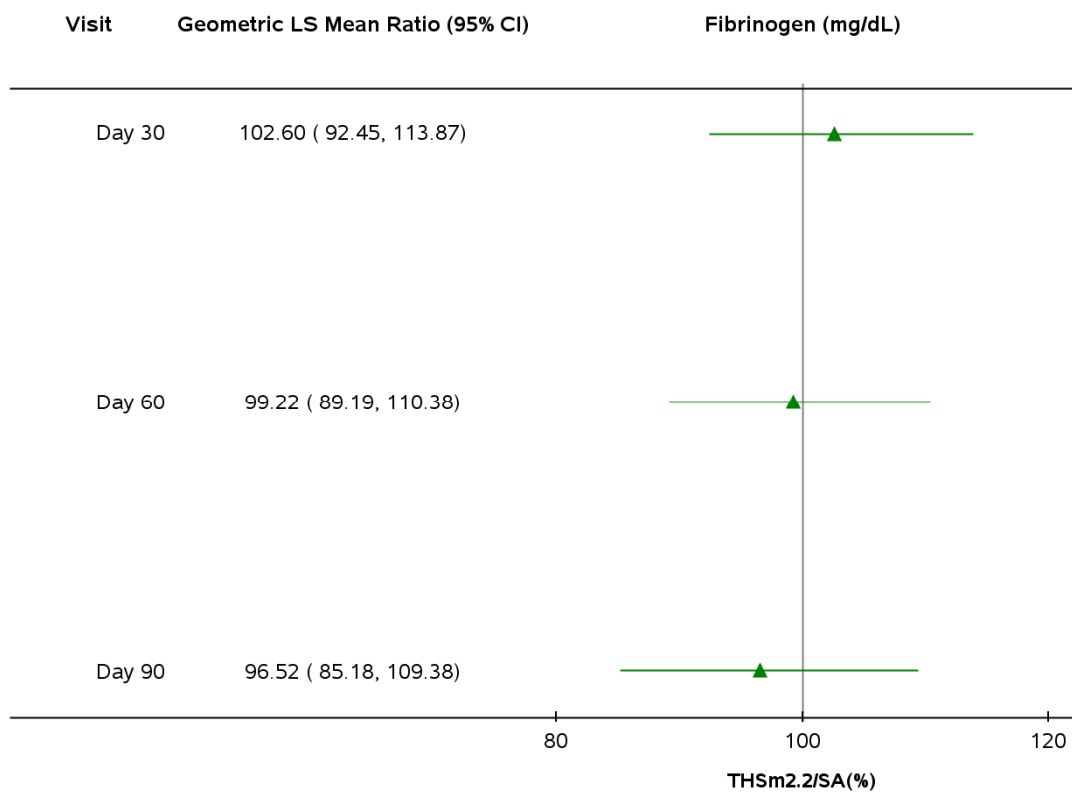
Study ID:ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 40 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 41 of 50)

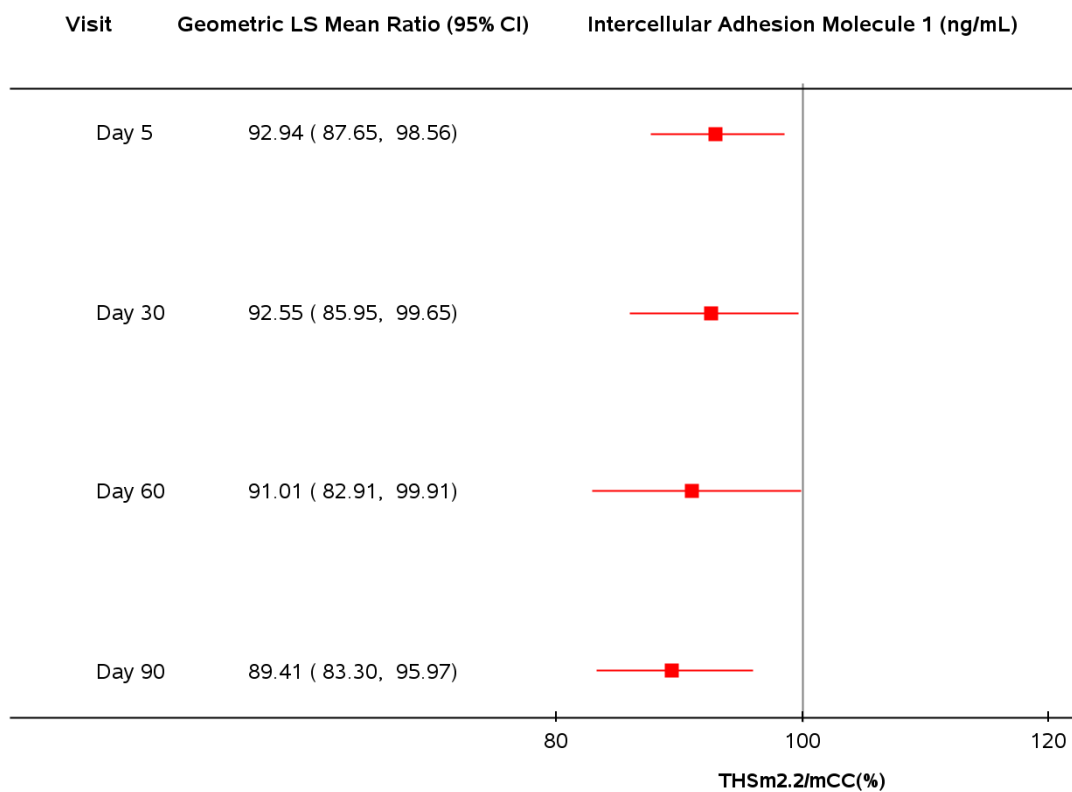
**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 42 of 50)

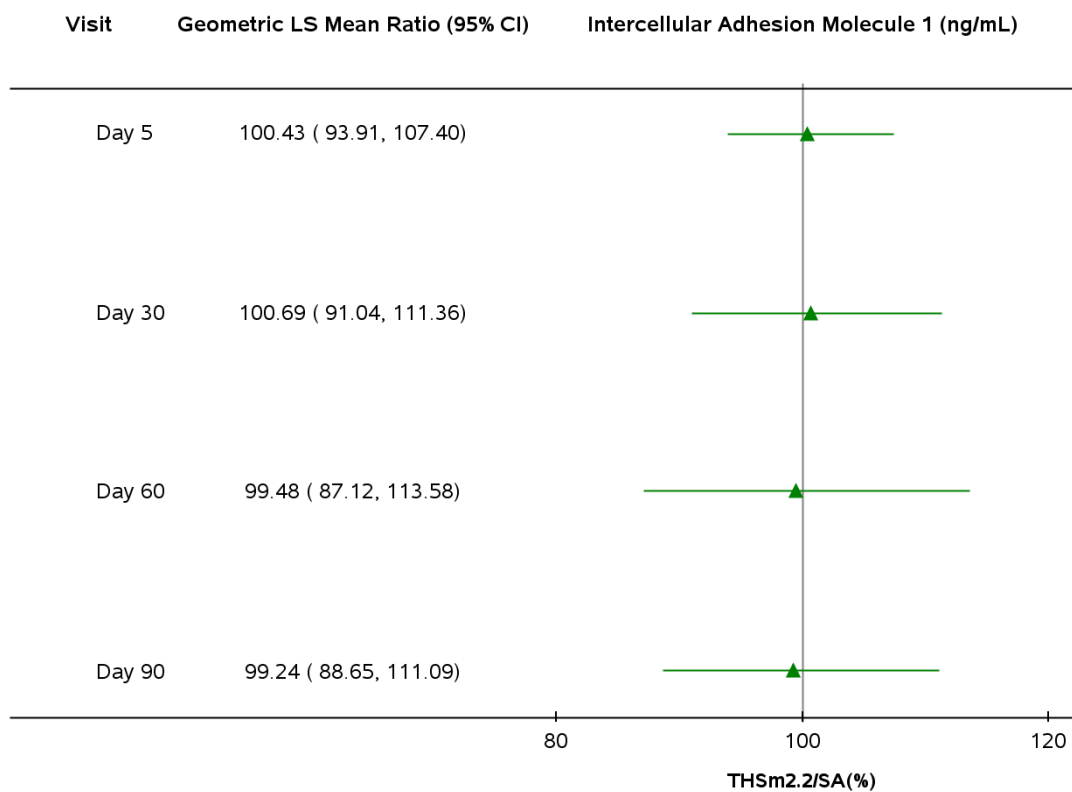


**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

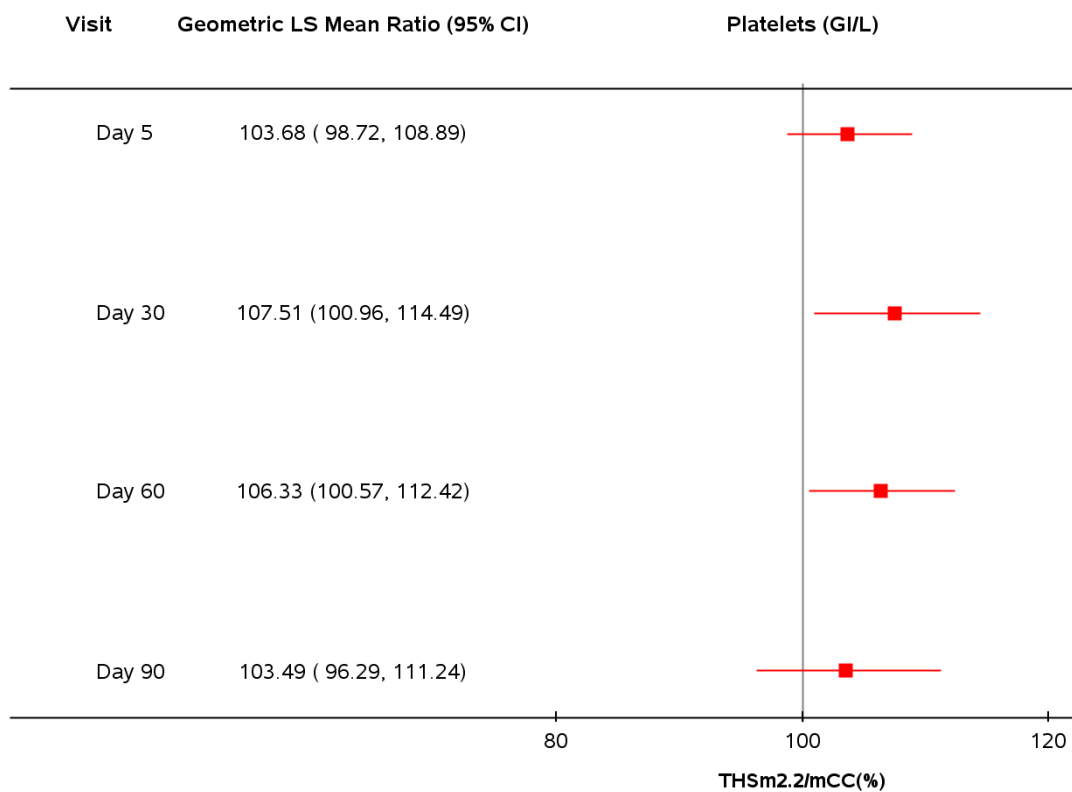
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 43 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

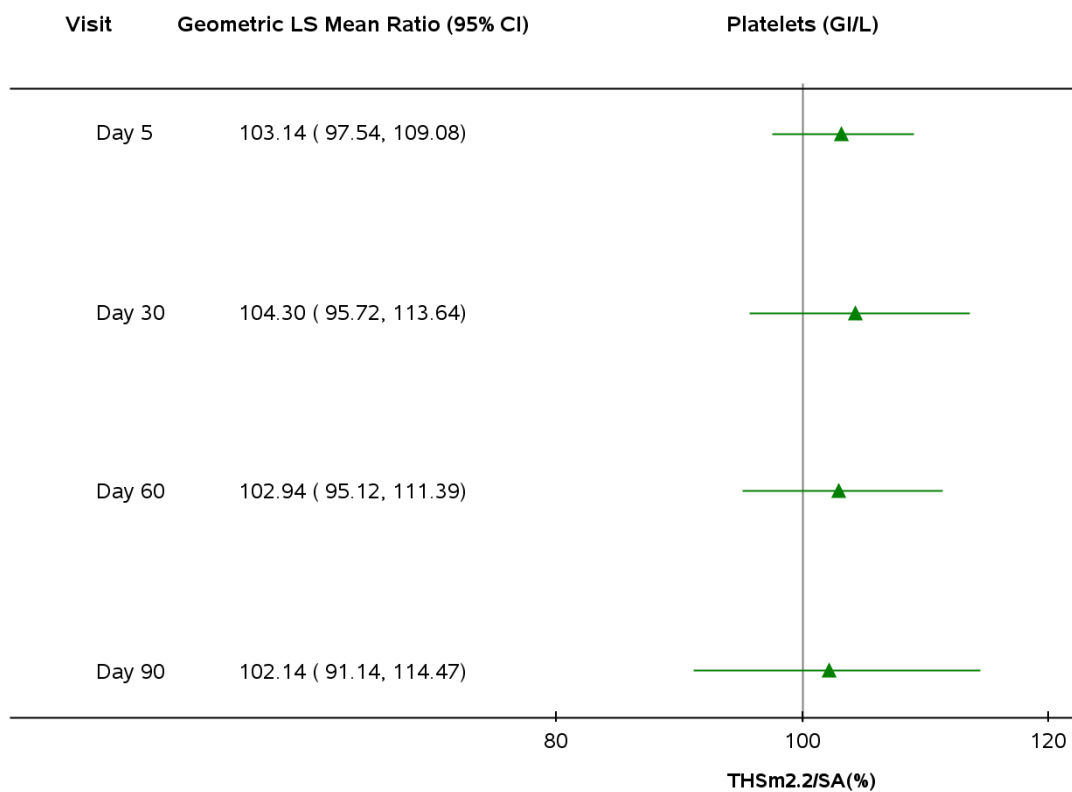
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 44 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

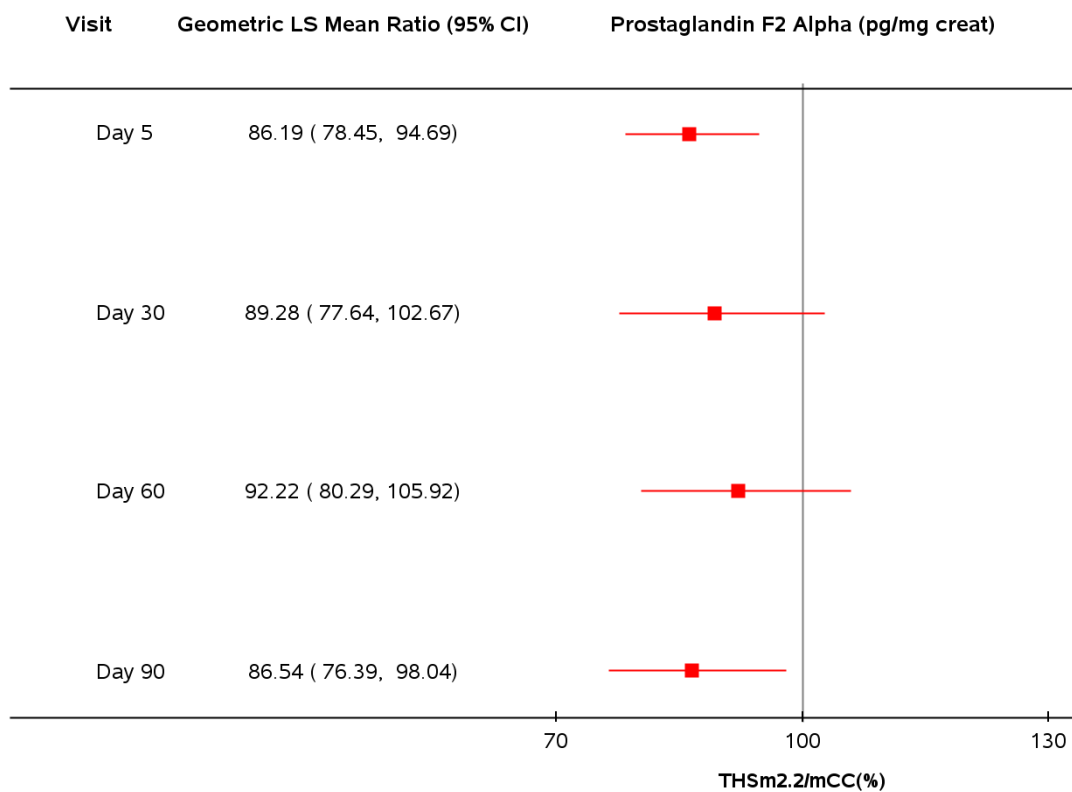
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 45 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

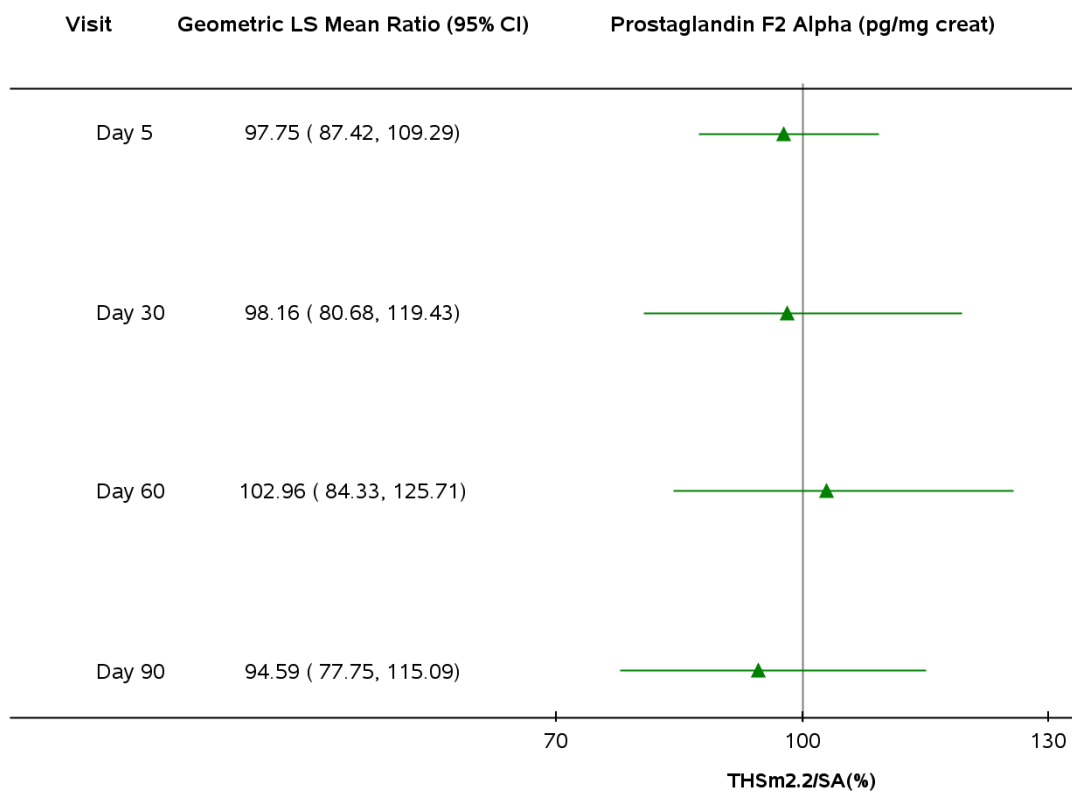
Study ID:ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 46 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

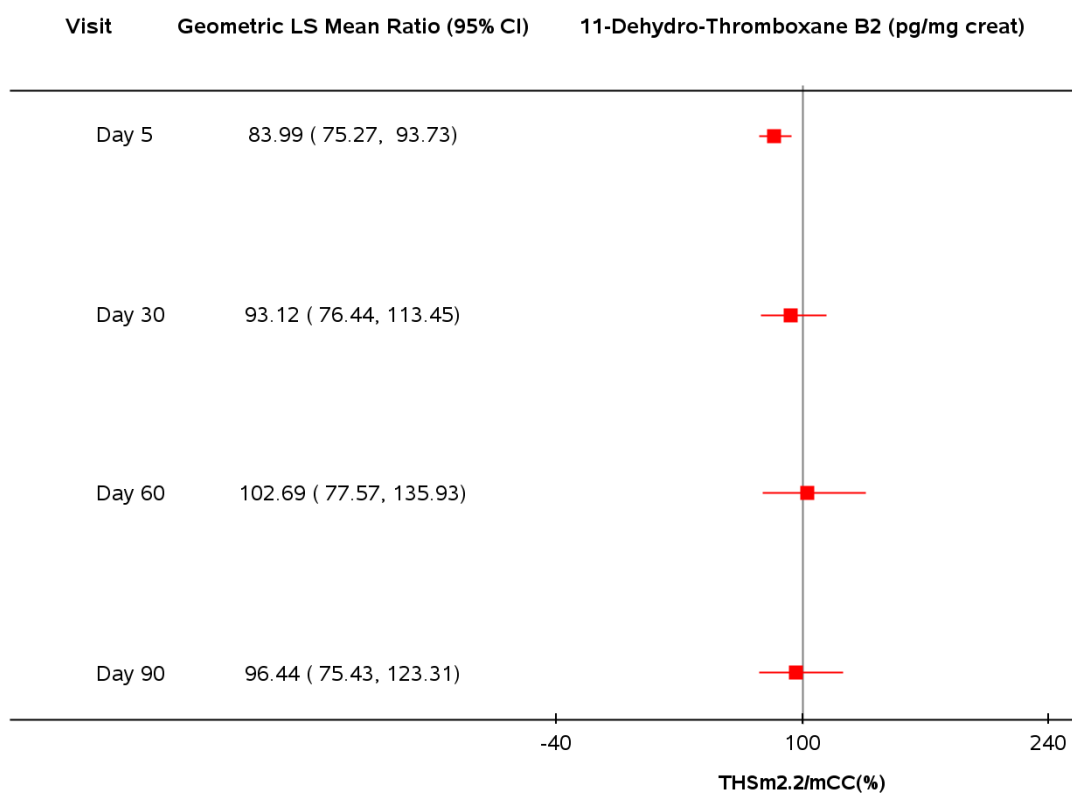
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 47 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

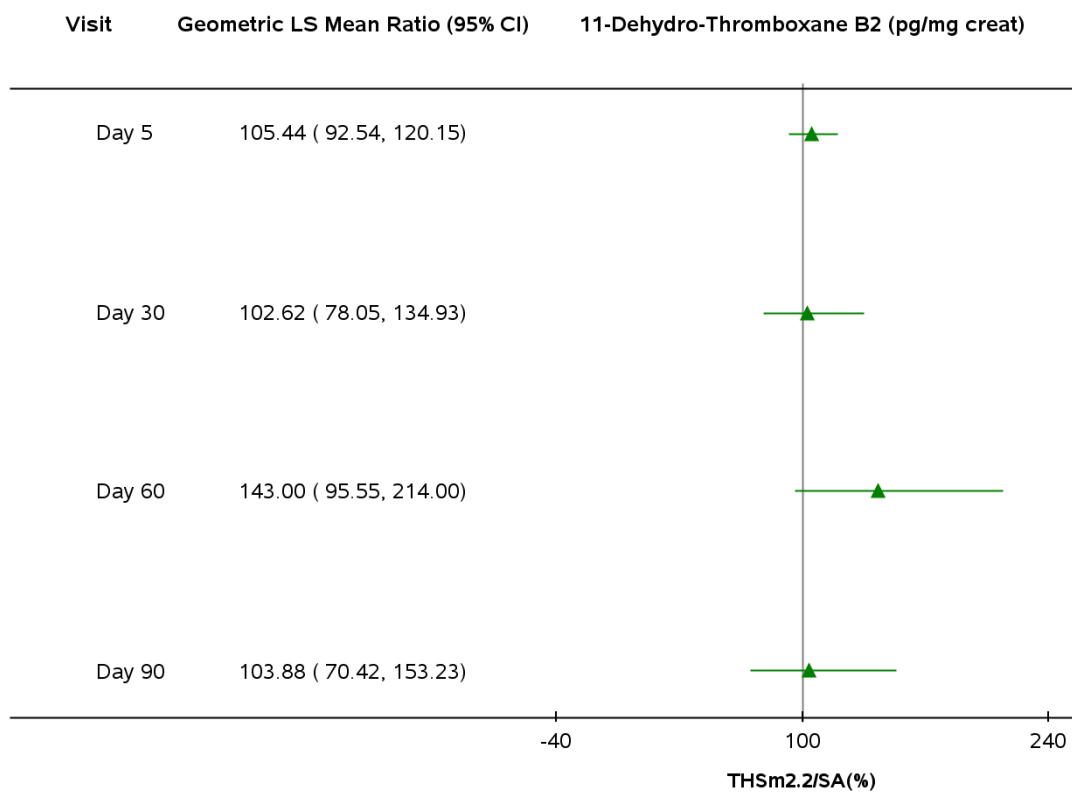
Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 48 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID: ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 49 of 50)

**Figure 15.1.2.2 Forest Plot of Statistical Analysis of Risk Markers - PP Set**

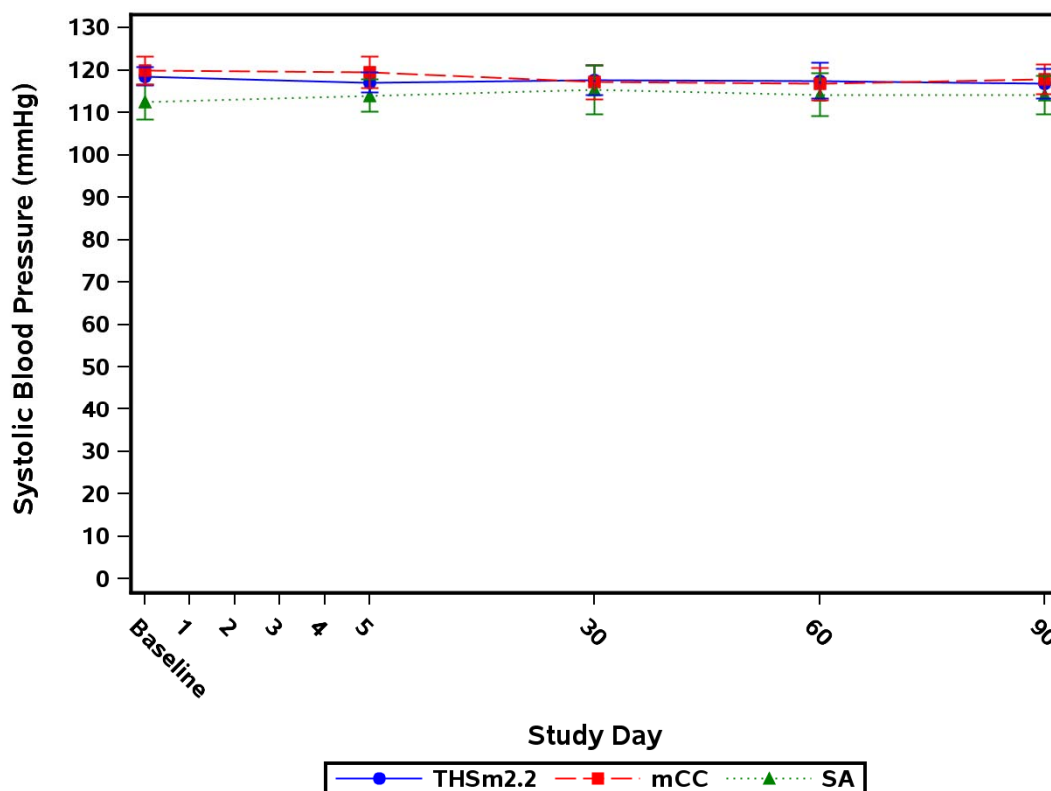
Ratio is displayed for C Reactive Protein (mg/L), Fibrinogen (mg/dL), Glucose (mg/dL), Homocysteine (umol/L), Intercellular Adhesion Molecule 1 (ng/mL), Platelets (GI/L), Prostaglandin F2 Alpha (pg/mg creat) and 11-Dehydro-Thromboxane B2 (pg/mg creat). All other risk markers are presented using difference.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.4.25.1

Study ID:ZRHM-REXA-08-US Program: f\_forest\_rm.sas 16MAR16 Status: Final (Page 50 of 50)



**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

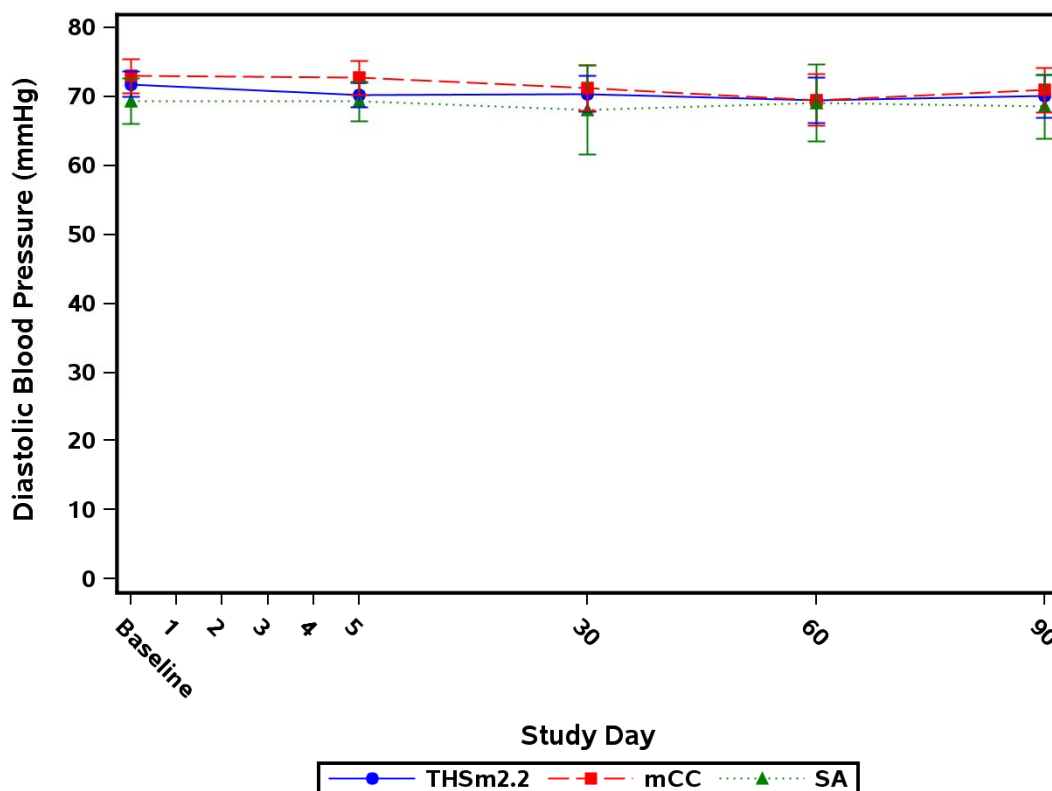
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 1 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

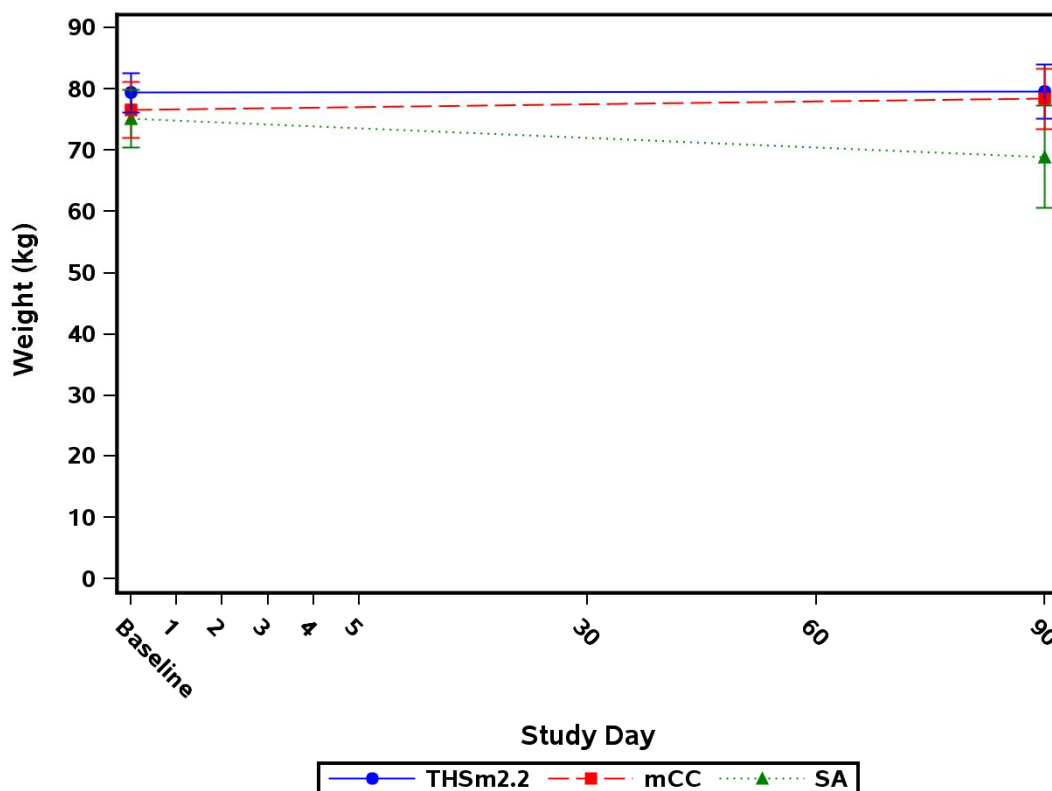
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 2 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

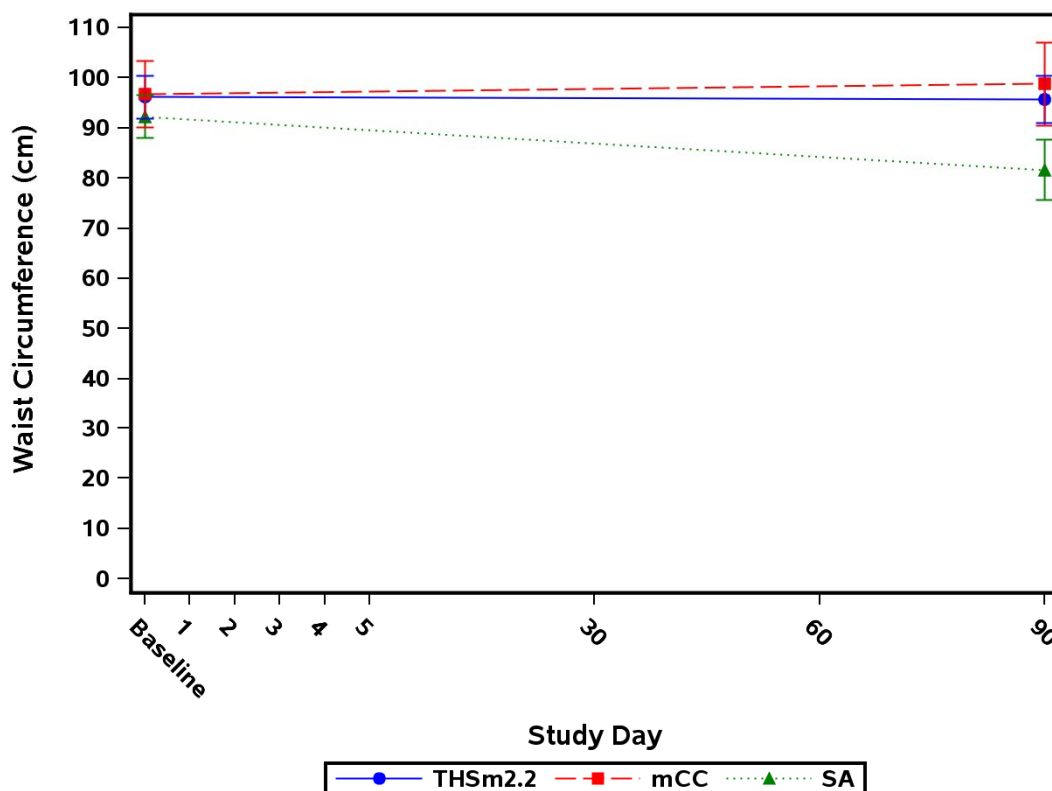
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 3 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

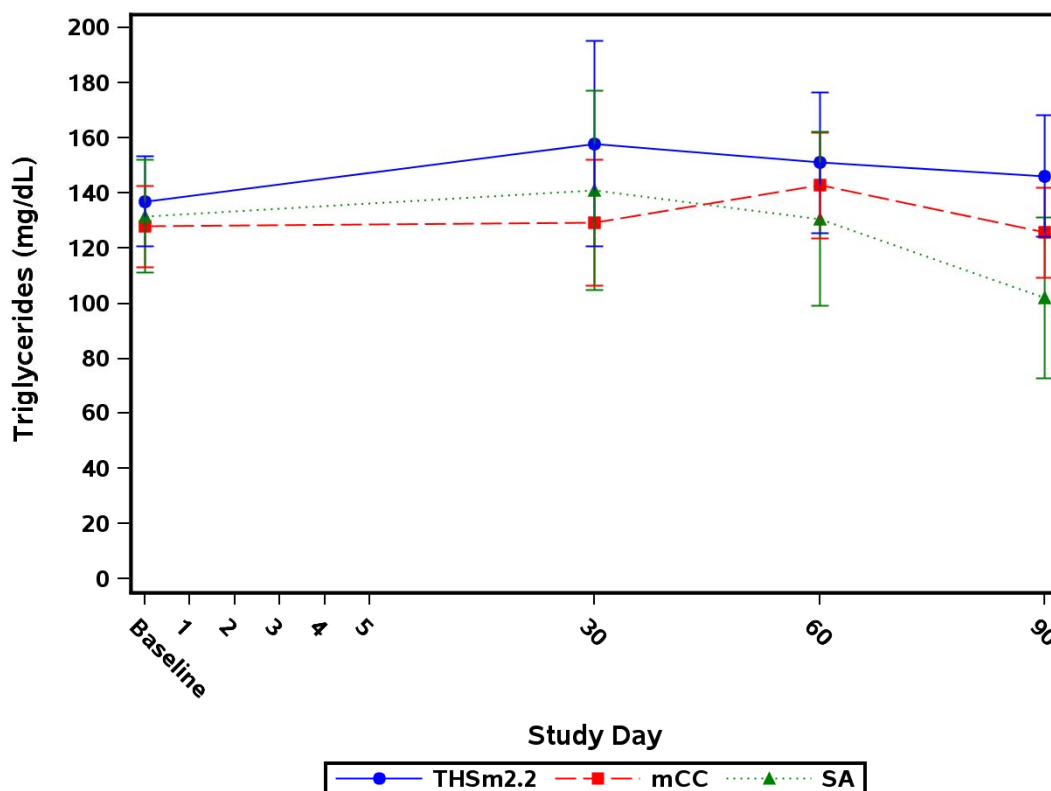
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 4 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

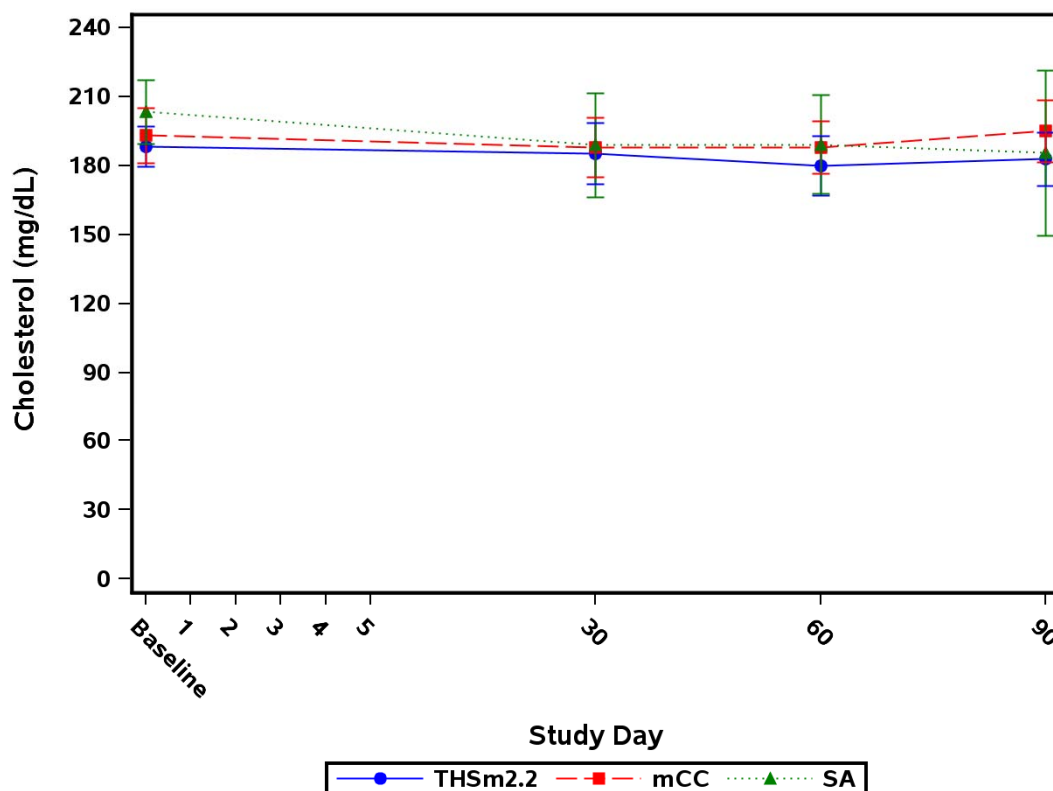
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 5 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

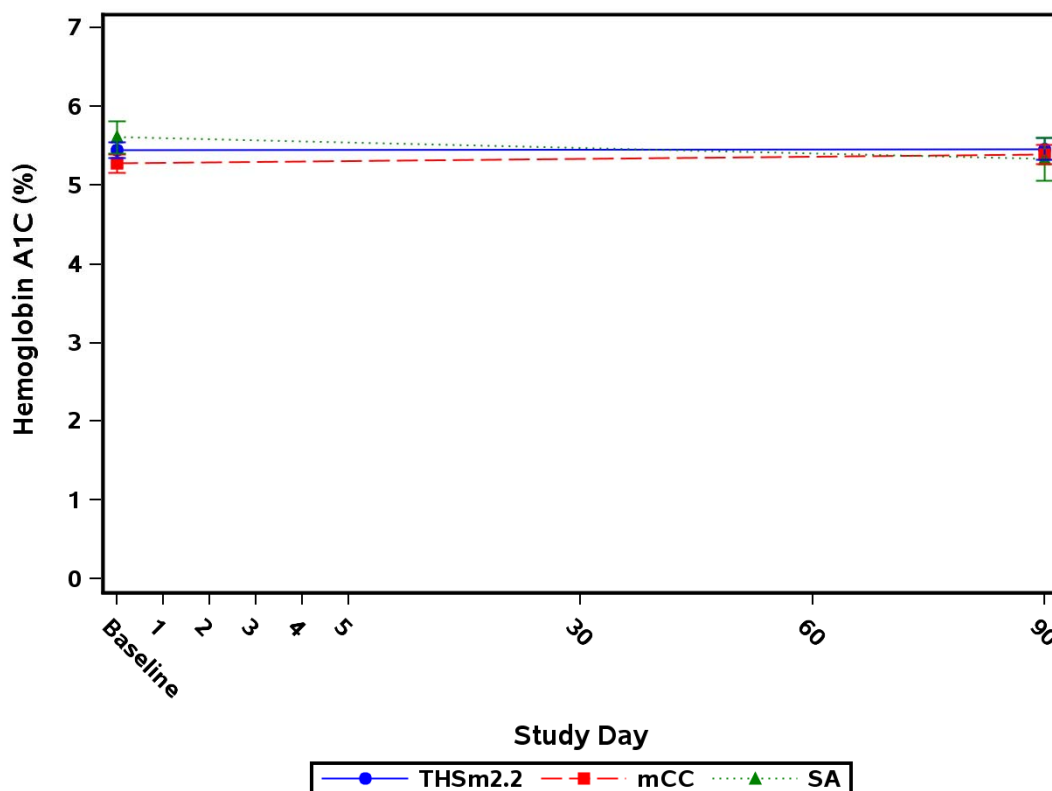
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 6 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

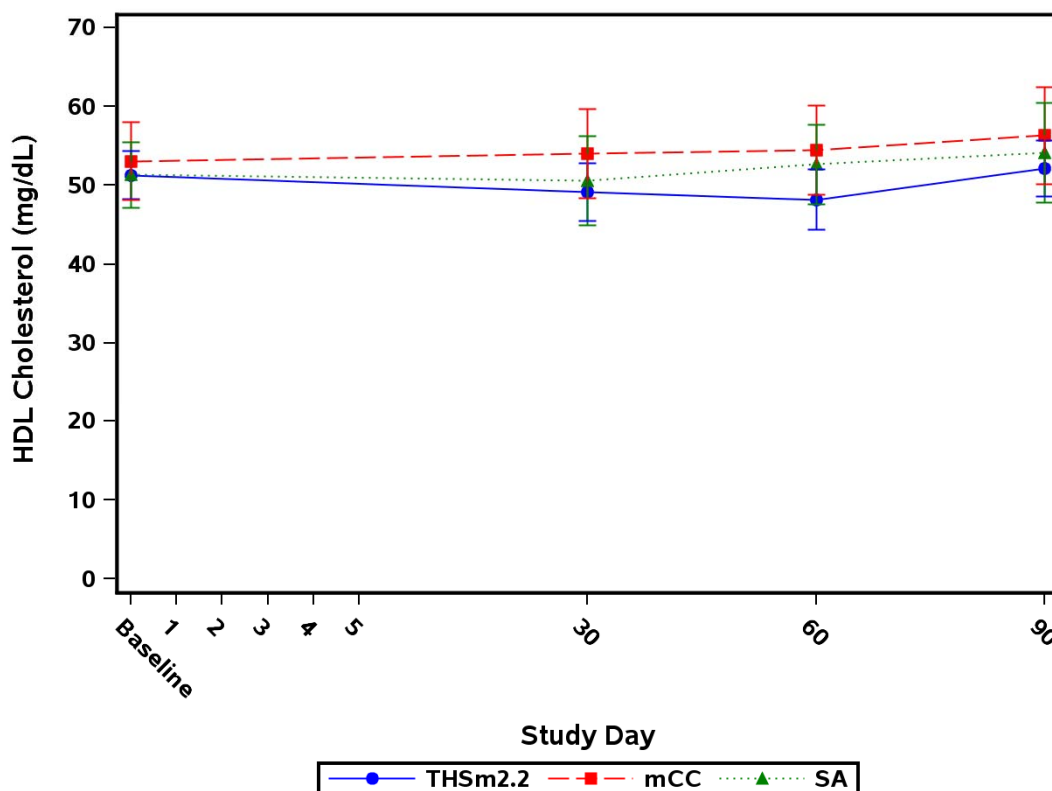
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

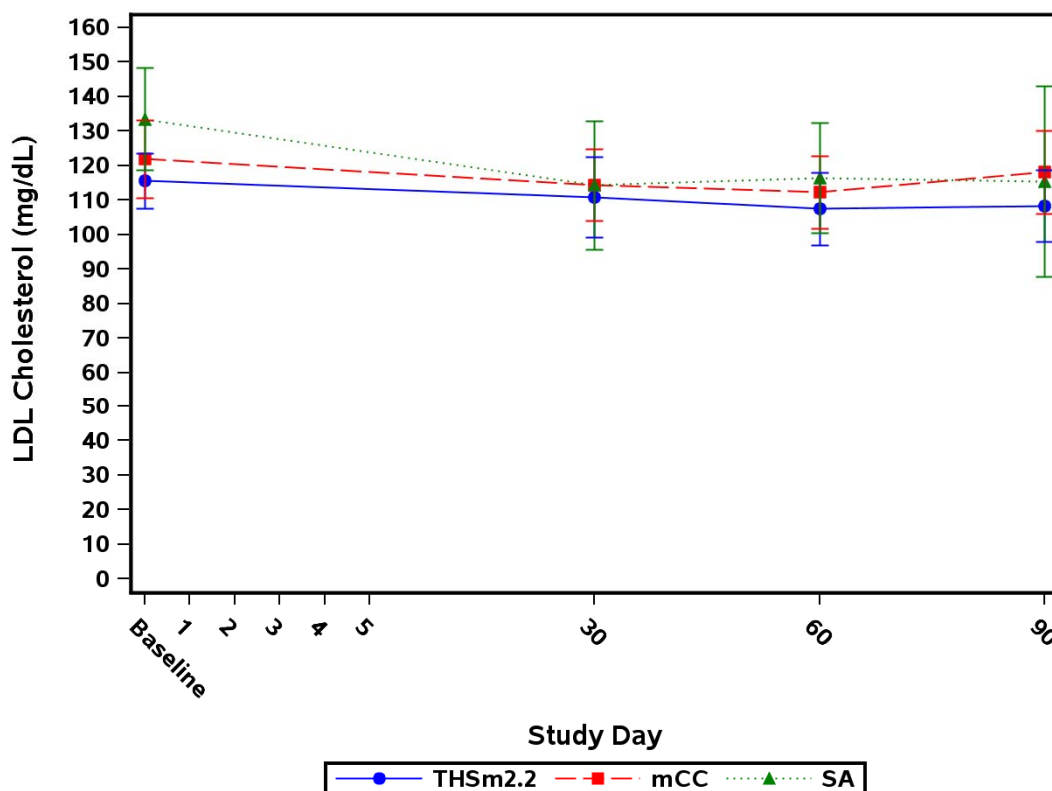
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 8 of 25)



**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

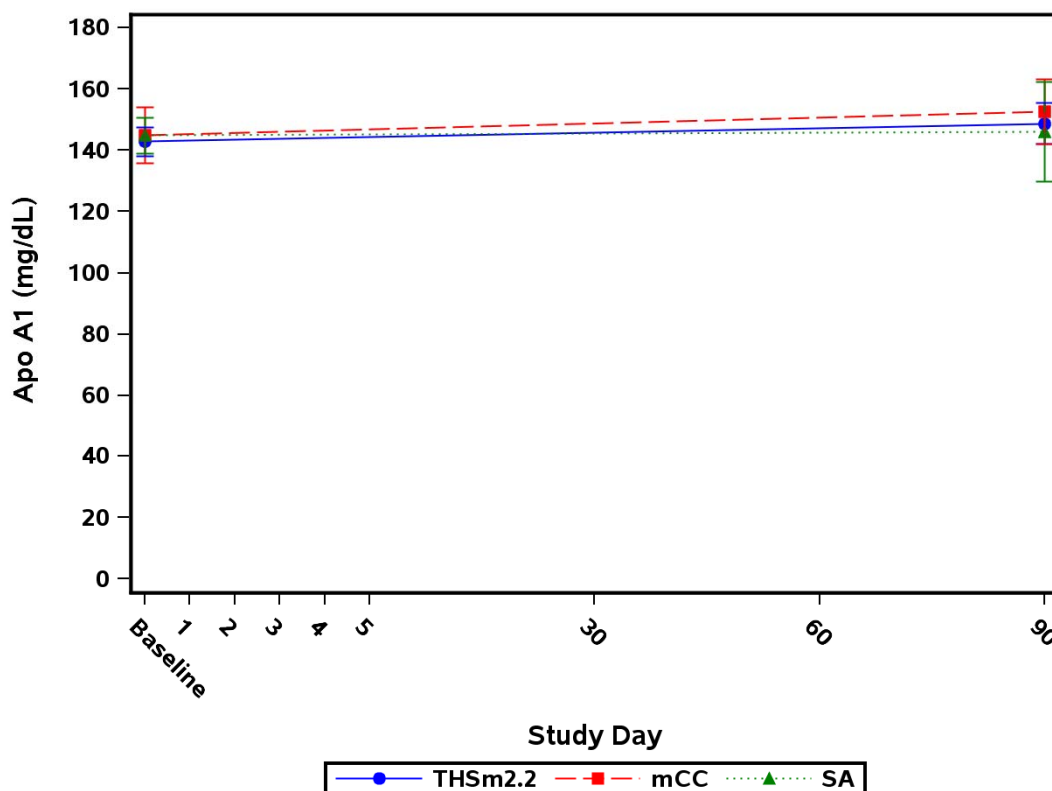
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 9 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

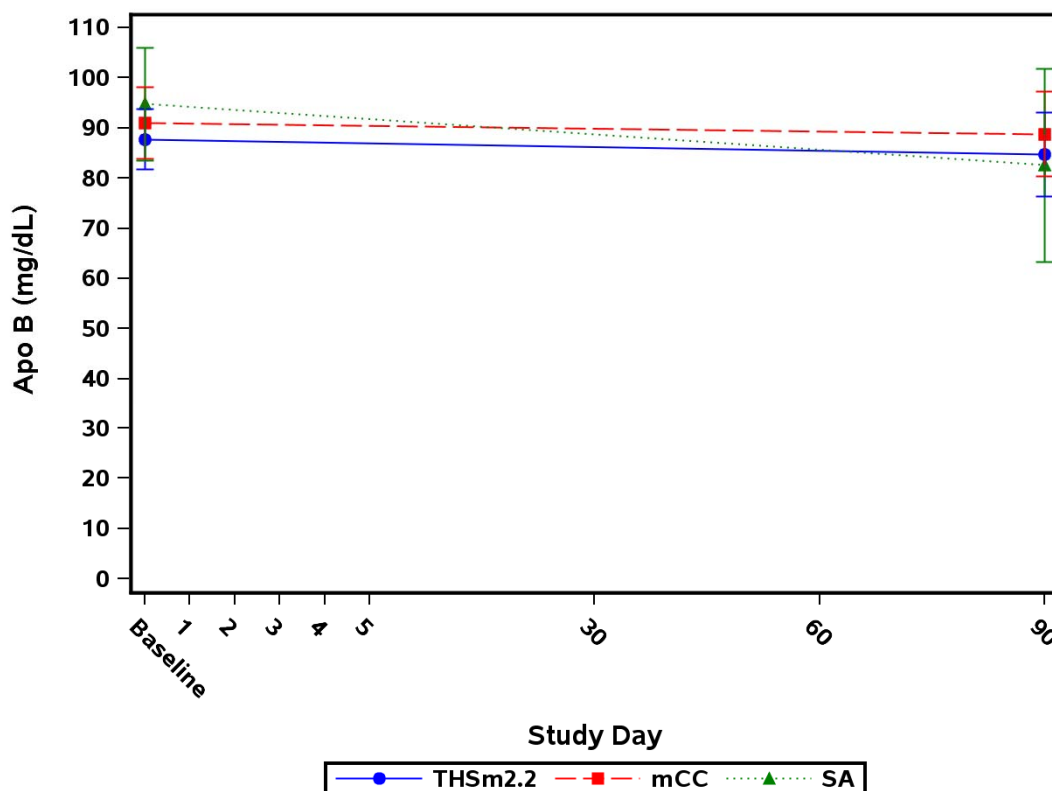
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 10 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

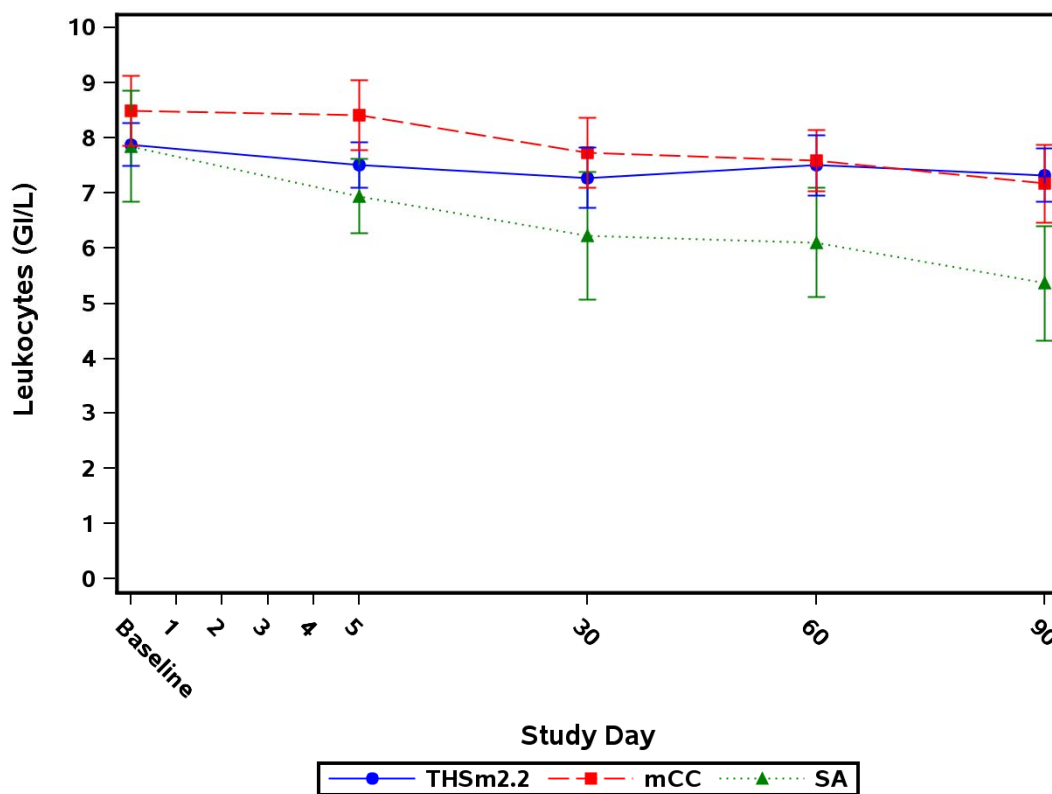
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 11 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

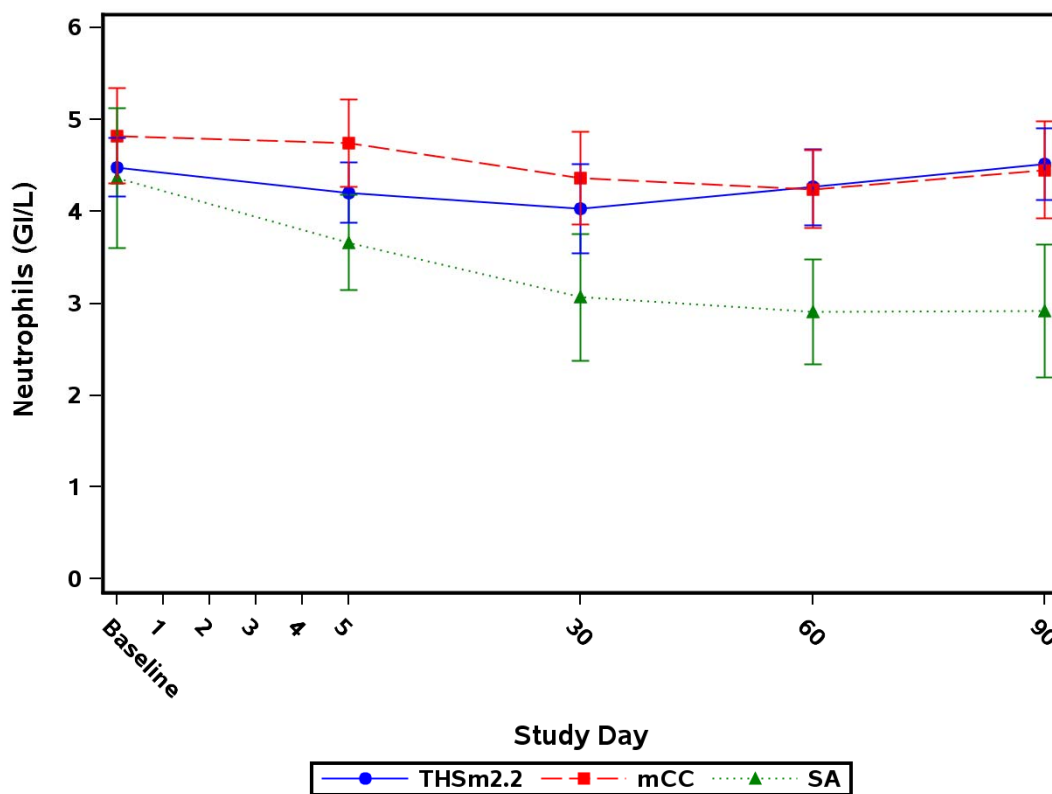
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

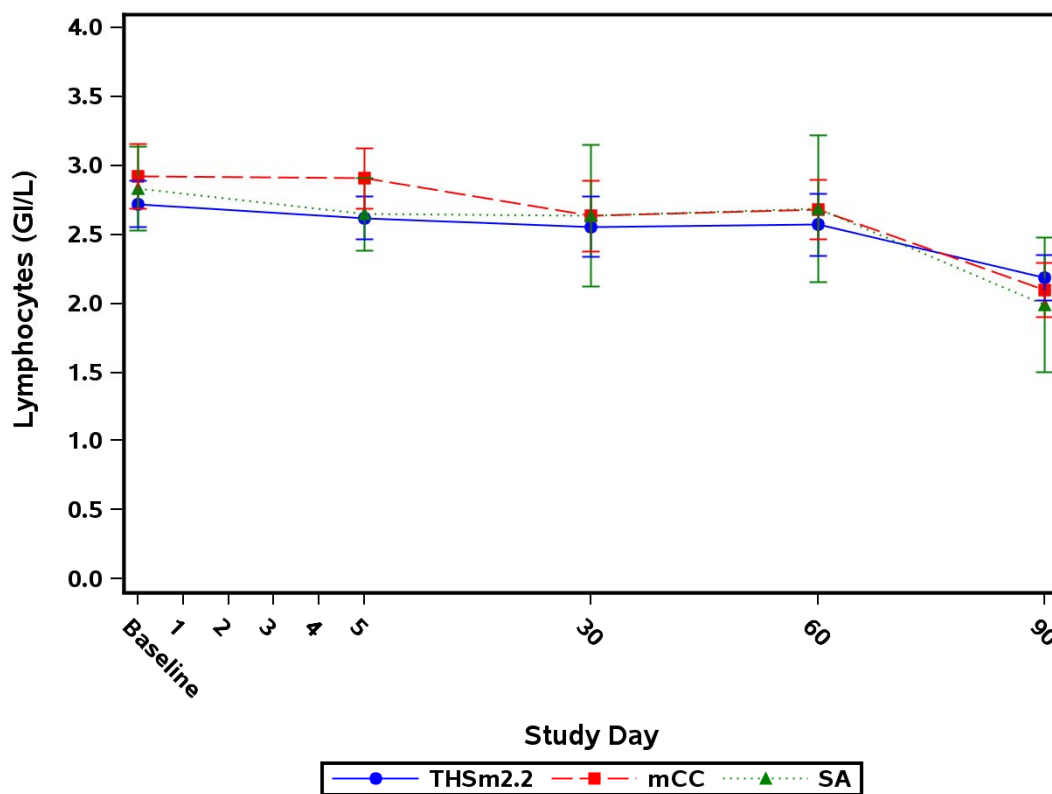
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 13 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

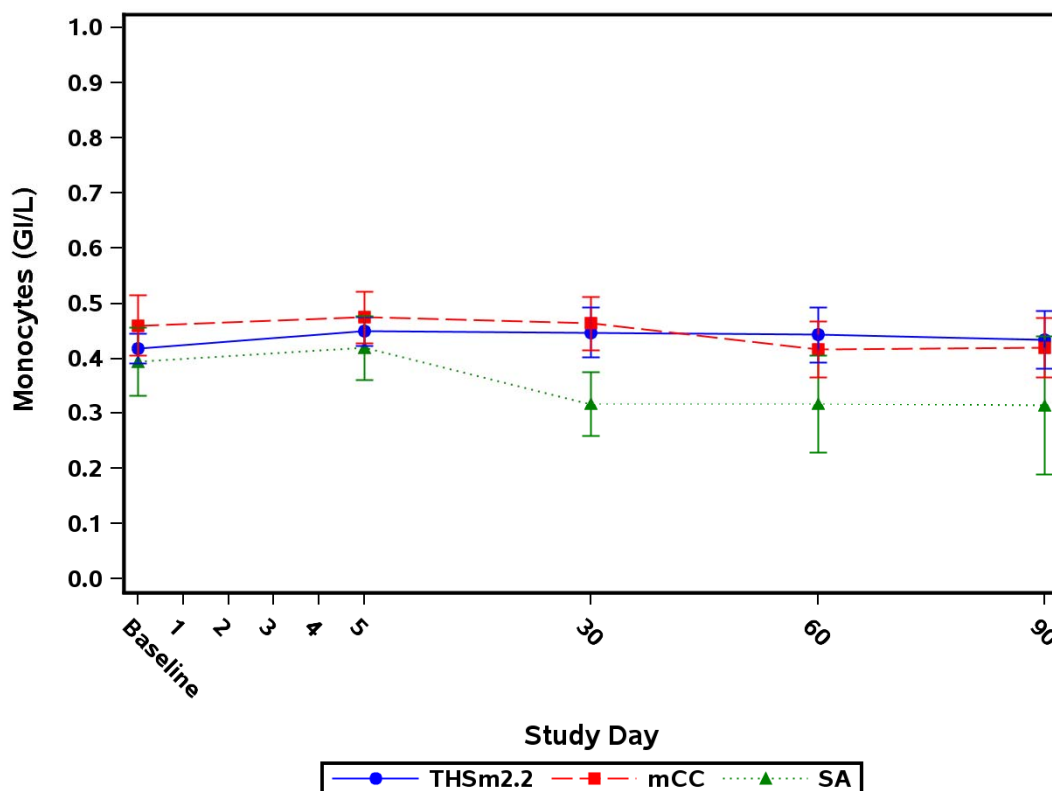
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 14 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

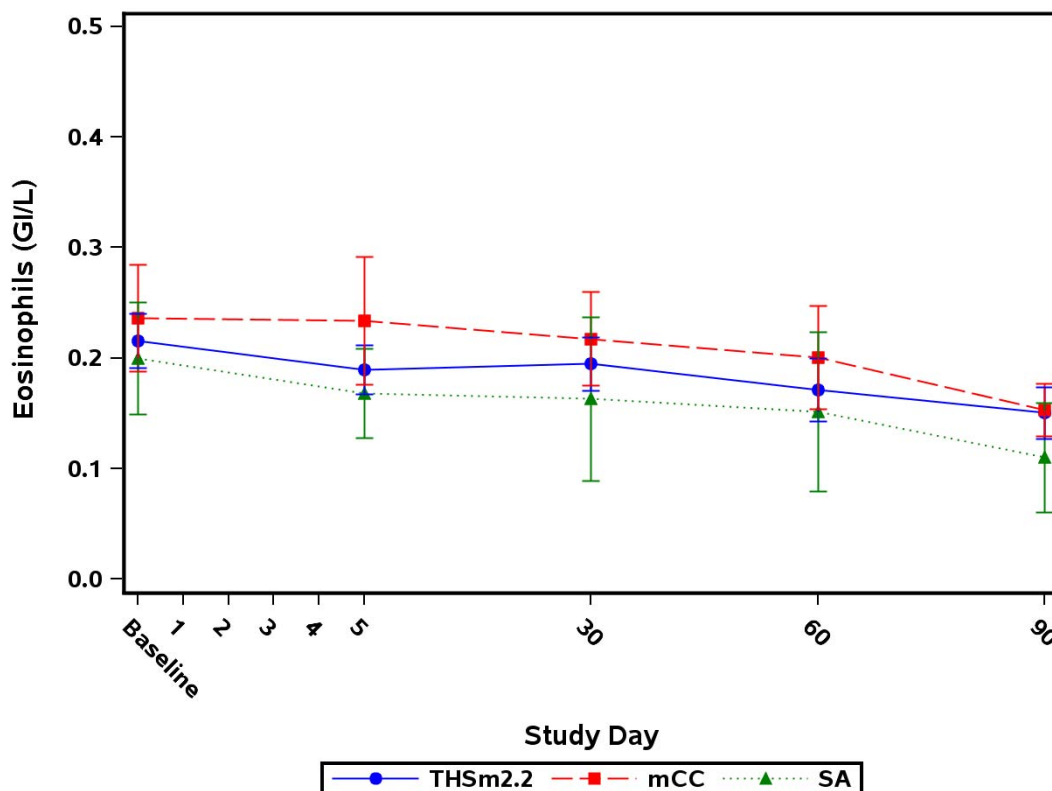
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 15 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

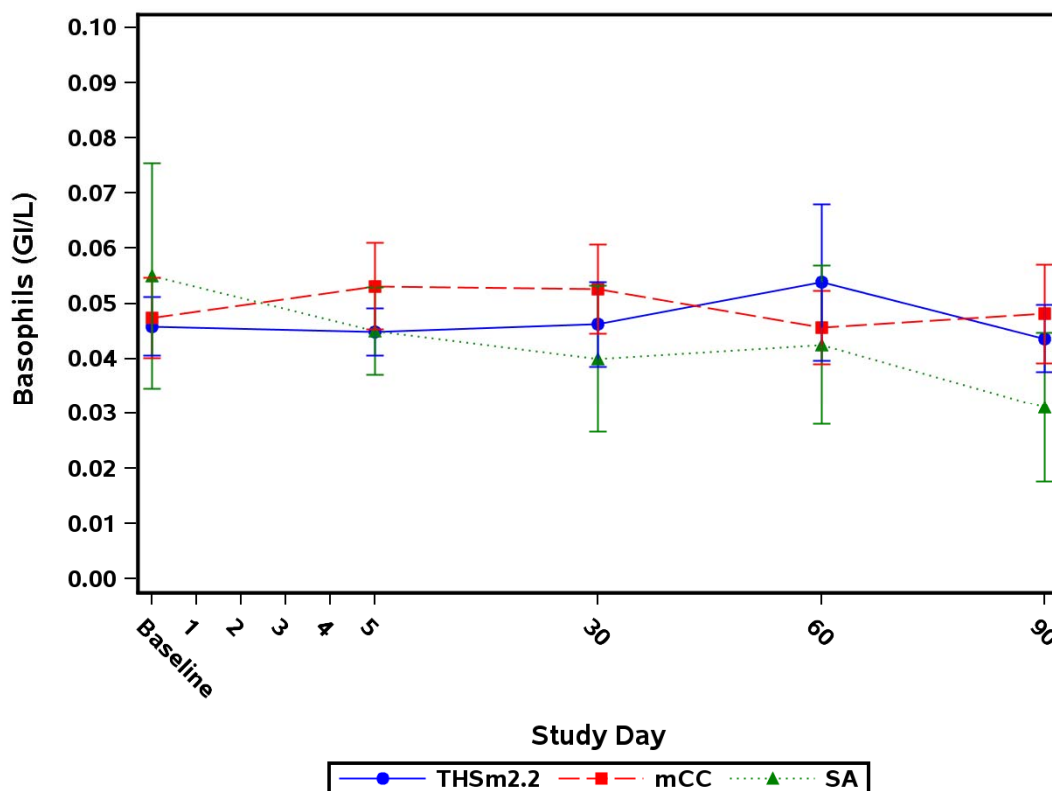
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

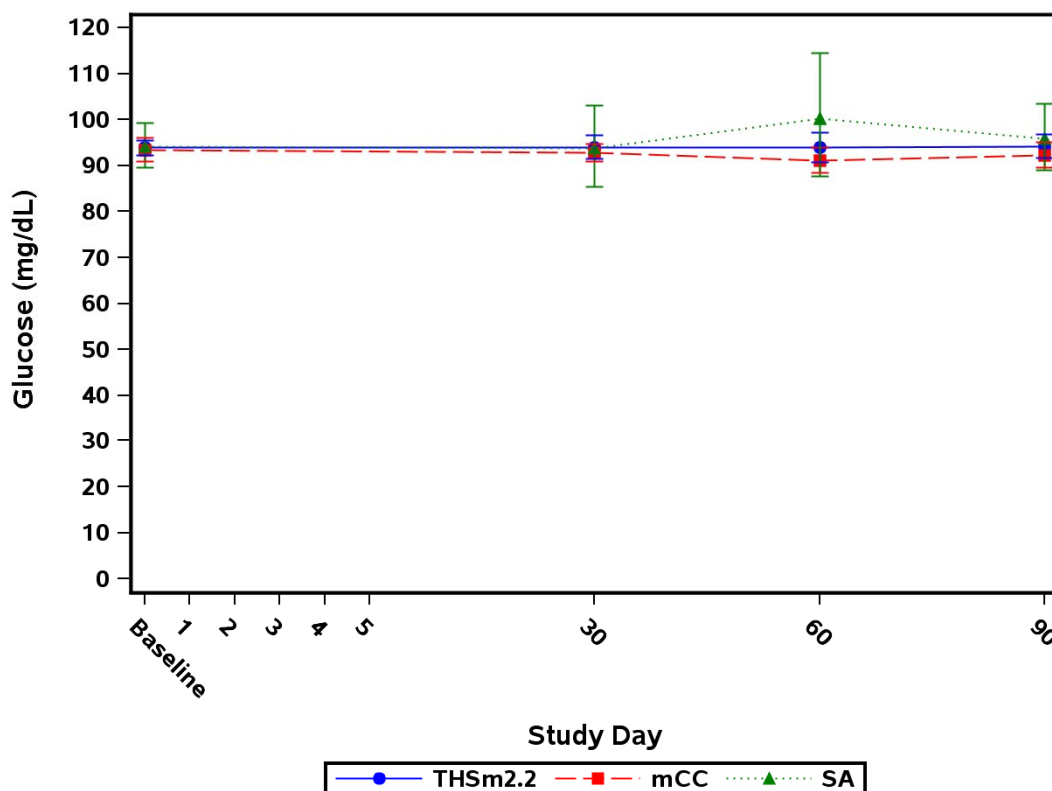
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 17 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

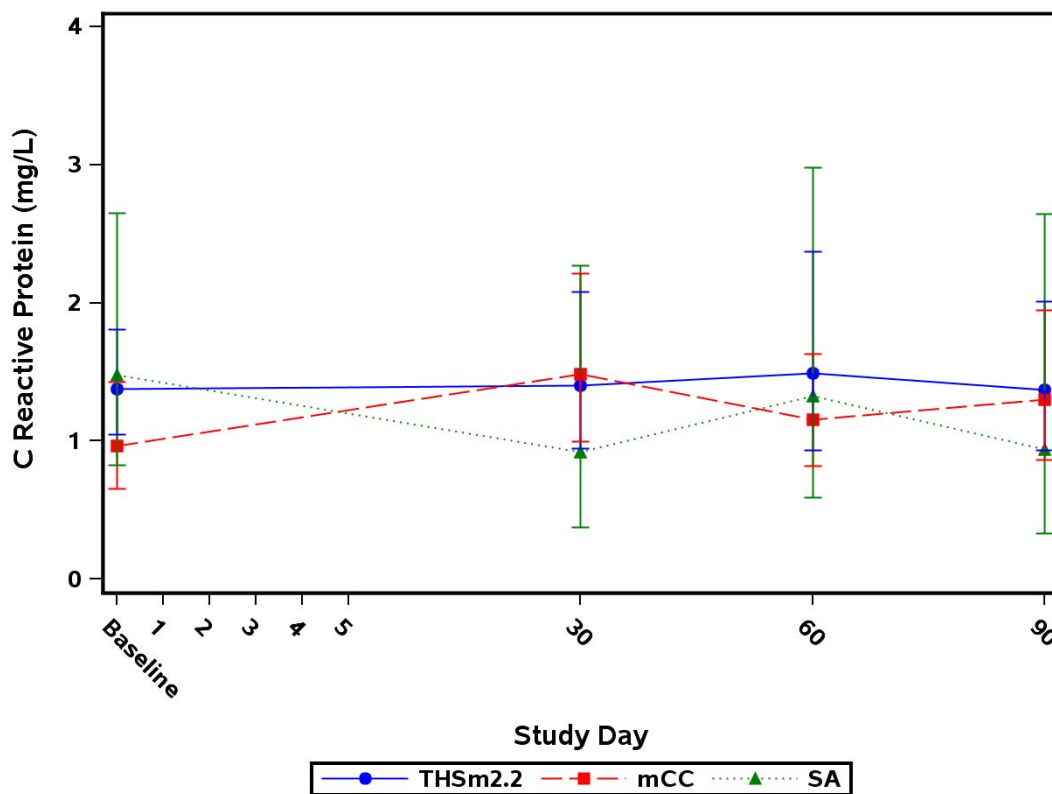
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

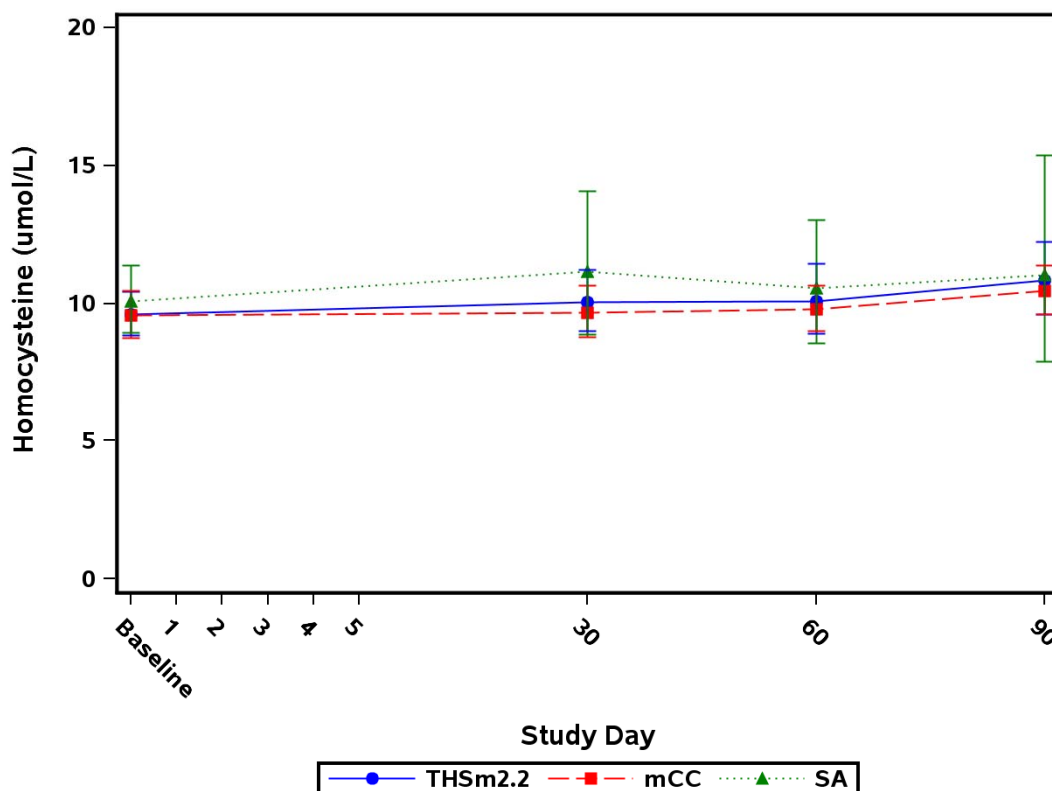
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

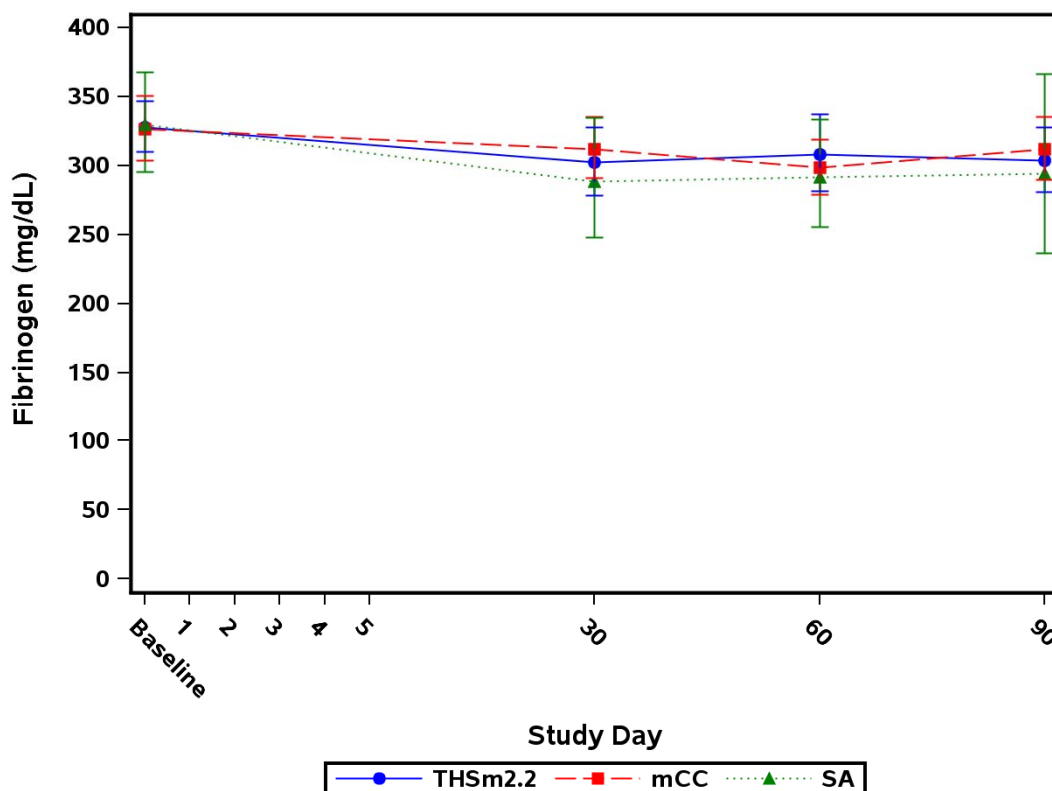
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 20 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

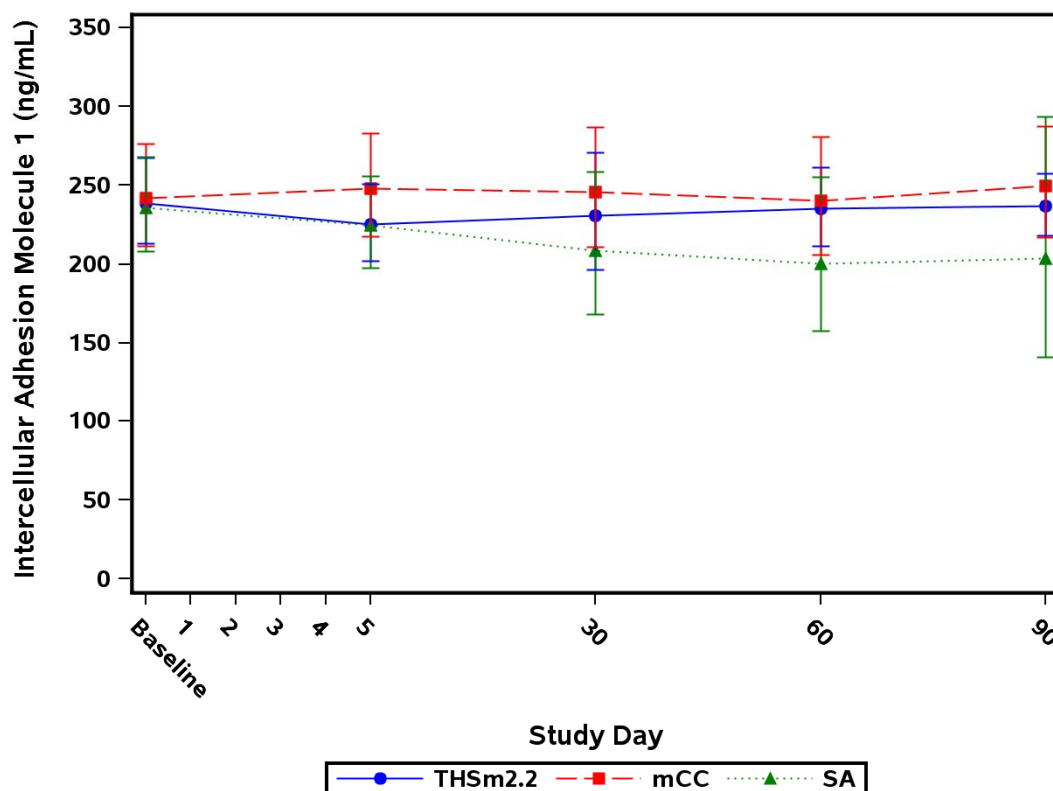
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 21 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

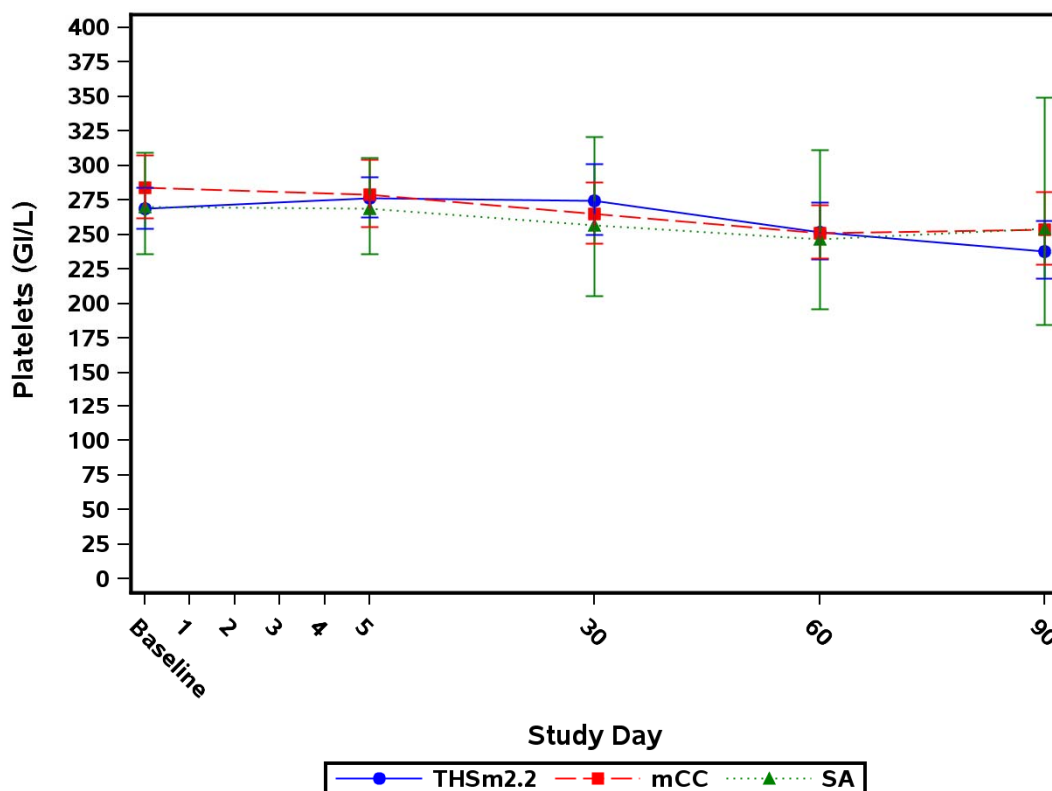
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 22 of 25)

**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

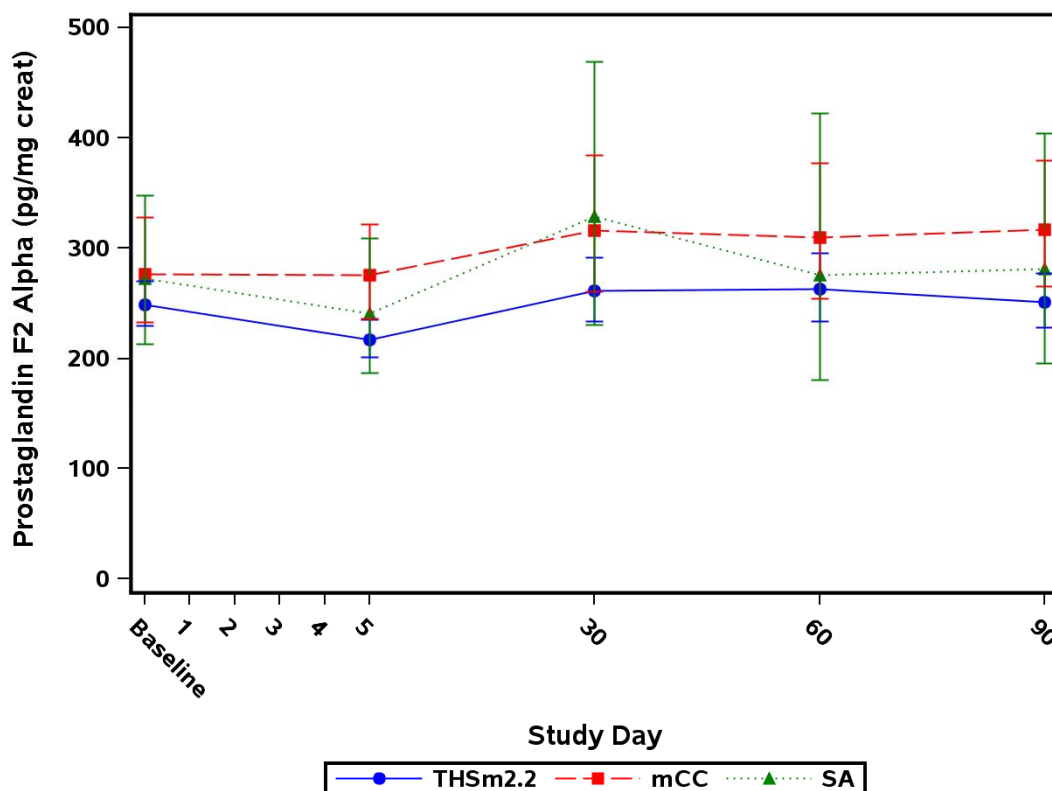
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.1, 15.2.4.27.1, 15.2.4.28.1, 15.2.4.29.1, 15.2.4.30.1, 15.2.4.31.1, 15.2.4.32.1, 15.2.4.33.1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

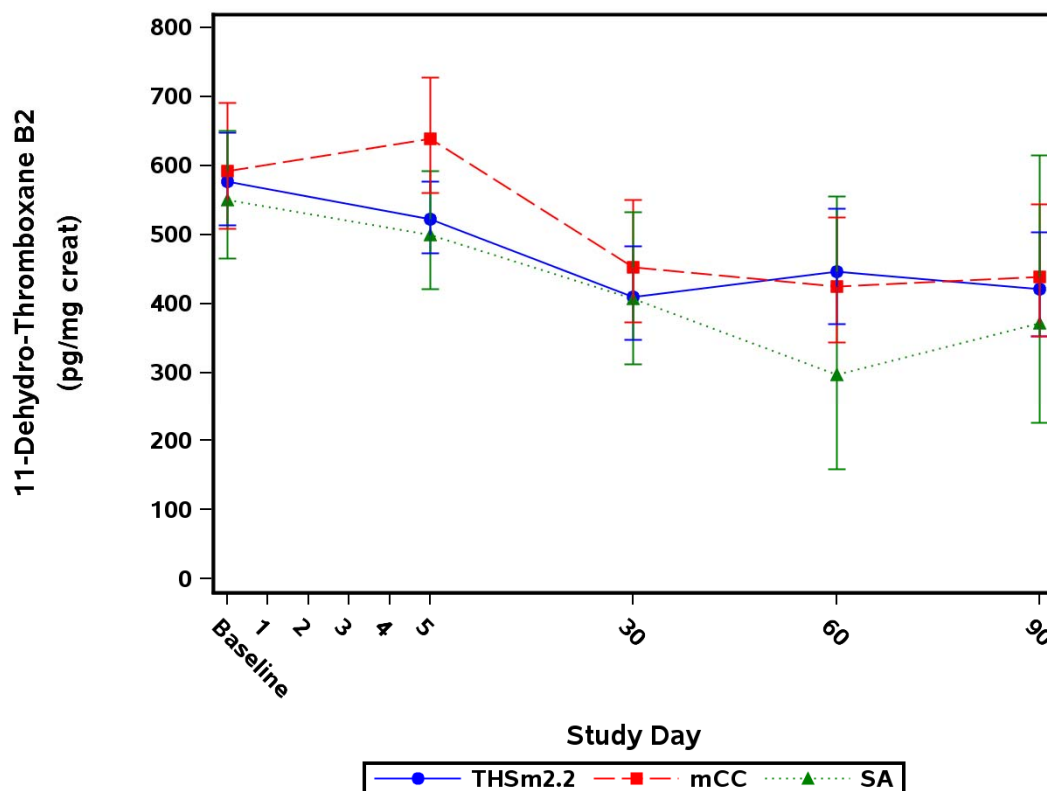
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.3.1 Risk Markers Mean and 95% CI - PP Set**

Geometric mean is displayed for C Reactive Protein (mg/L), Fibrinogen (mg/dL), Glucose (mg/dL), Homocysteine (umol/L), Intercellular Adhesion Molecule 1 (ng/mL), Platelets (GI/L), Prostaglandin F2 Alpha (pg/mg creat) and 11-Dehydro-Thromboxane B2 (pg/mg creat). All other risk markers are presented using arithmetic mean.

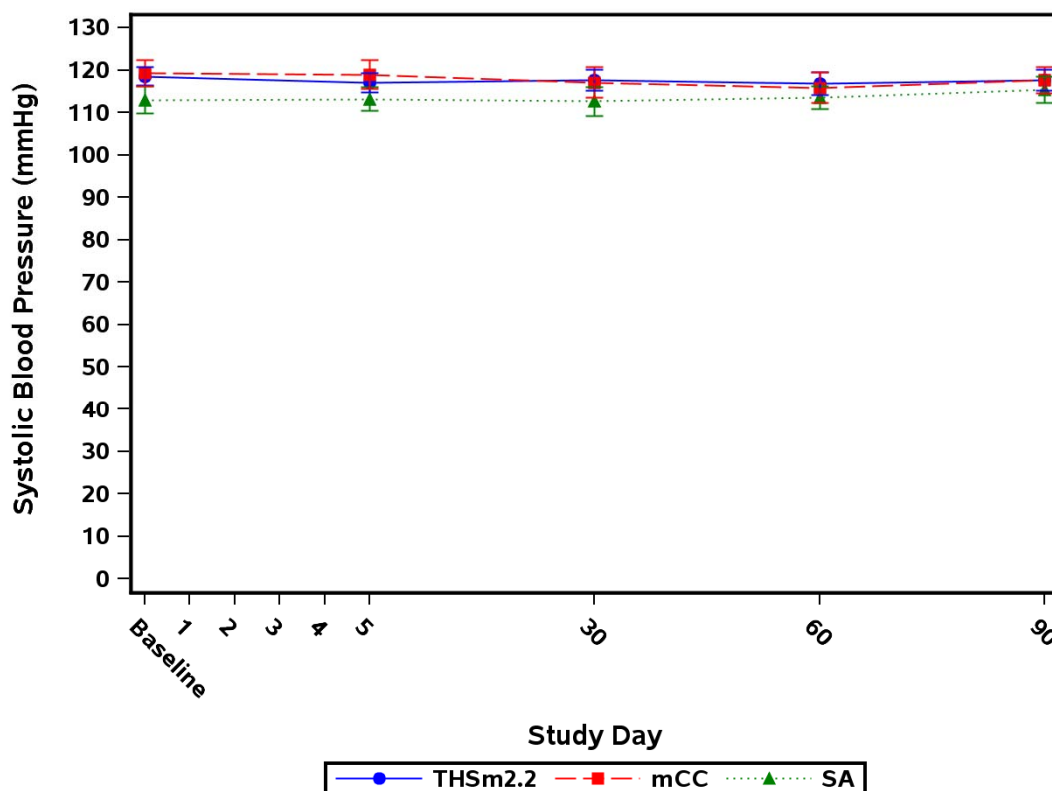
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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Study ID: ZRHM-REXA-08-US Program: f\_riskmrk.sas 16MAR16 Status: Final (Page 25 of 25)

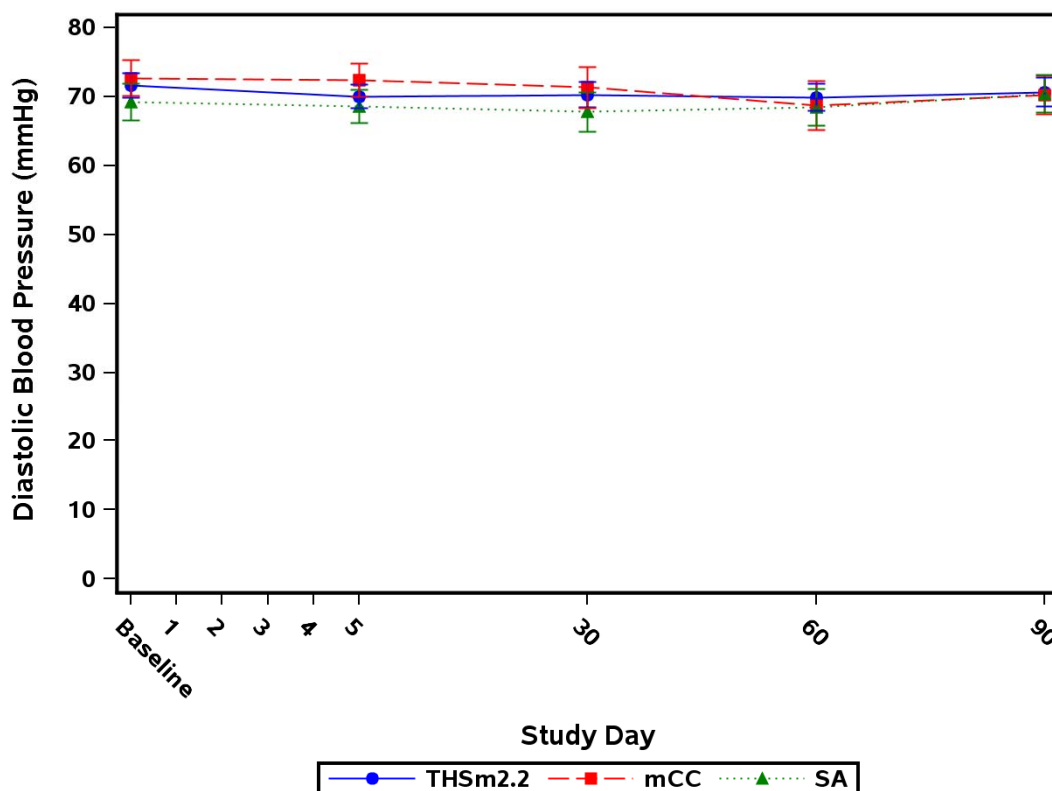
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 1 of 25)

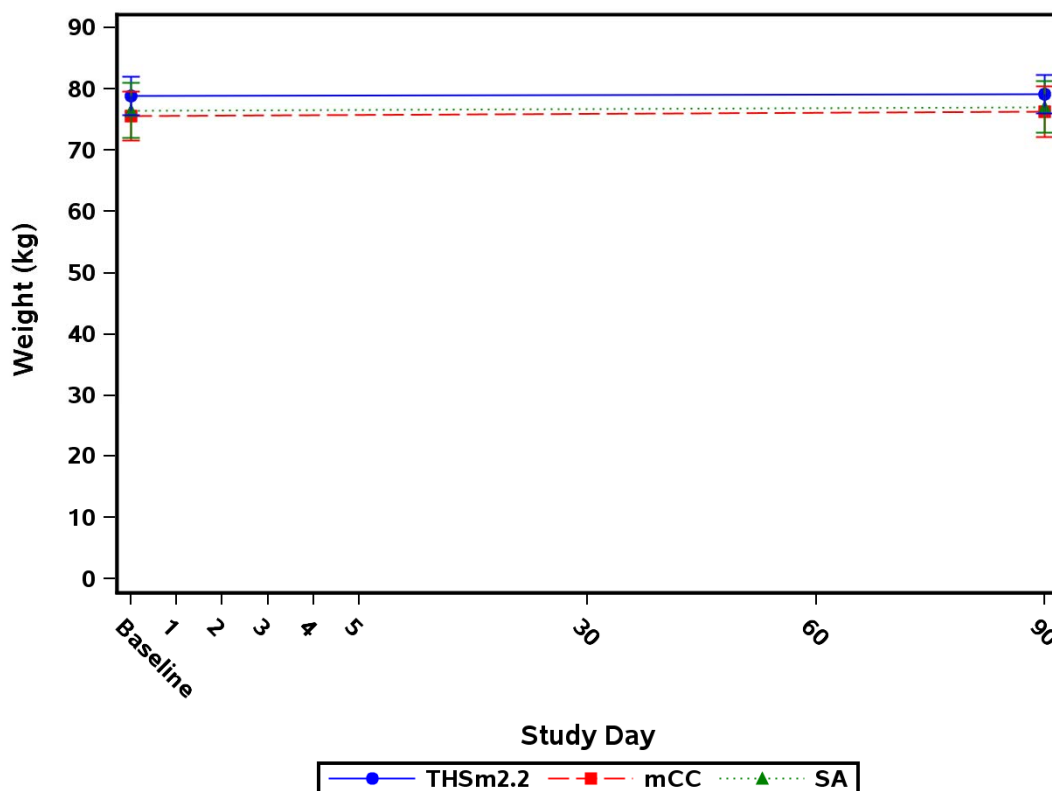
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 2 of 25)

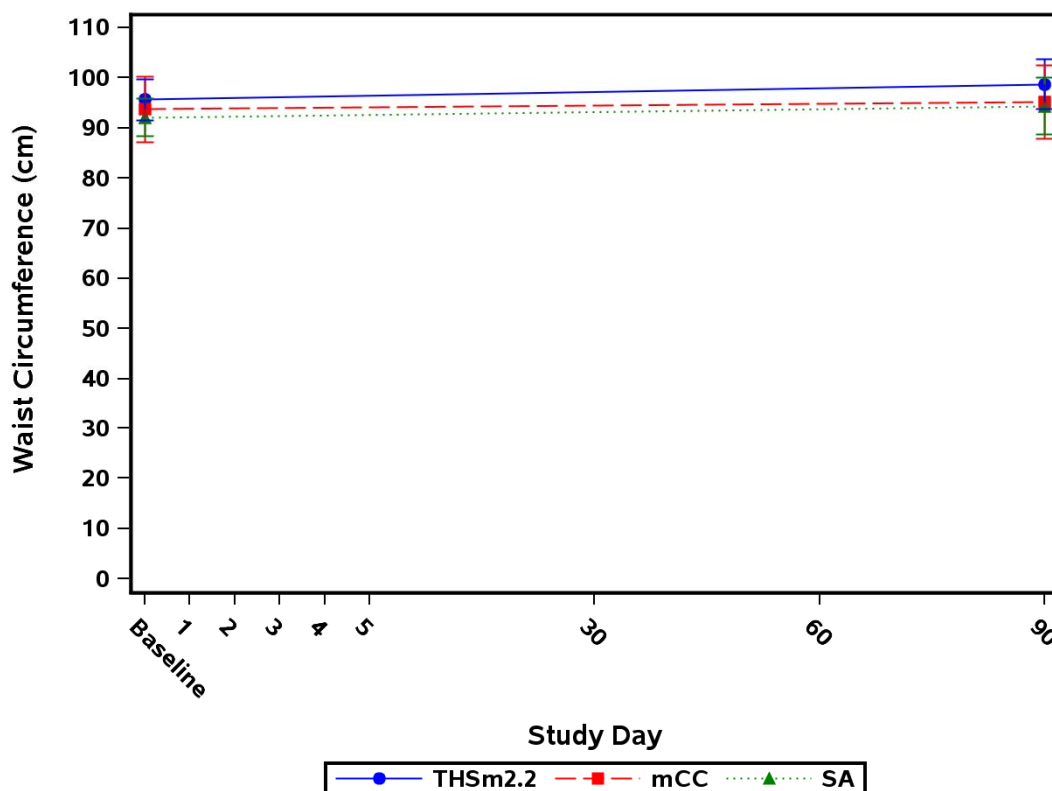
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 3 of 25)

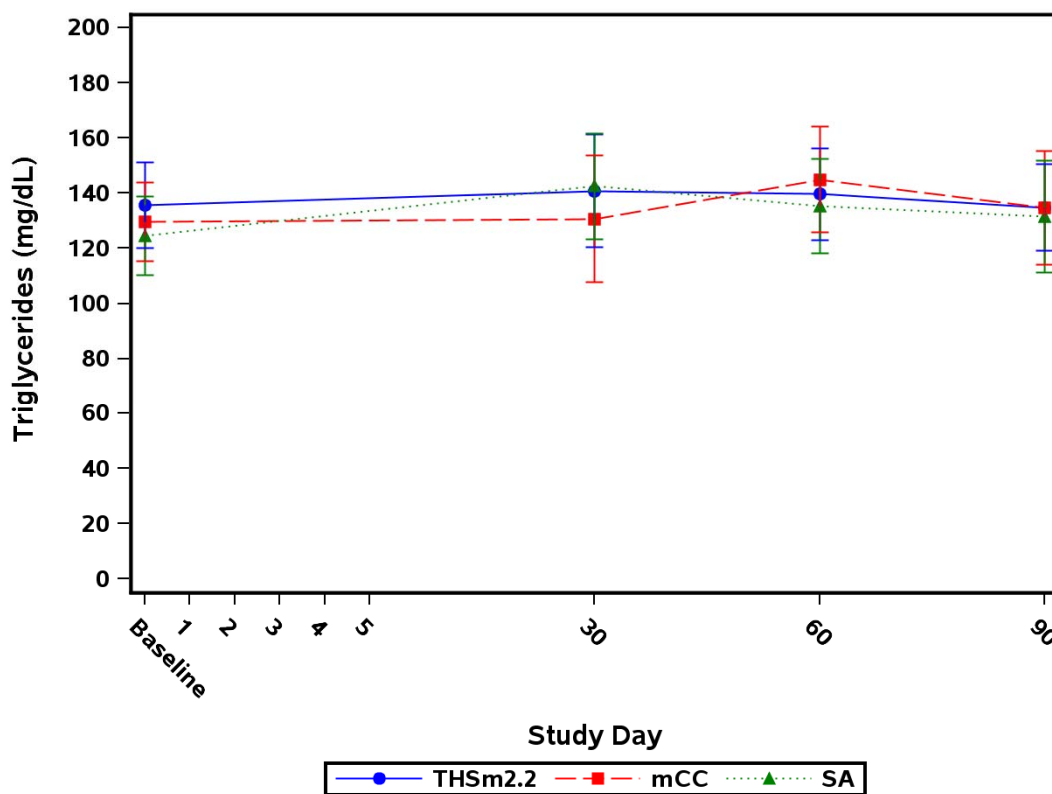
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 4 of 25)

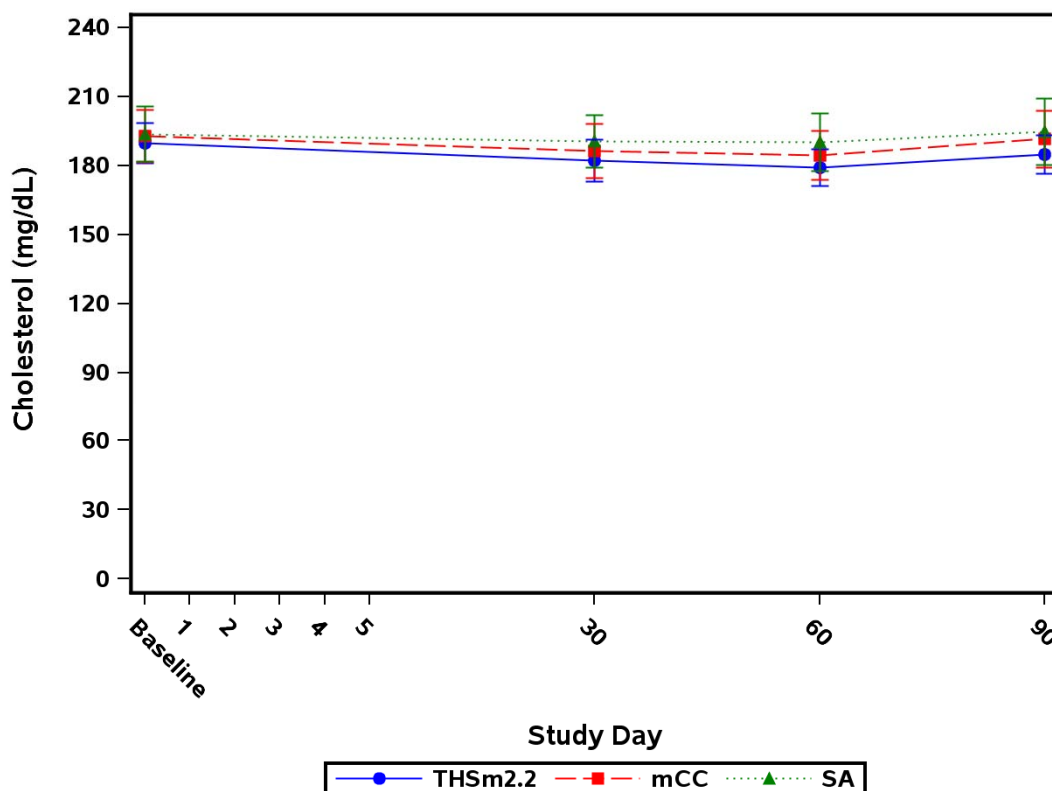
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 5 of 25)

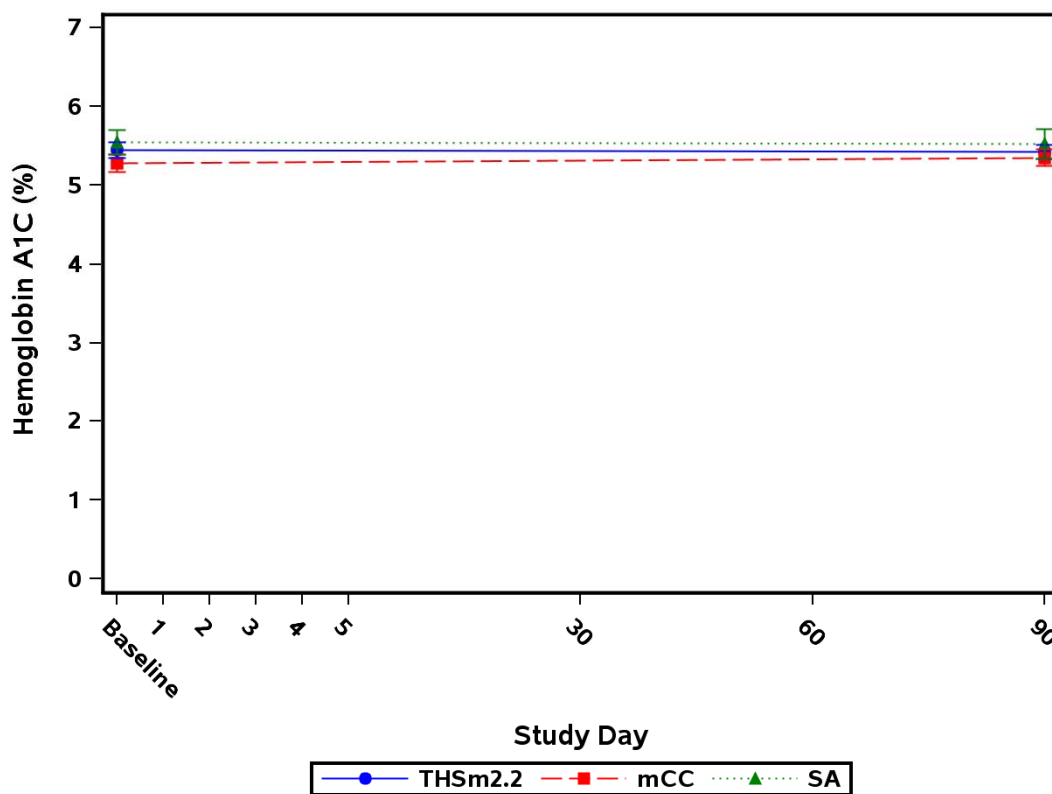
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

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**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

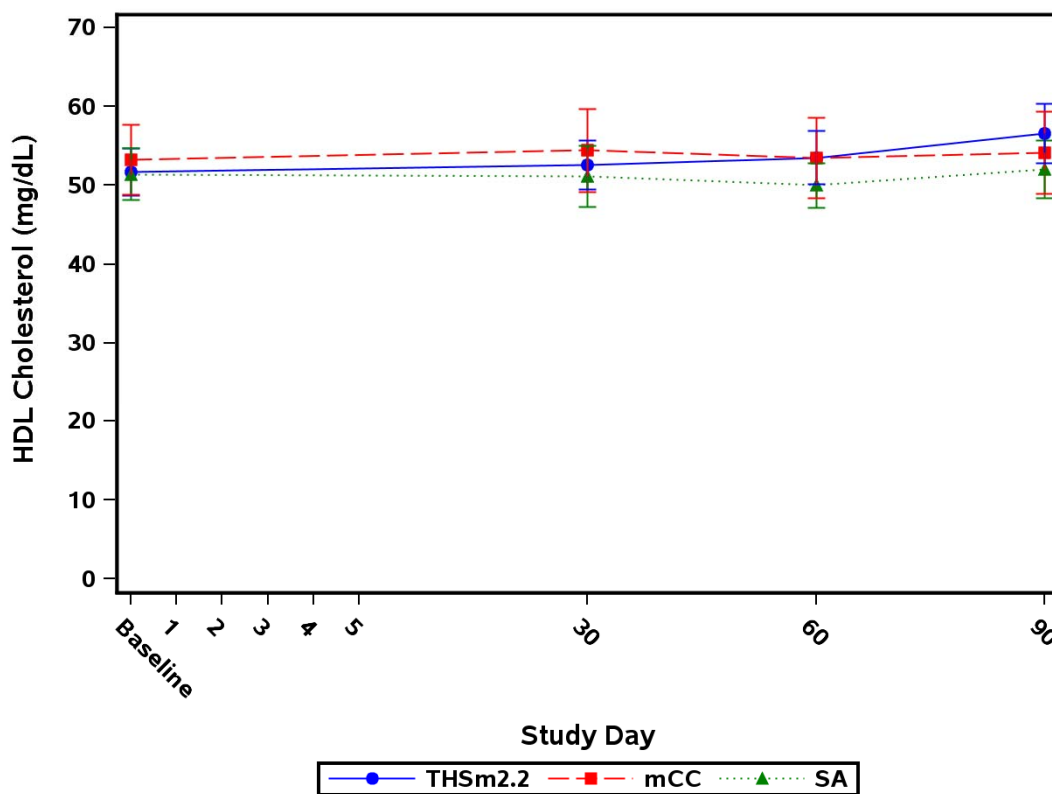
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 7 of 25)



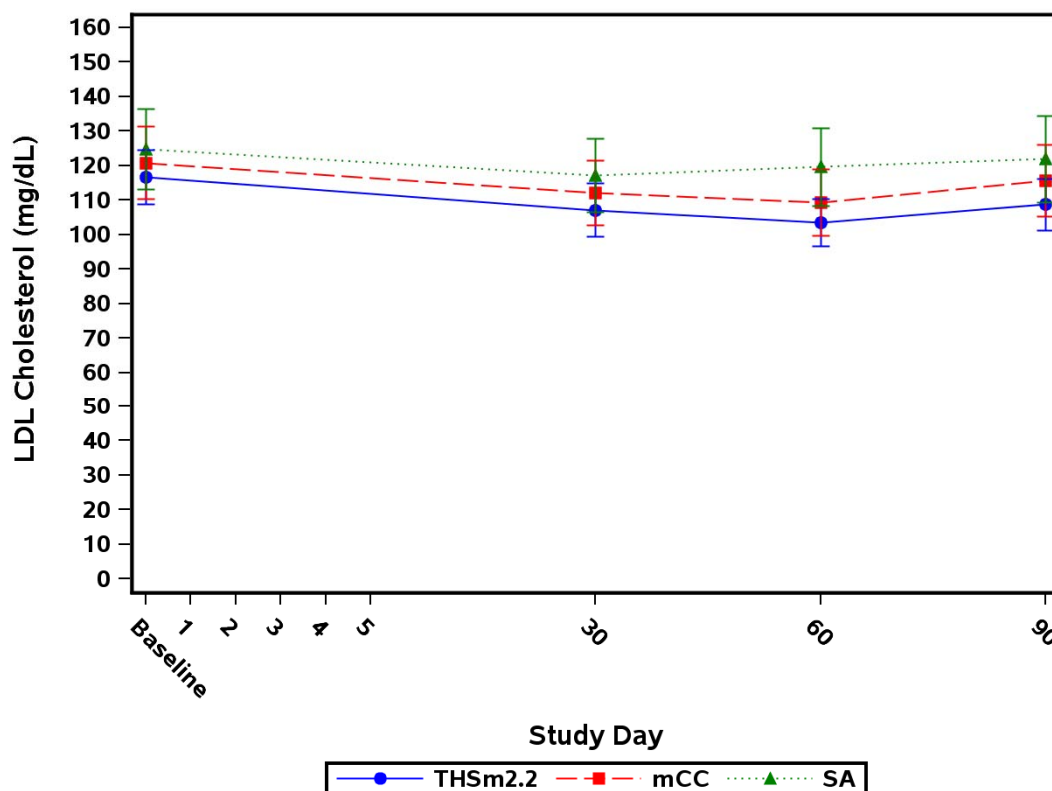
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 8 of 25)

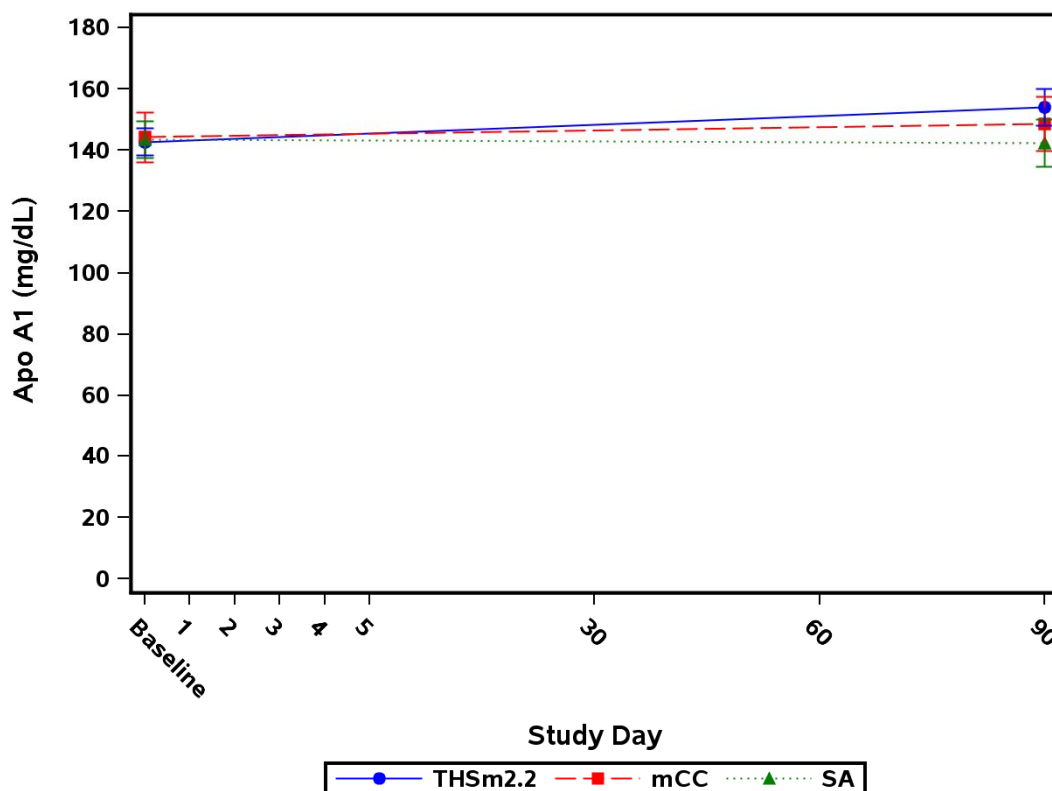
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 9 of 25)

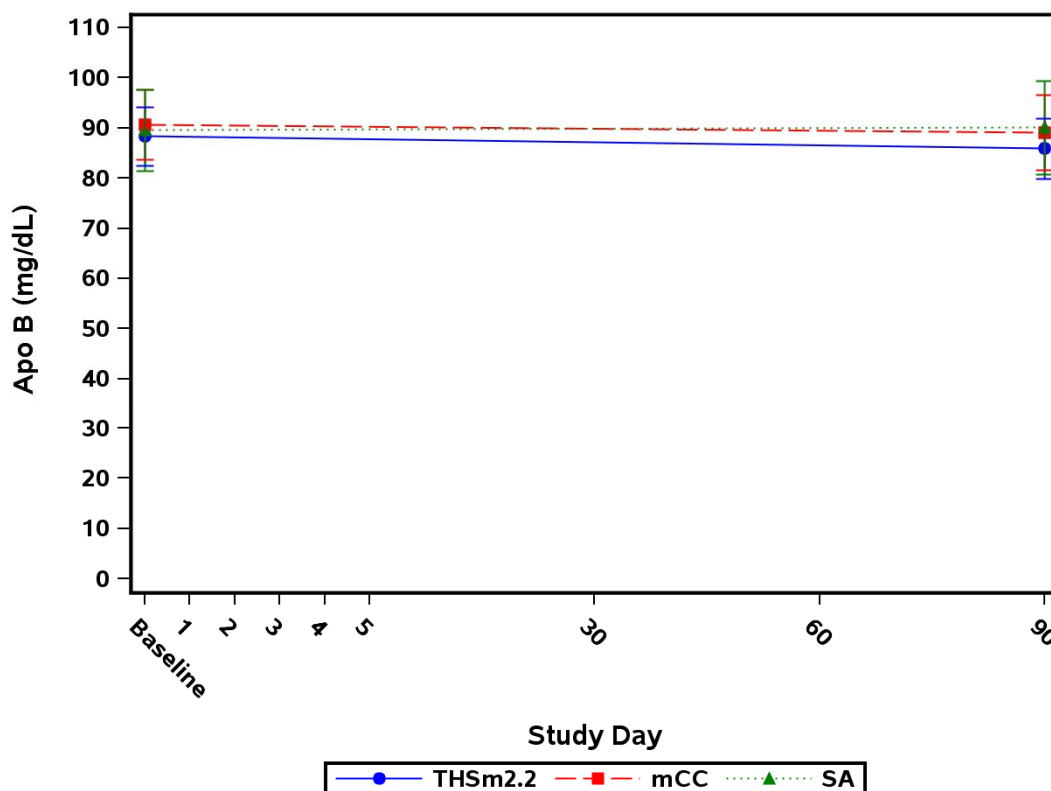
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 10 of 25)

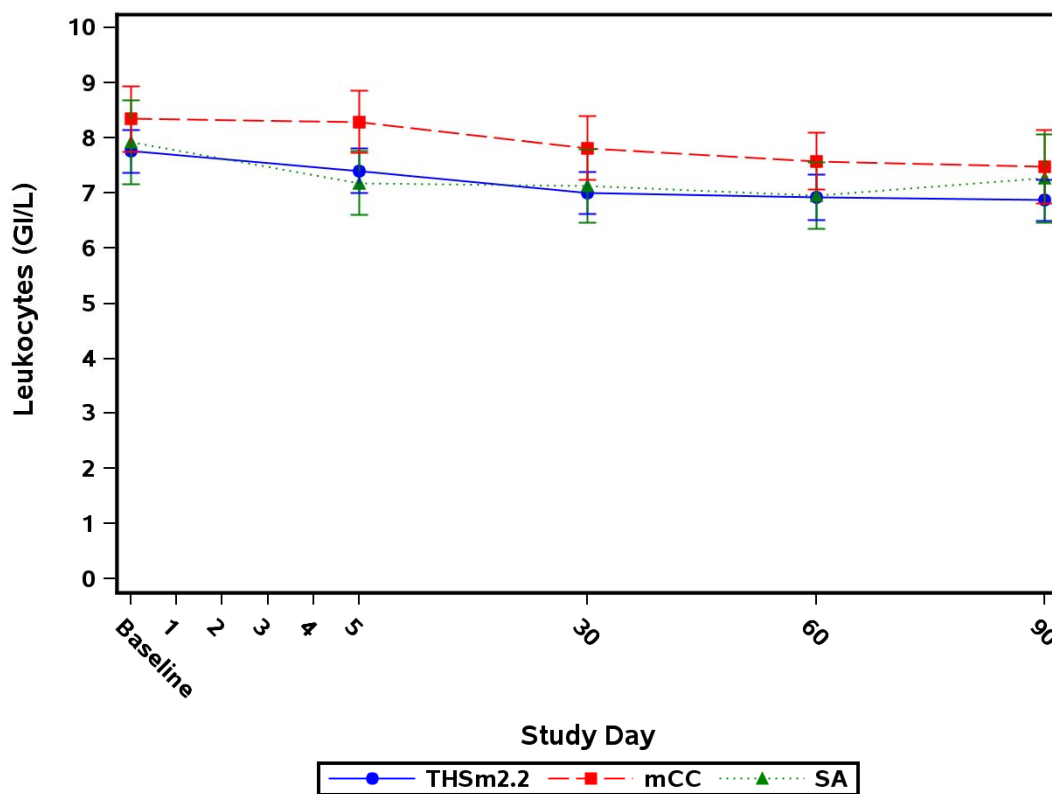
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 11 of 25)

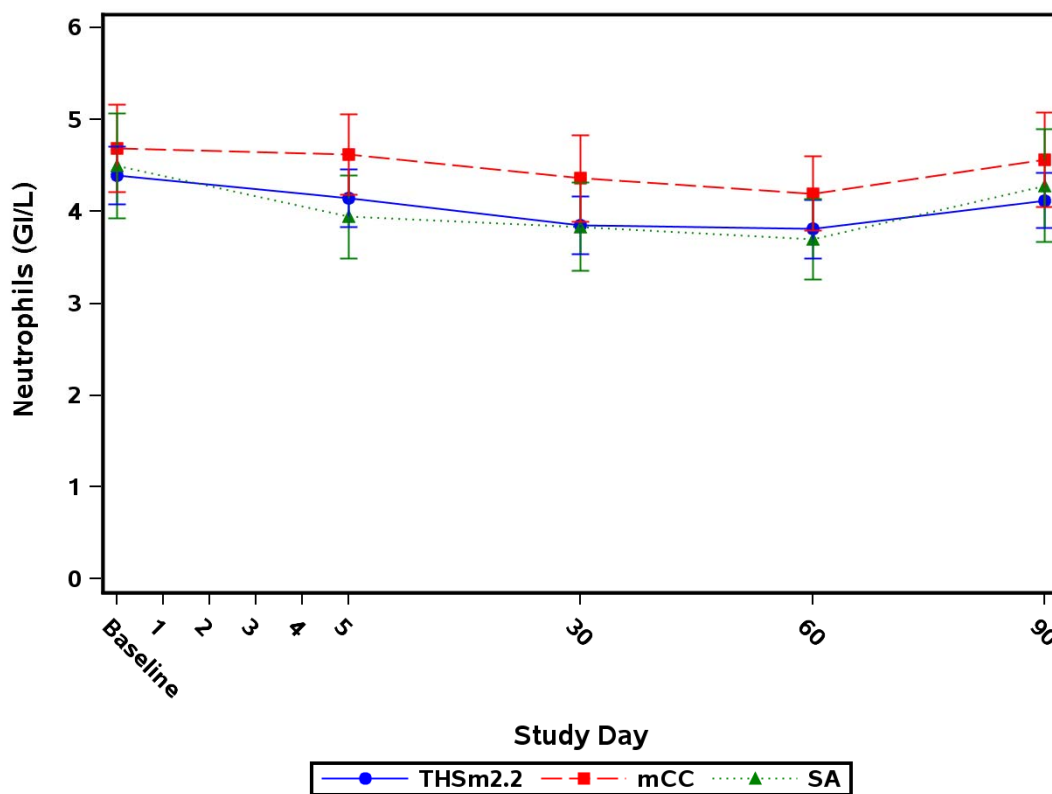
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 12 of 25)

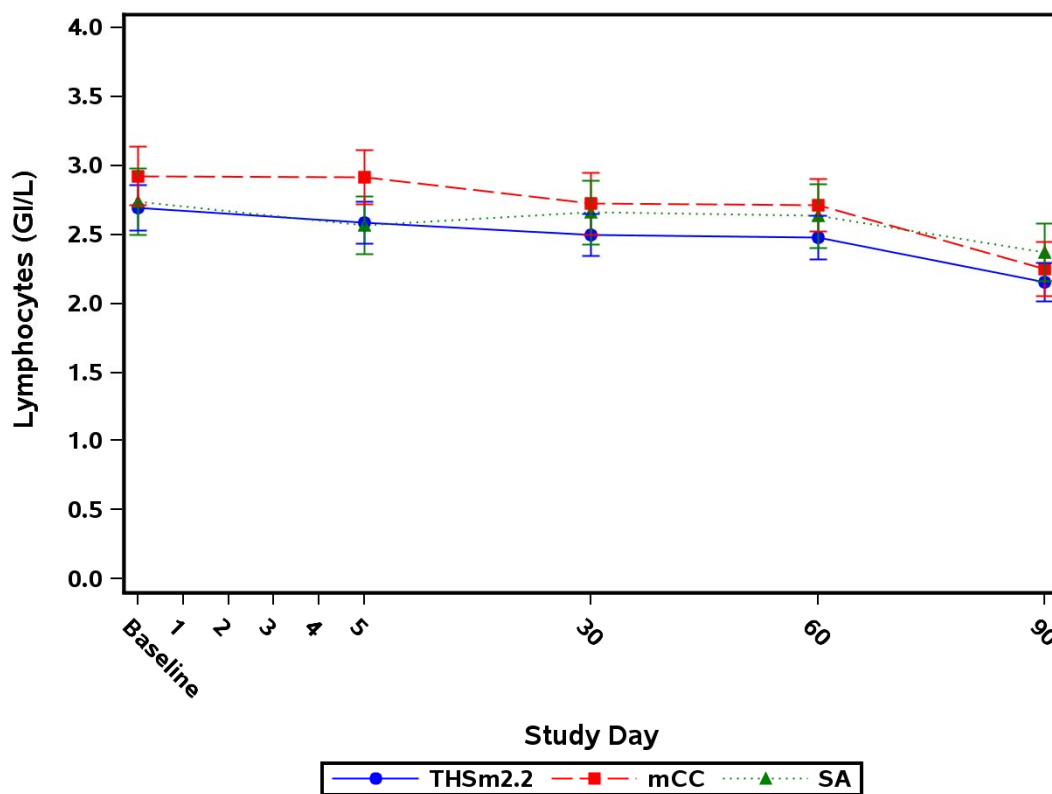
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 13 of 25)

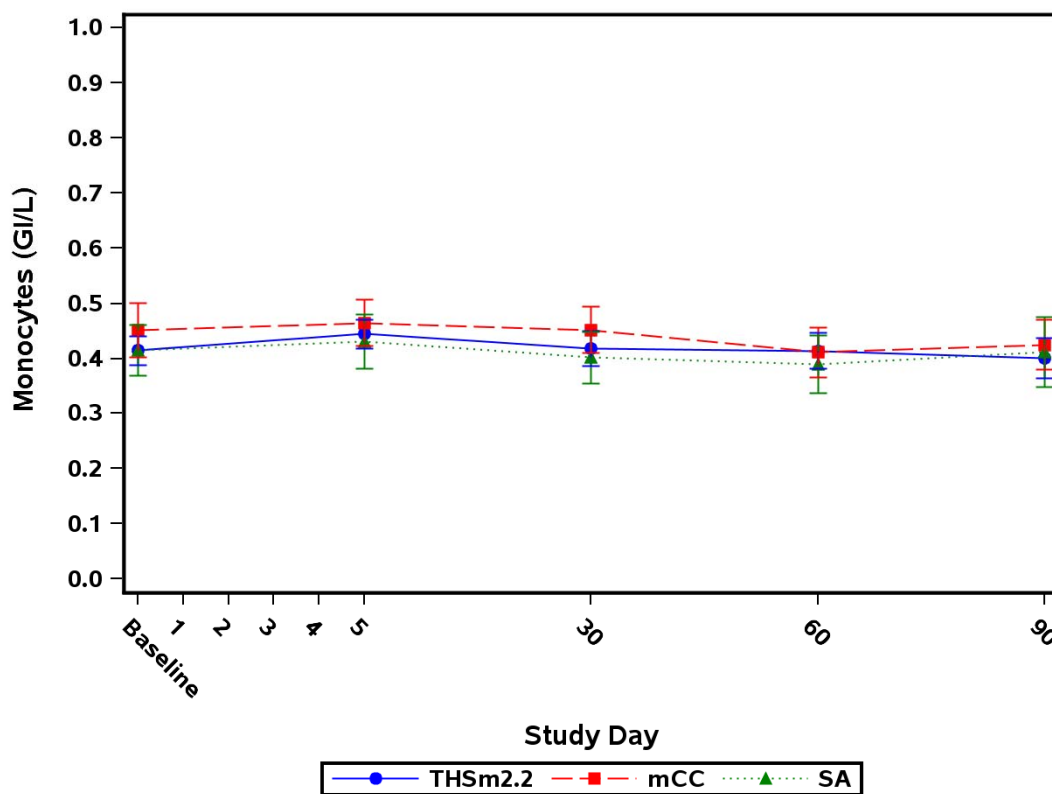
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 14 of 25)

**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

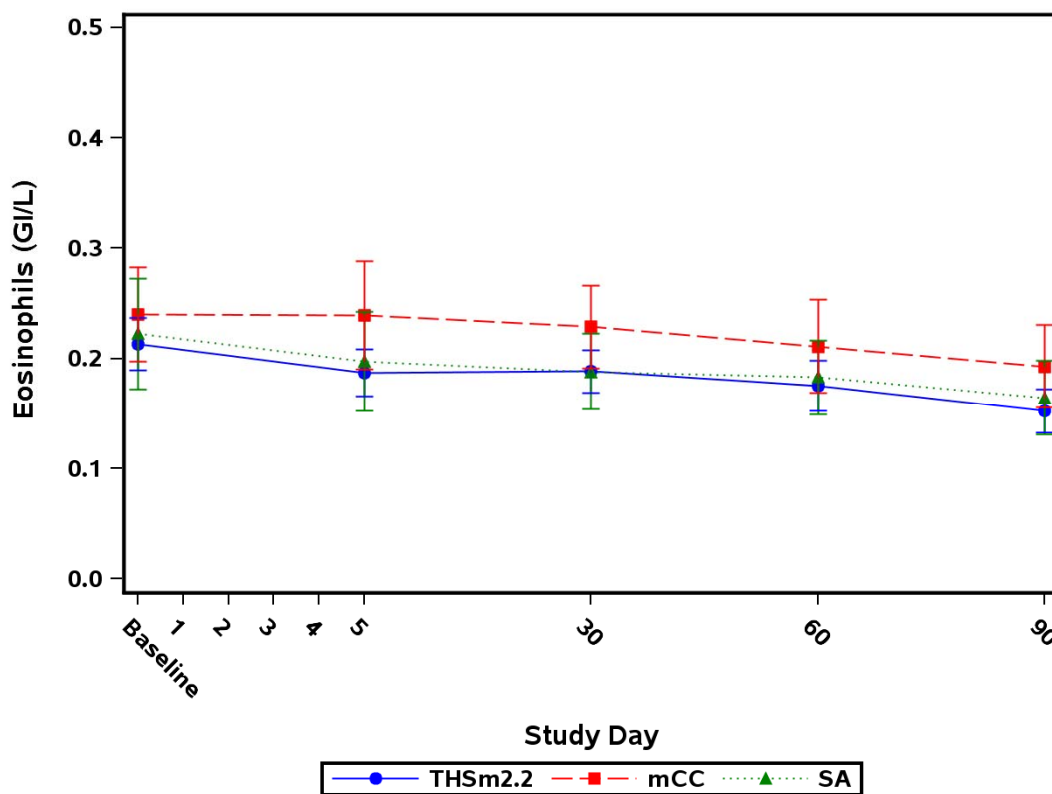
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 15 of 25)



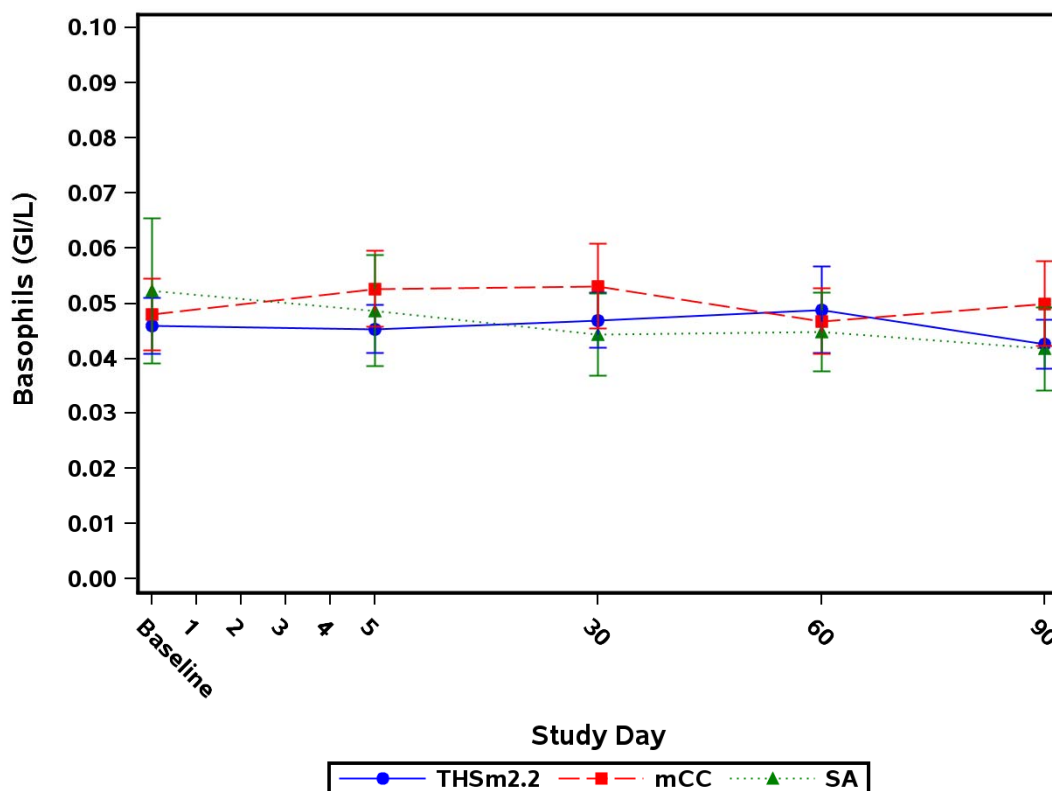
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 16 of 25)

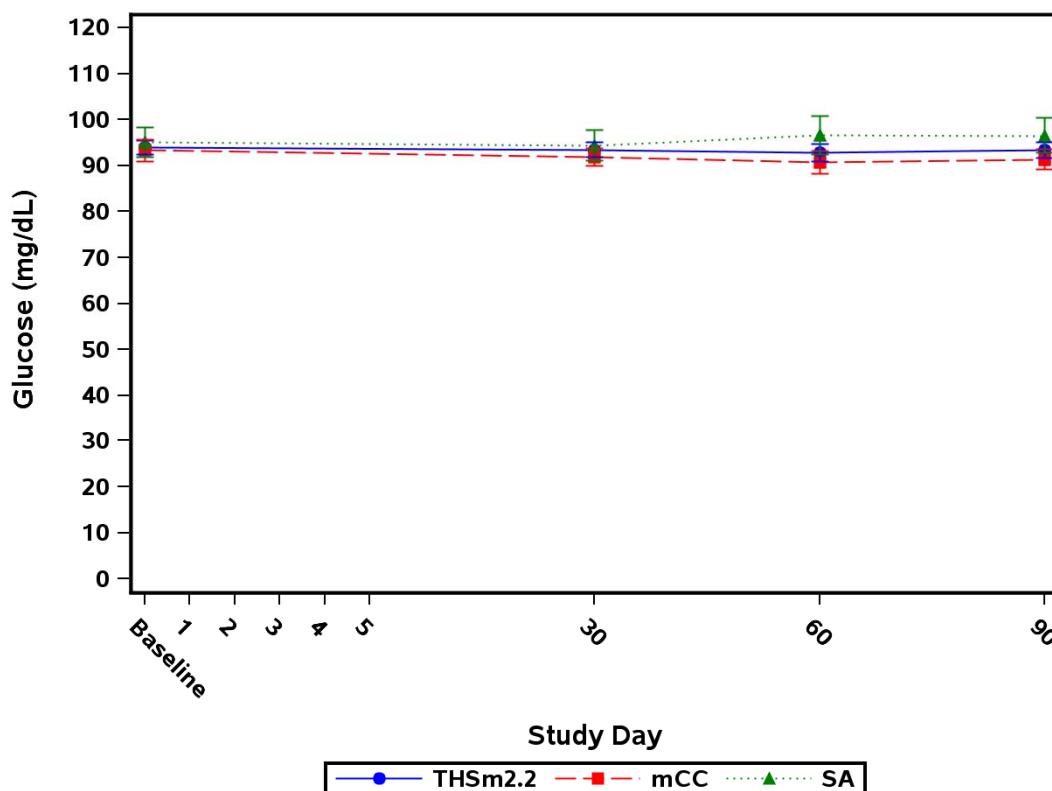
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 17 of 25)

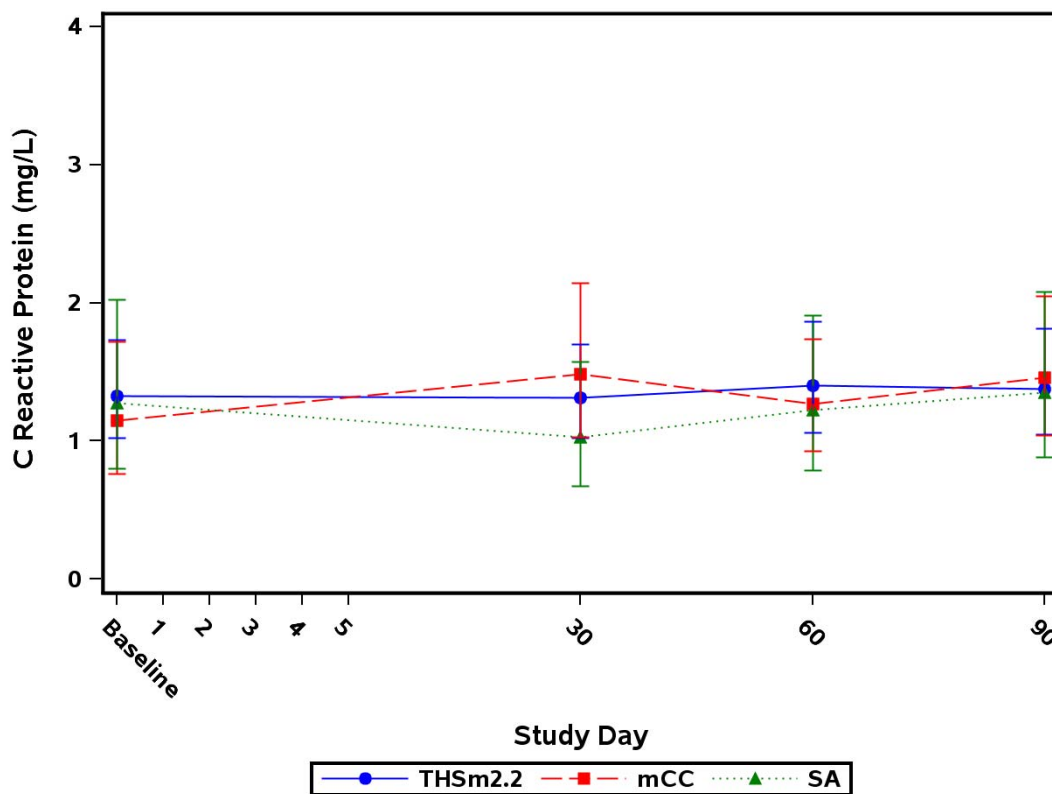
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 18 of 25)

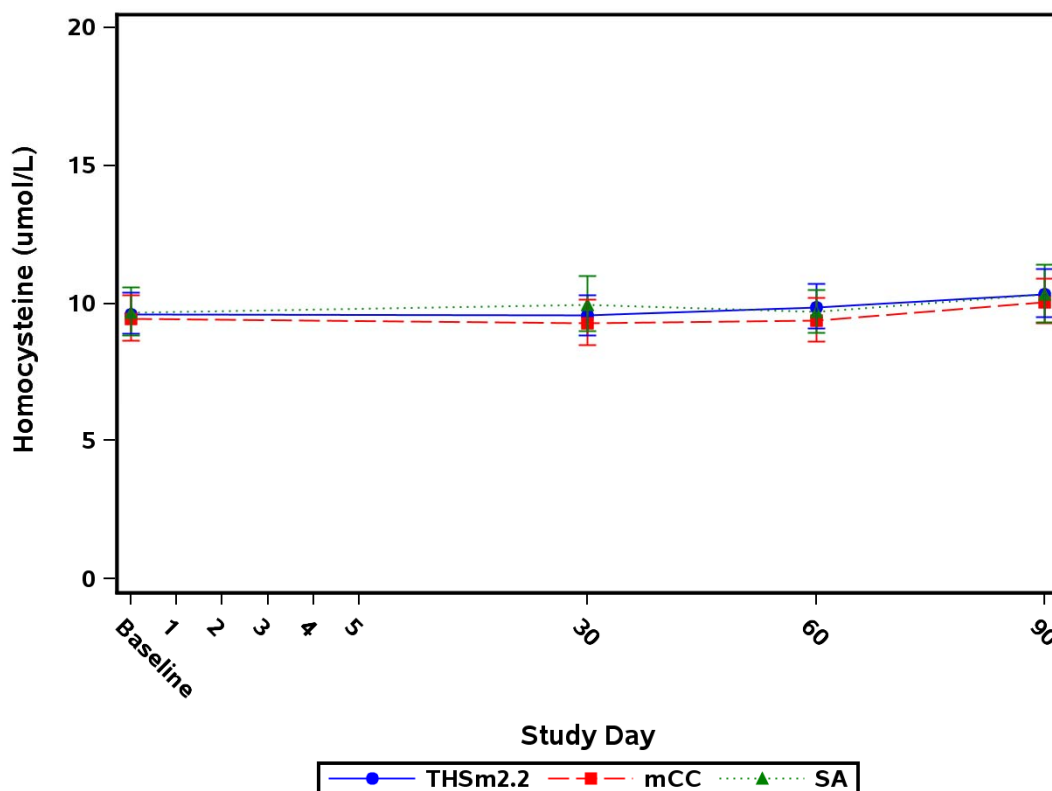
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 19 of 25)

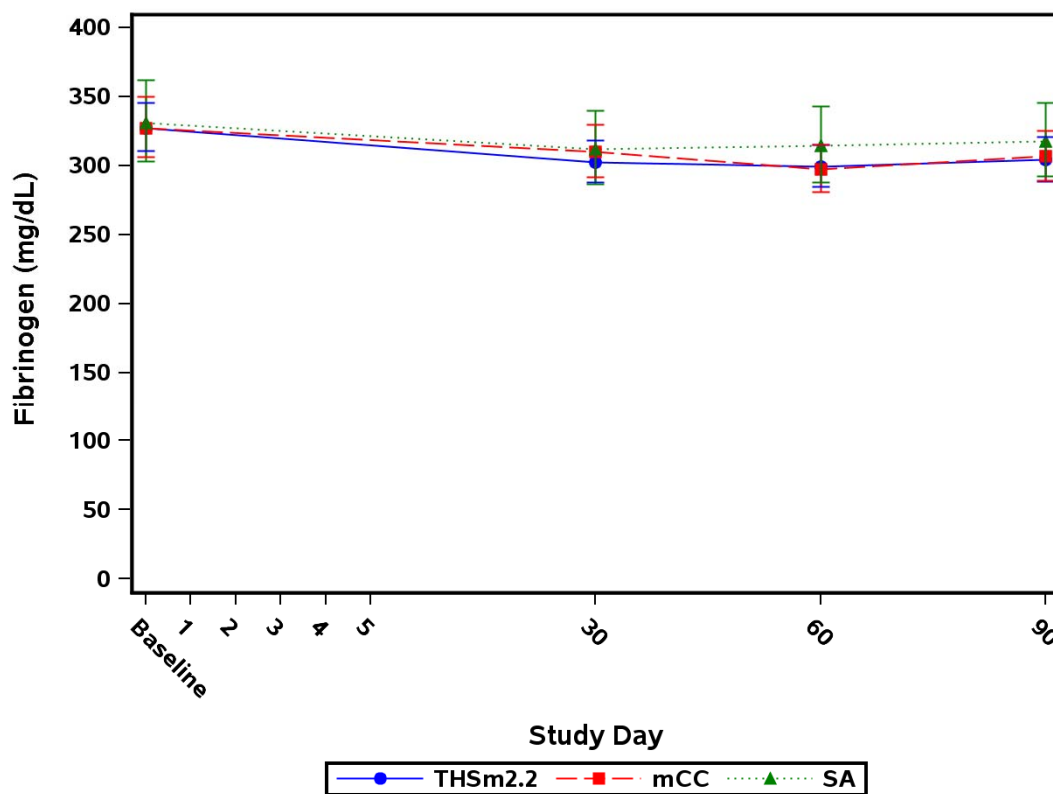
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 20 of 25)

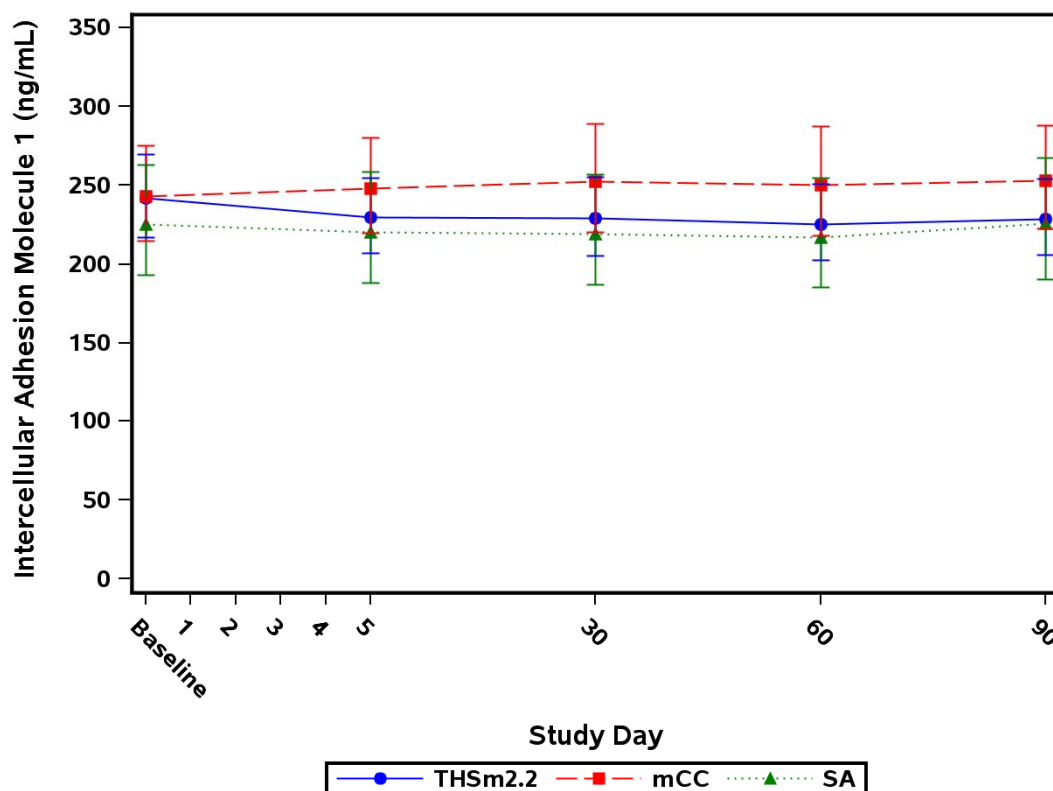
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 21 of 25)

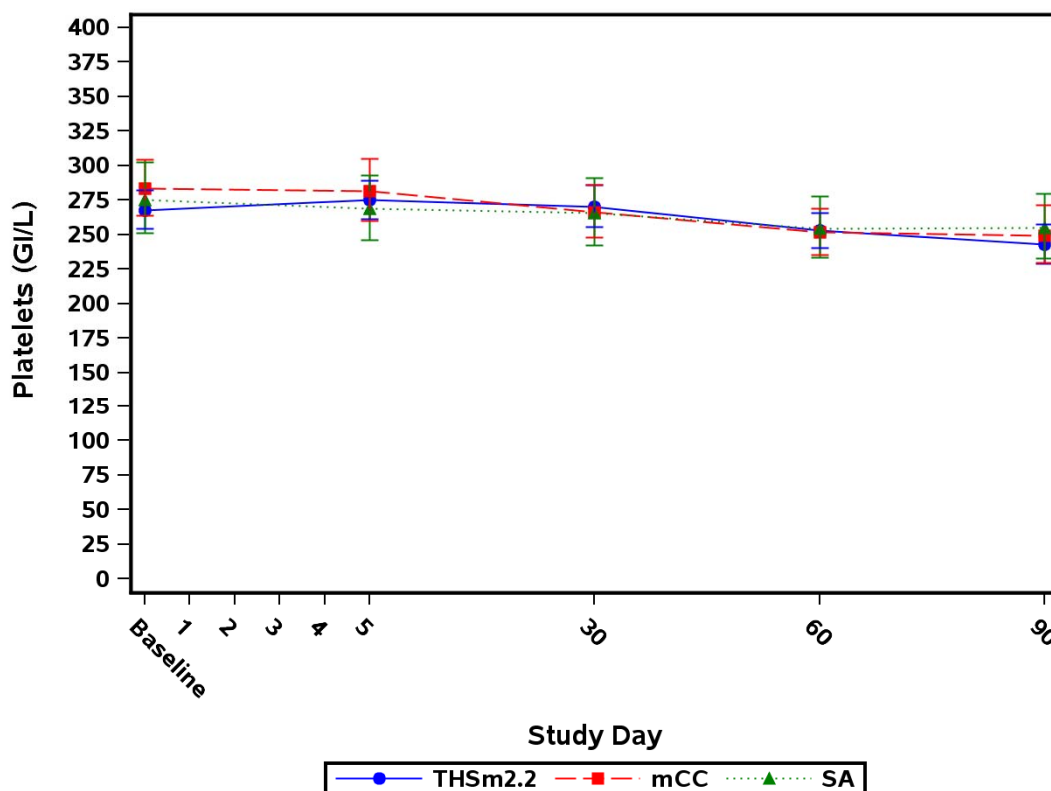
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 22 of 25)

**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

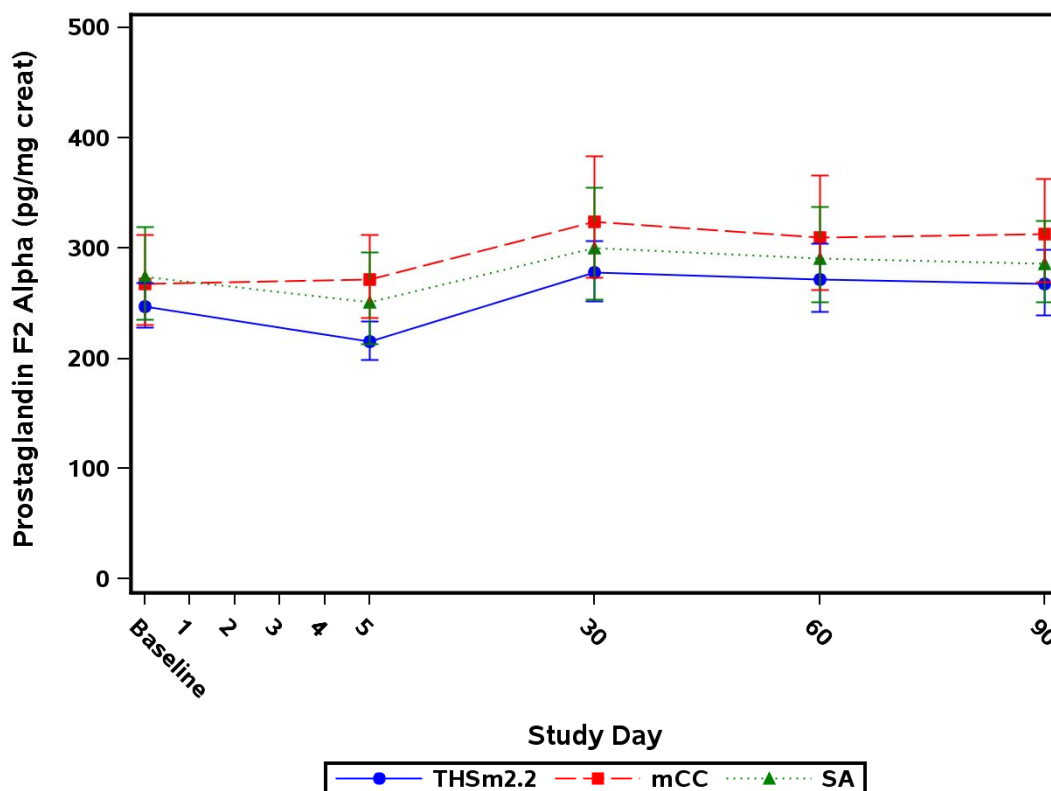
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 23 of 25)



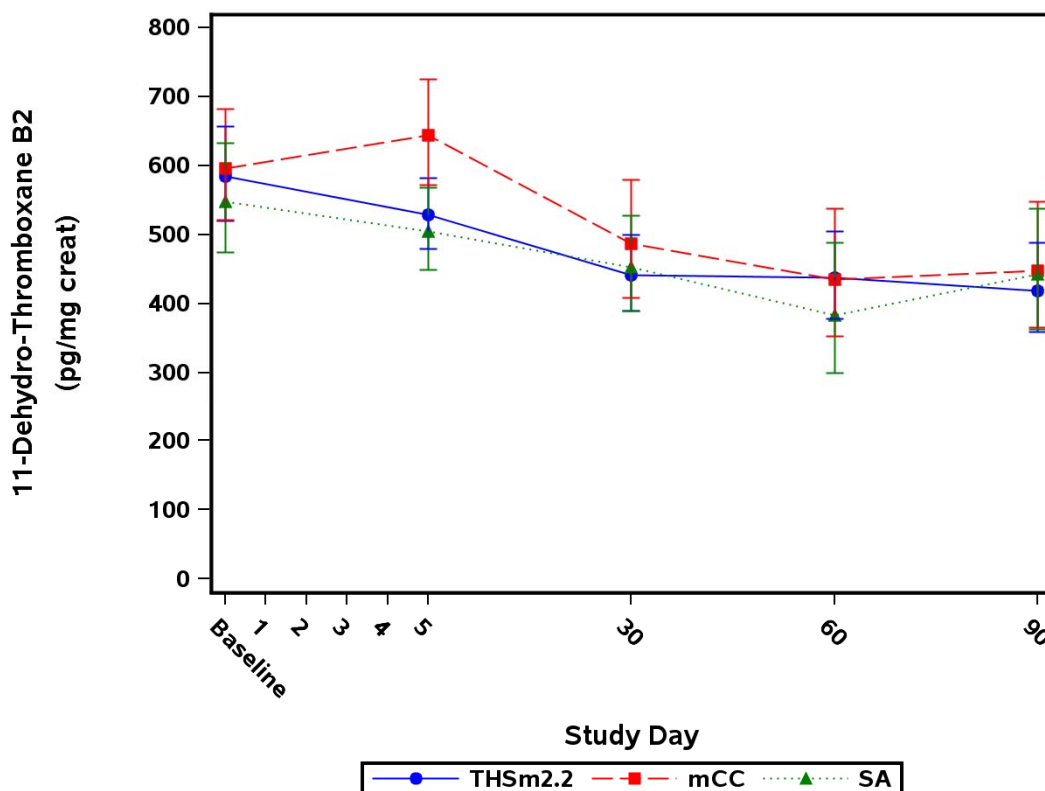
**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID: ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 24 of 25)

**Figure 15.1.2.3.2 Risk Markers Mean and 95% CI - FAS**

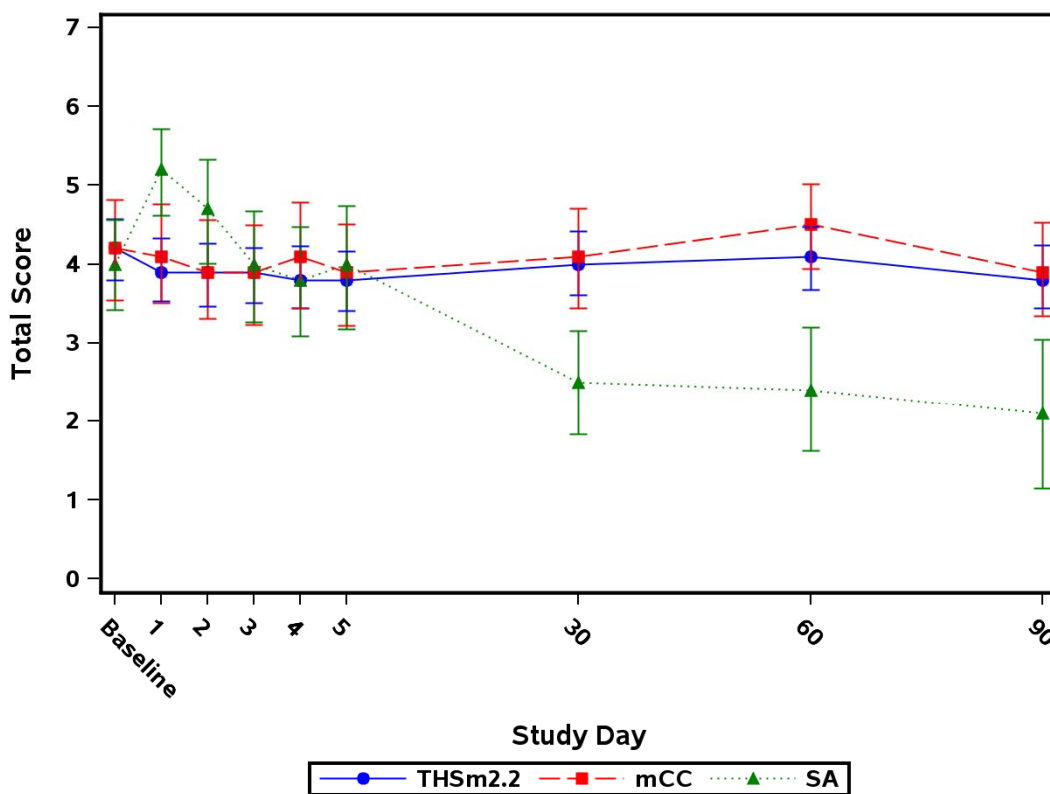
Geometric mean is displayed for C Reactive Protein (mg/L), Fibrinogen (mg/dL), Glucose (mg/dL), Homocysteine (umol/L), Intercellular Adhesion Molecule 1 (ng/mL), Platelets (GI/L), Prostaglandin F2 Alpha (pg/mg creat) and 11-Dehydro-Thromboxane B2 (pg/mg creat). All other risk markers are presented using arithmetic mean.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.26.2, 15.2.4.27.2, 15.2.4.28.2, 15.2.4.29.2, 15.2.4.30.2, 15.2.4.31.2, 15.2.4.32.2, 15.2.4.33.2.

Study ID:ZRHM-REXA-08-US Program: f\_riskmrk\_fas.sas 16MAR16 Status: Final (Page 25 of 25)

**Figure 15.1.2.4.1 QSU-brief Total Scores Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

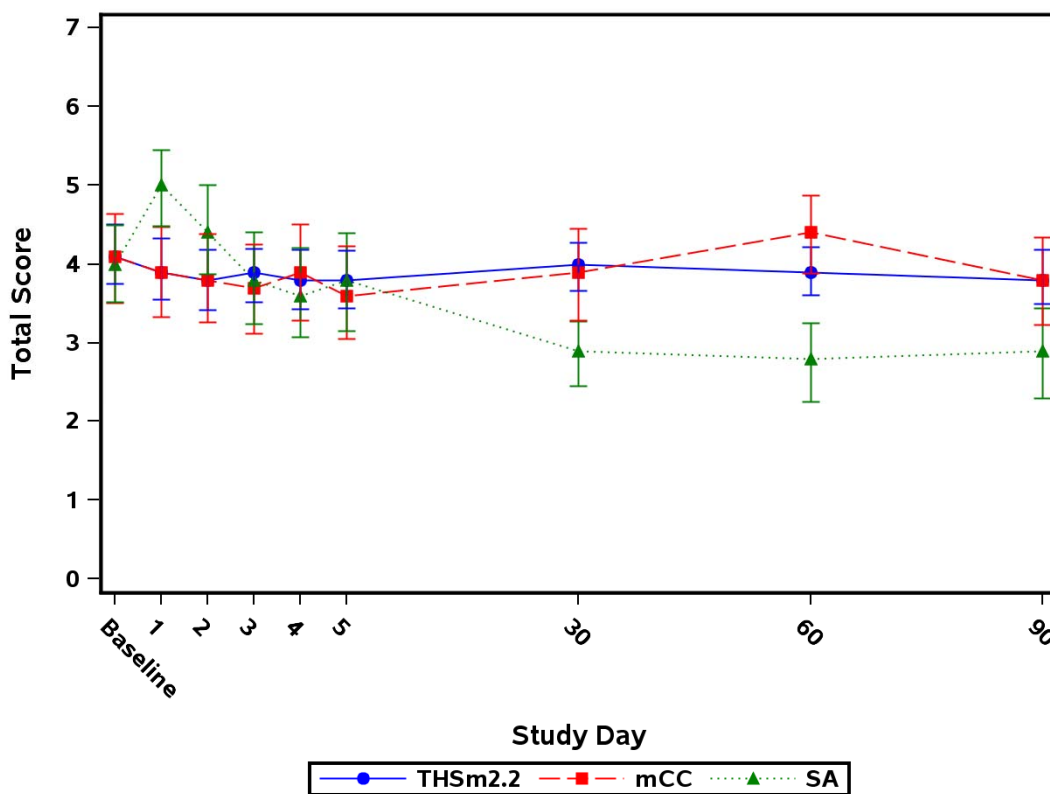
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: QSU-brief scores reported on a 7-point scale. Higher values indicate greater intensity of urge.

Appendix 15.2.4.52.1

Study ID: ZRHM-REXA-08-US Program: f\_qsutotal\_pp.sas 21SEP15 Status: Final (Page 1 of 1)

**Figure 15.1.2.4.2 QSU-brief Total Scores Arithmetic Mean and 95% CI – FAS**

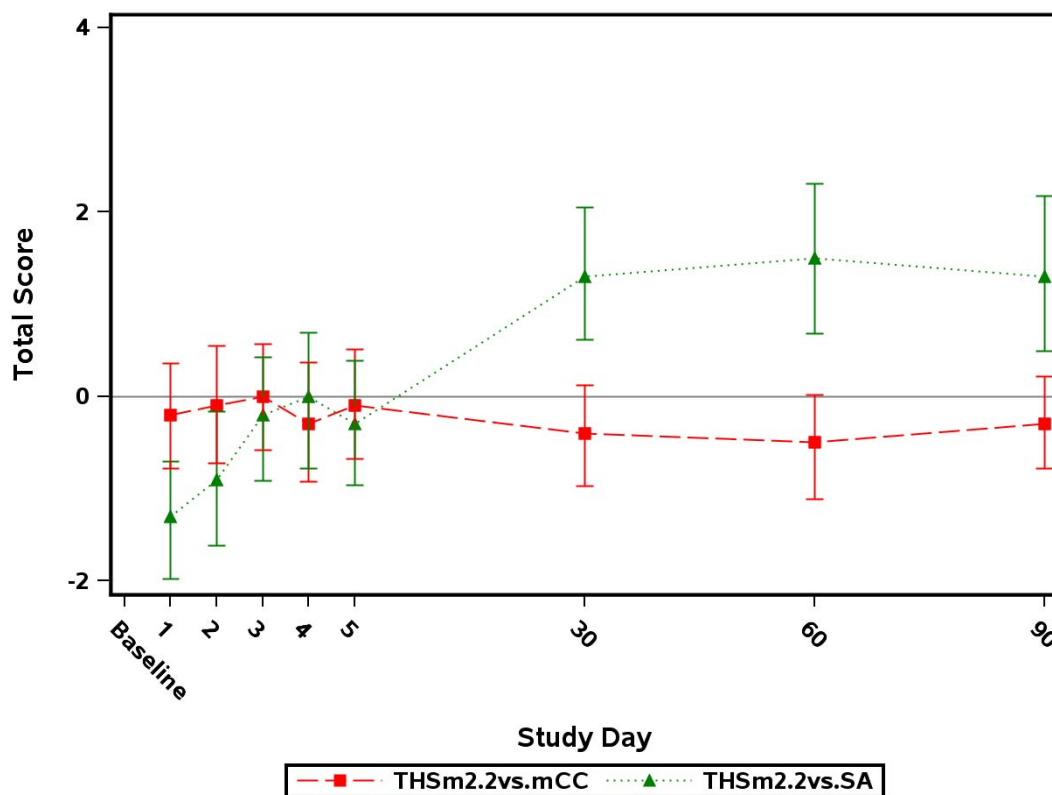
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: QSU-brief scores reported on a 7-point scale. Higher values indicate greater intensity of urge.

Appendix 15.2.4.52.2

Study ID: ZRHM-REXA-08-US Program: f\_qsutotal\_fas.sas 21SEP15 Status: Final (Page 1 of 1)

**Figure 15.1.2.5.1 QSU-brief Total Scores Least Squares Mean and 95% CI - PP Set**

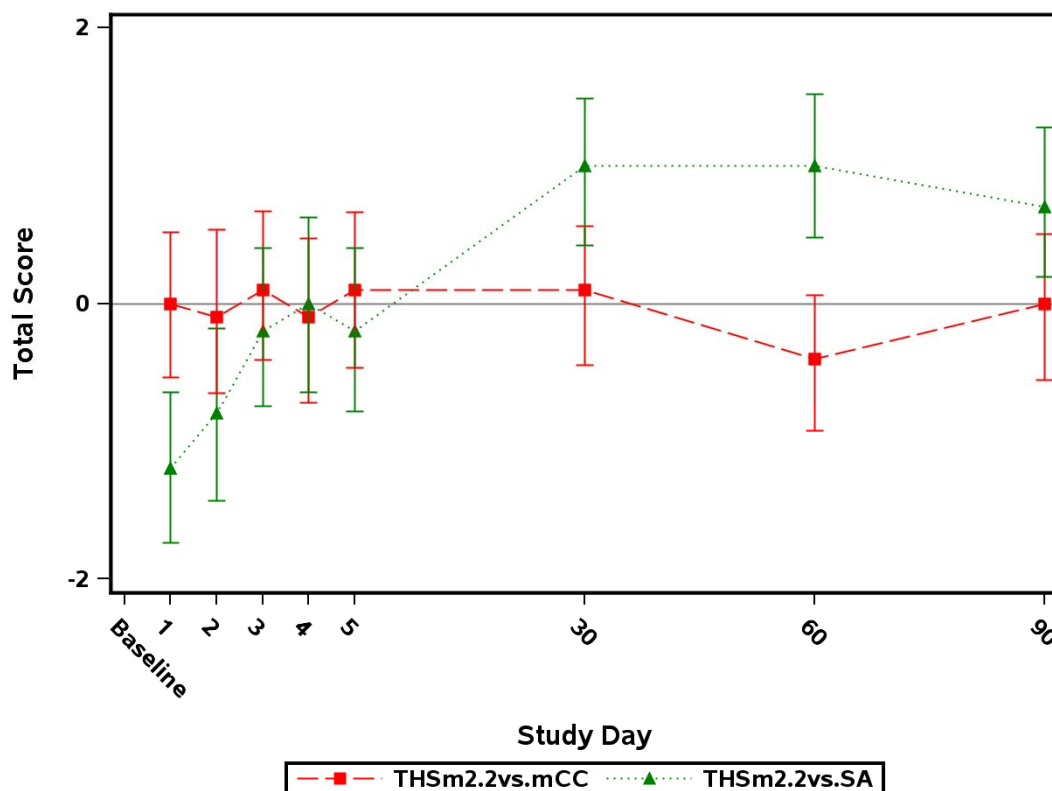
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: QSU-brief scores reported on a 7-point scale. Higher values indicate greater intensity of urge.

Appendix 15.2.4.53.1

Study ID: ZRHM-REXA-08-US Program: f\_qsu\_ls\_pp.sas 21SEP15 Status: Final (Page 1 of 1)

**Figure 15.1.2.5.2 QSU-brief Total Scores Least Squares Mean and 95% CI - FAS**

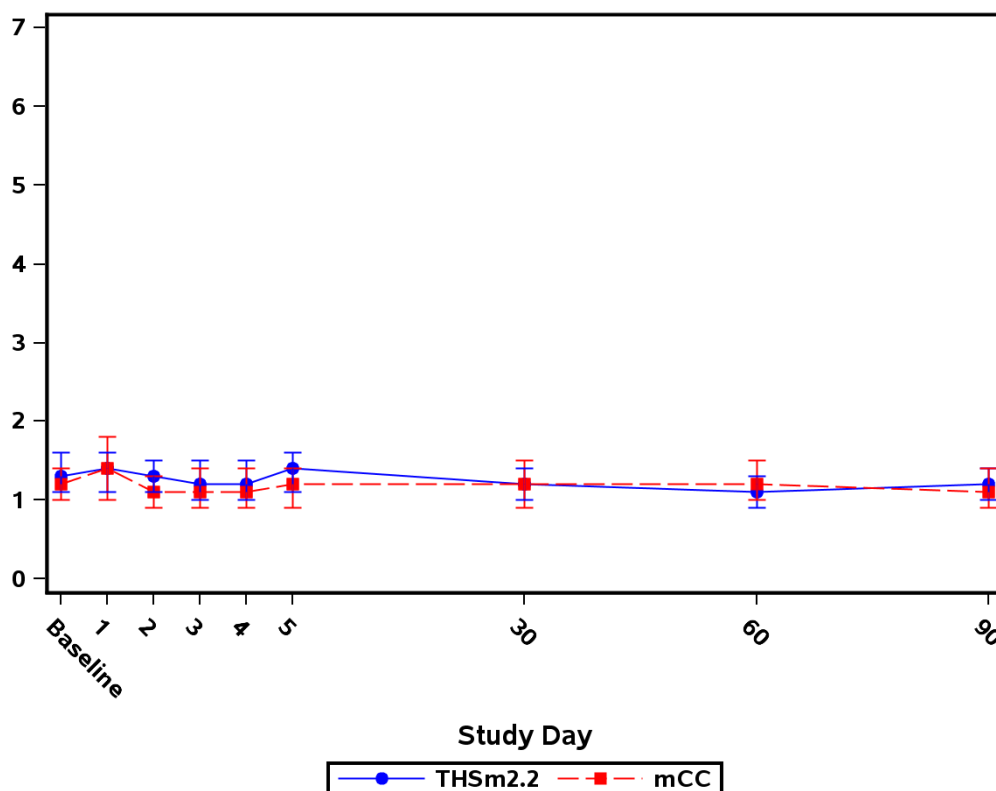
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: QSU-brief scores reported on a 7-point scale. Higher values indicate greater intensity of urge.

Appendix 15.2.4.53.2

Study ID: ZRHM-REXA-08-US. Program: f\_qsu\_ls\_fas.sas 21SEP15 Status: Final (Page 1 of 1)

**Figure 15.1.2.6.1 MCEQ Subscales Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

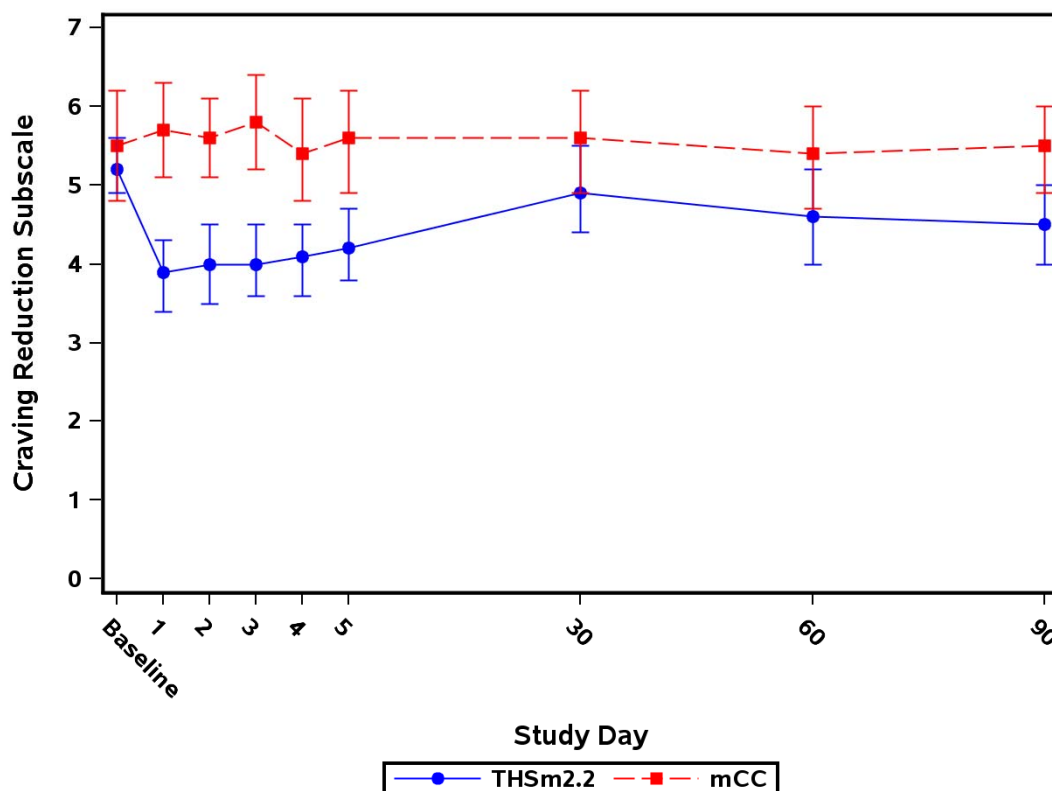
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.1

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_pp.sas 21SEP15 Status: Final (Page 1 of 5)

**Figure 15.1.2.6.1 MCEQ Subscales Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

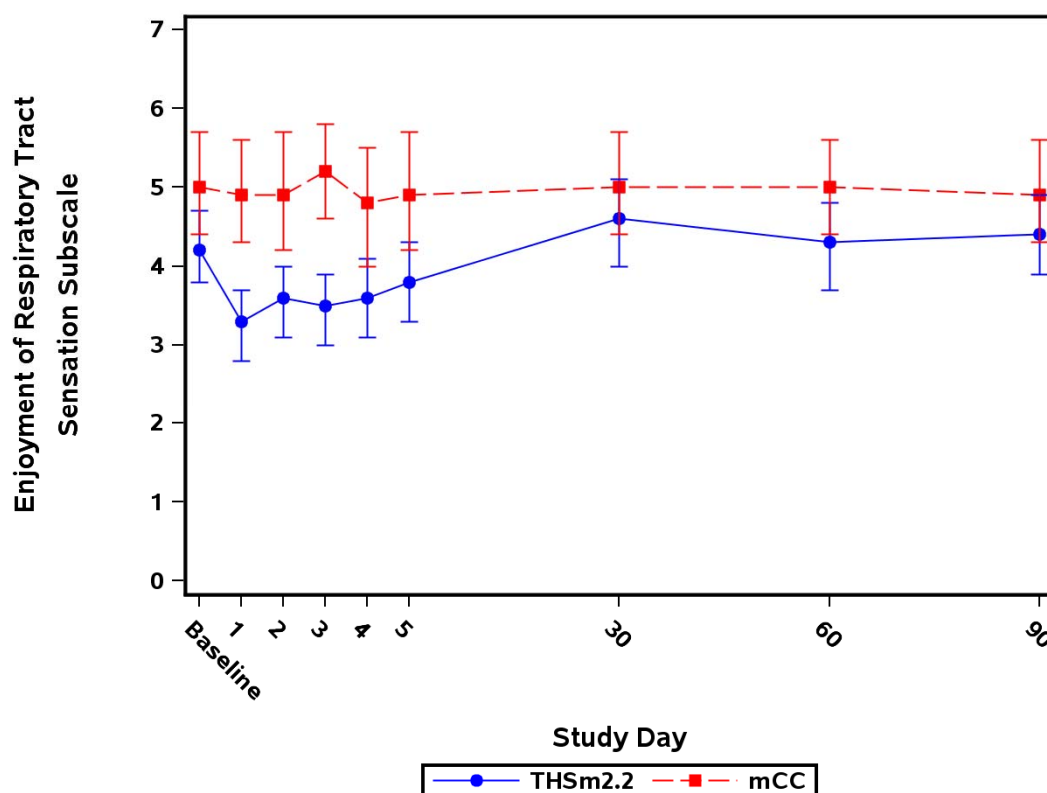
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.1

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_pp.sas 21SEP15 Status: Final (Page 2 of 5)



**Figure 15.1.2.6.1 MCEQ Subscales Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

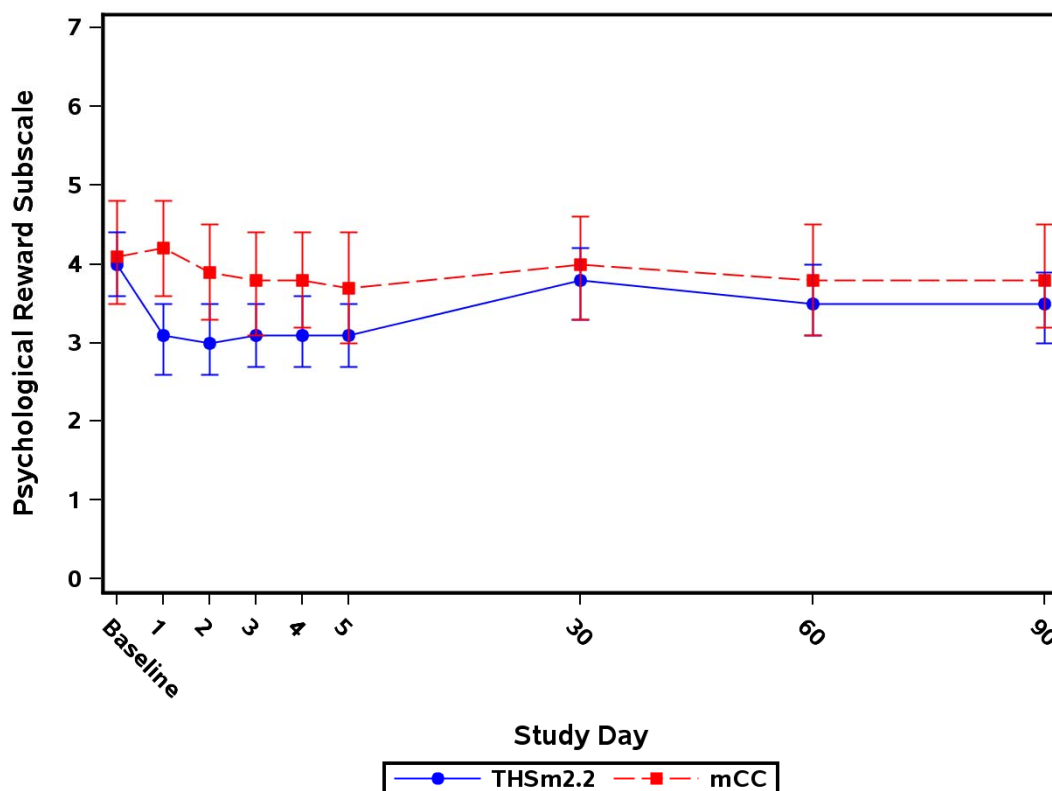
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.1

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_pp.sas 21SEP15 Status: Final (Page 3 of 5)

**Figure 15.1.2.6.1 MCEQ Subscales Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

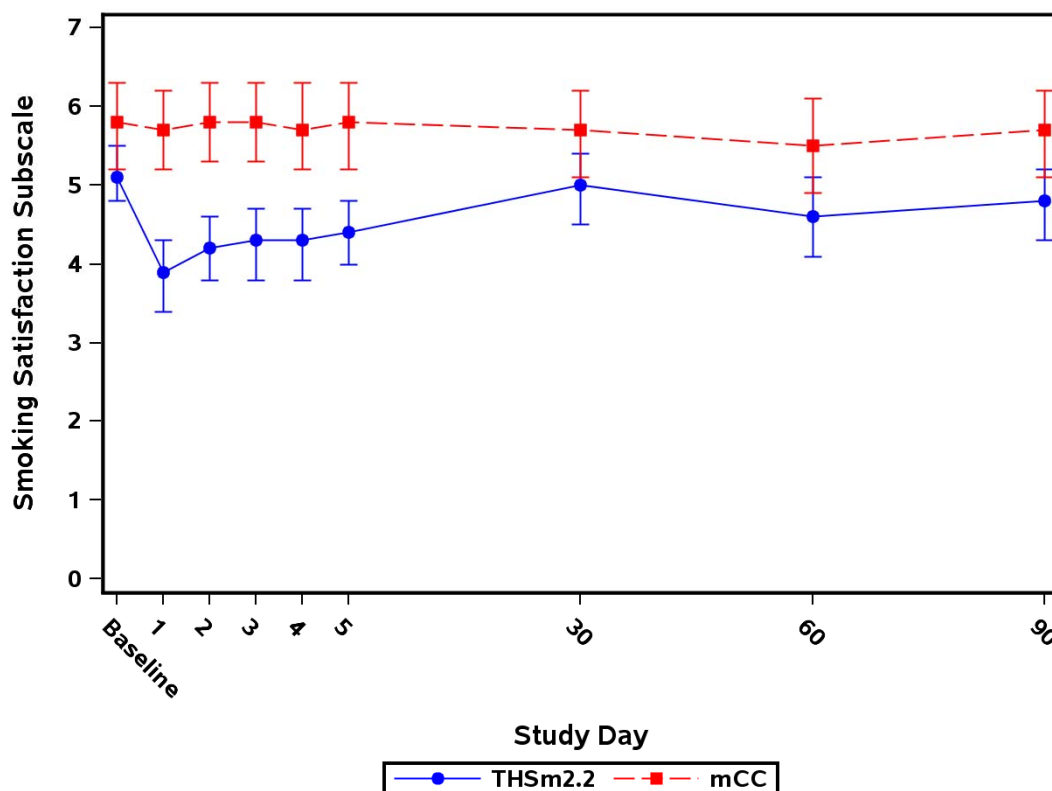
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.1

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_pp.sas 21SEP15 Status: Final (Page 4 of 5)

**Figure 15.1.2.6.1 MCEQ Subscales Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

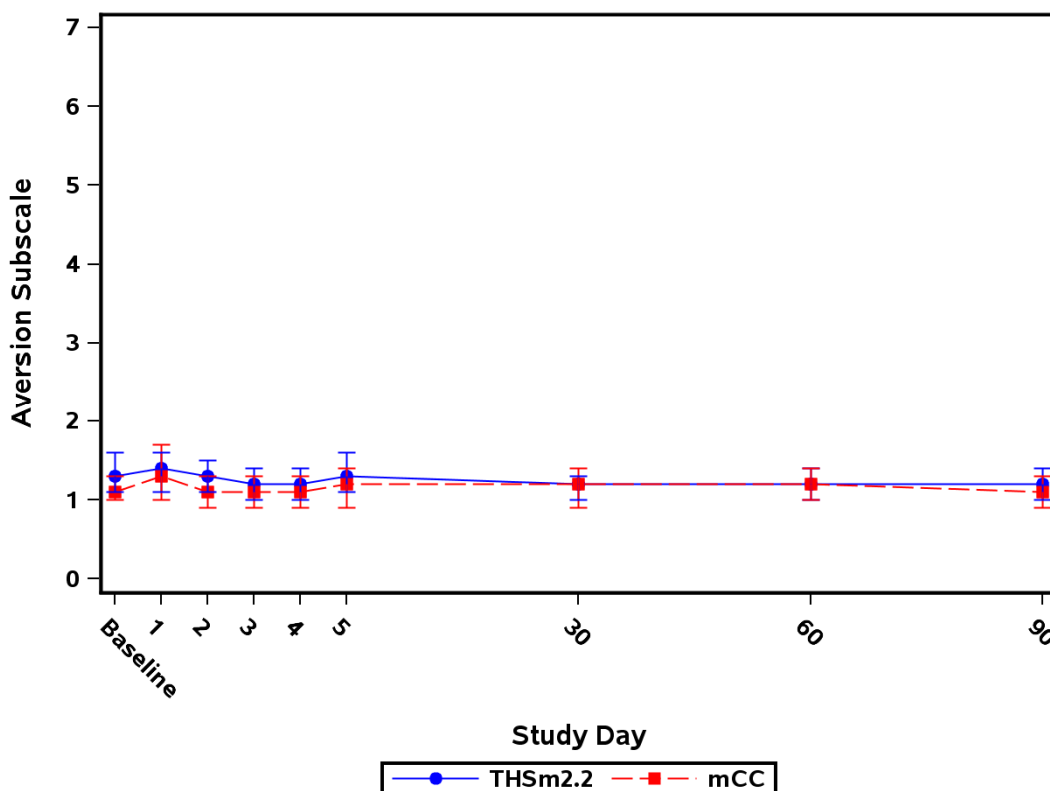
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.1

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**Figure 15.1.2.6.2 MCEQ Subscales Arithmetic Mean and 95% CI - FAS**

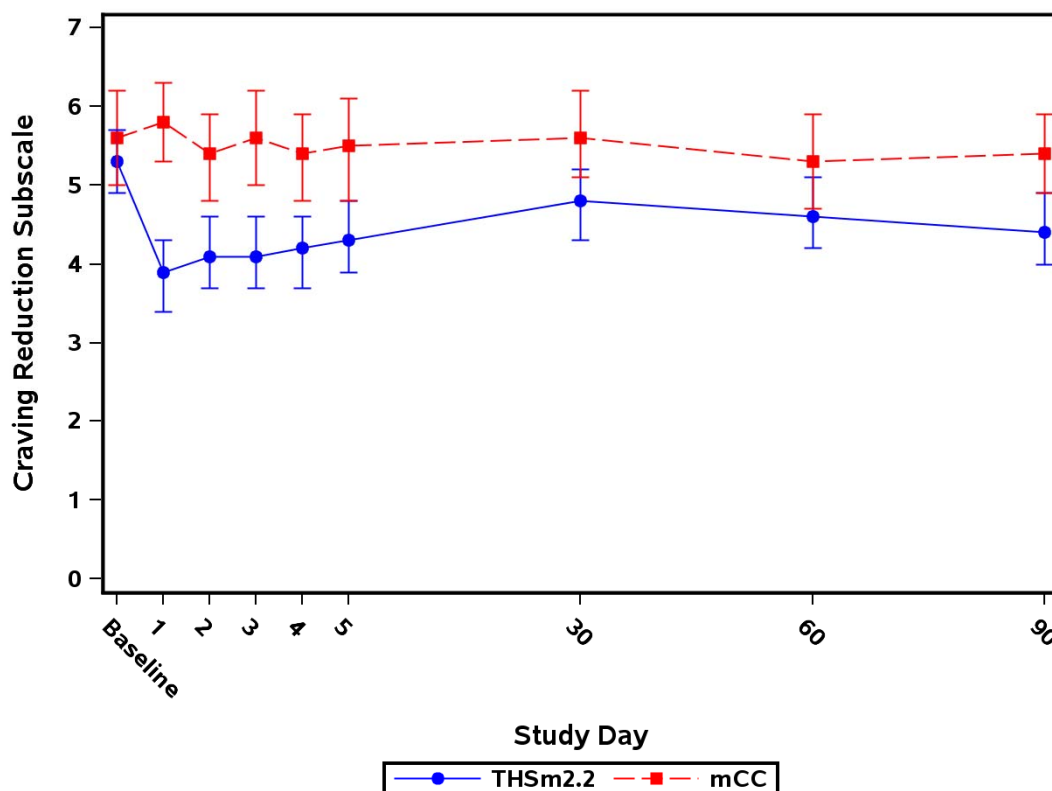
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.2

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_fas.sas 21SEP15 Status: Final (Page 1 of 5)

**Figure 15.1.2.6.2 MCEQ Subscales Arithmetic Mean and 95% CI - FAS**

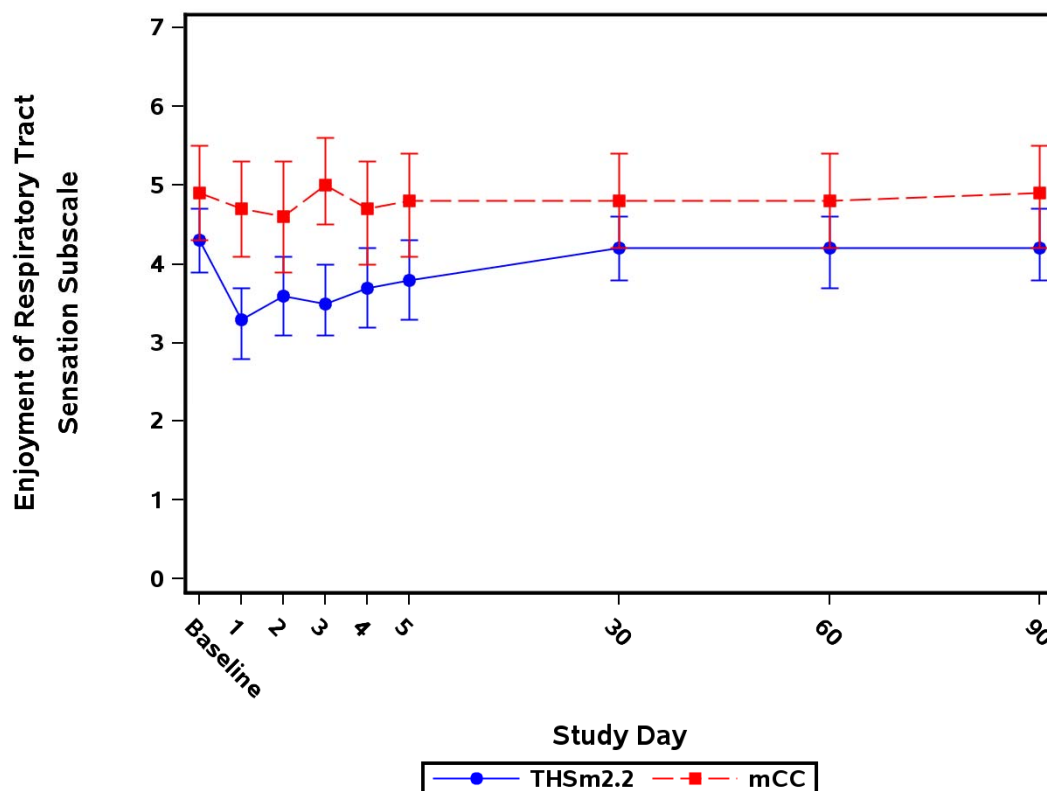
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.2

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**Figure 15.1.2.6.2 MCEQ Subscales Arithmetic Mean and 95% CI - FAS**

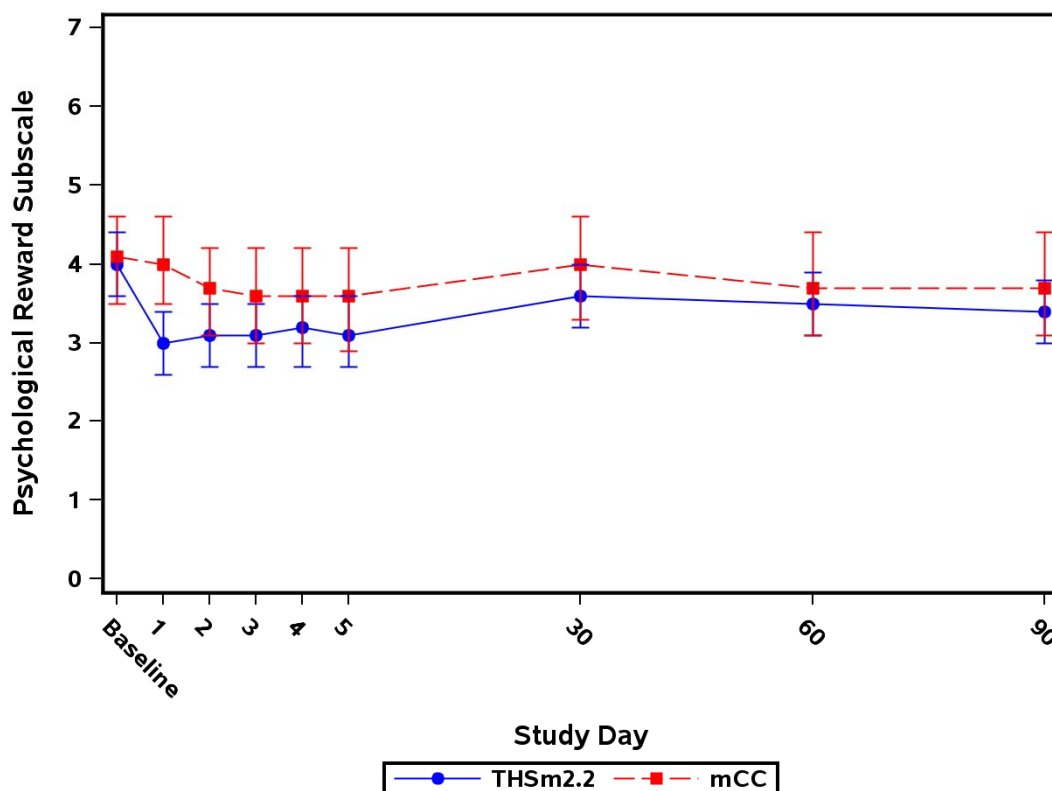
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.2

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**Figure 15.1.2.6.2 MCEQ Subscales Arithmetic Mean and 95% CI - FAS**

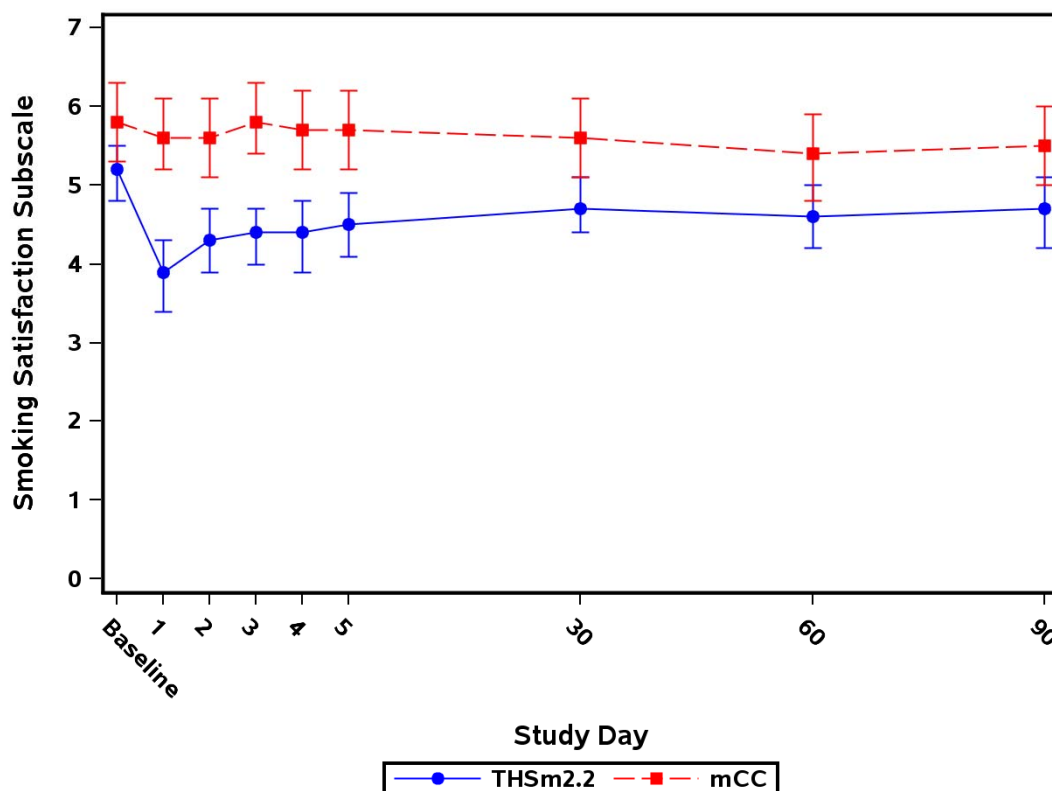
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.54.2

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_fas.sas 21SEP15 Status: Final (Page 4 of 5)

**Figure 15.1.2.6.2 MCEQ Subscales Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

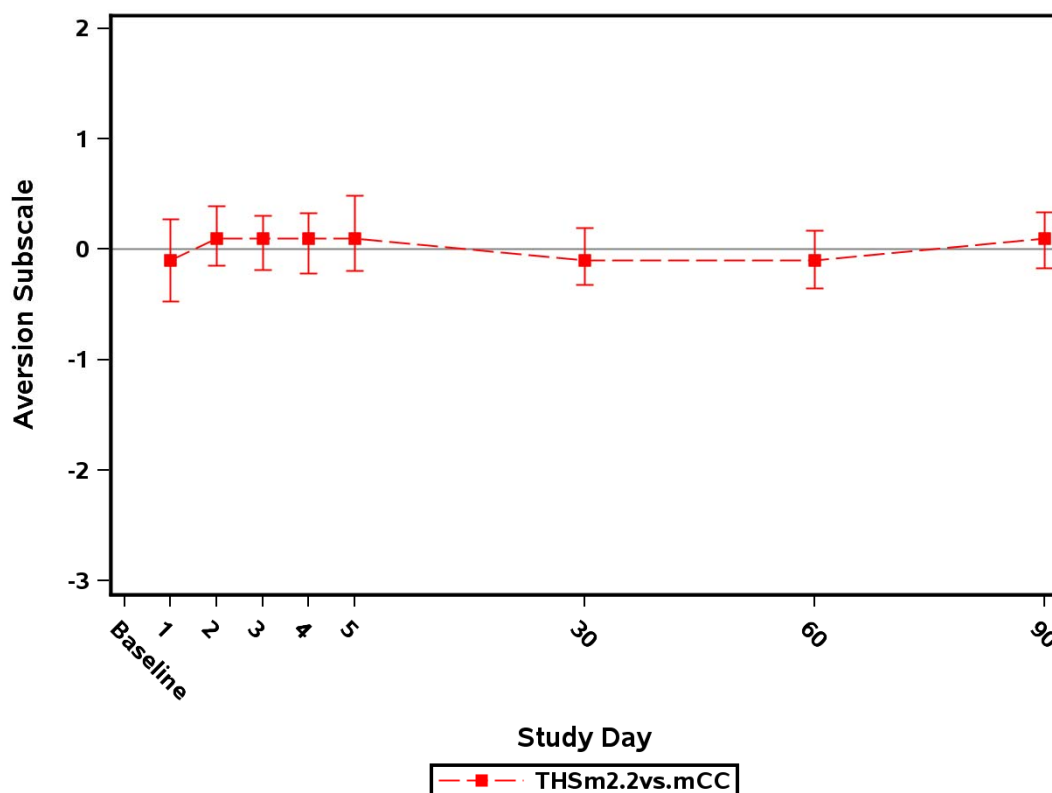
Appendix 15.2.4.54.2

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**Figure 15.1.2.7.1 MCEQ Subscales Least Squares Means Differences and 95% CI - PP Set**



Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

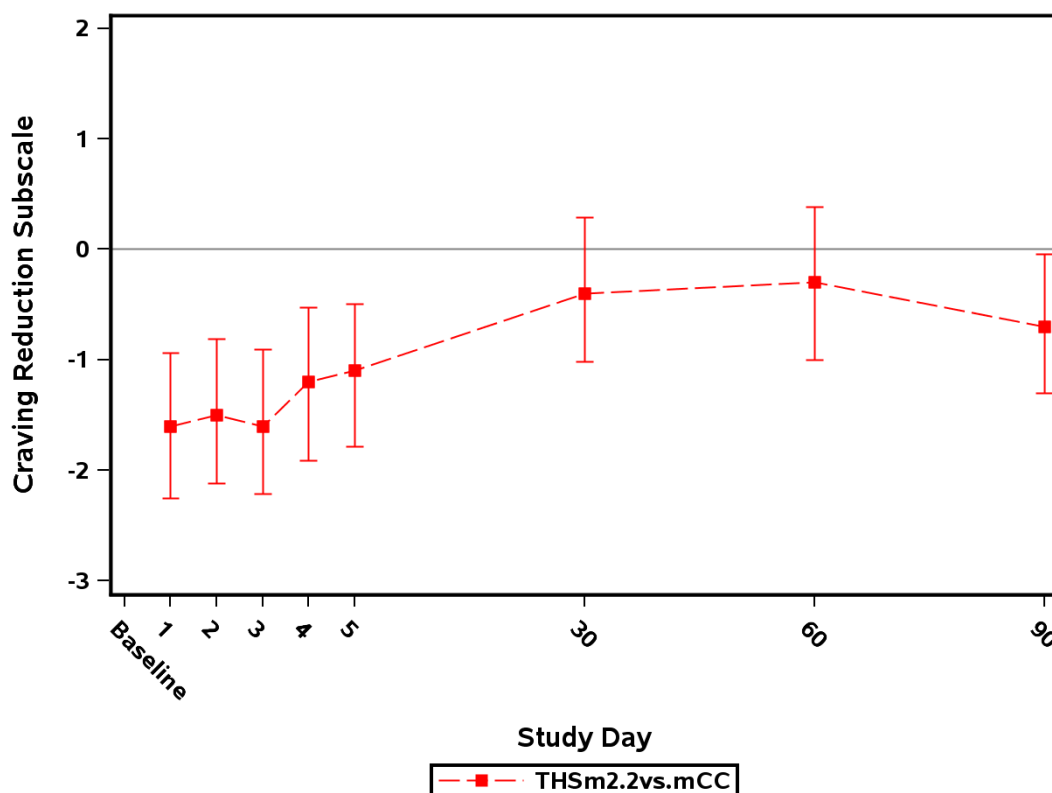
Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.1

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**Figure 15.1.2.7.1 MCEQ Subscales Least Squares Means Differences and 95% CI - PP Set**



Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

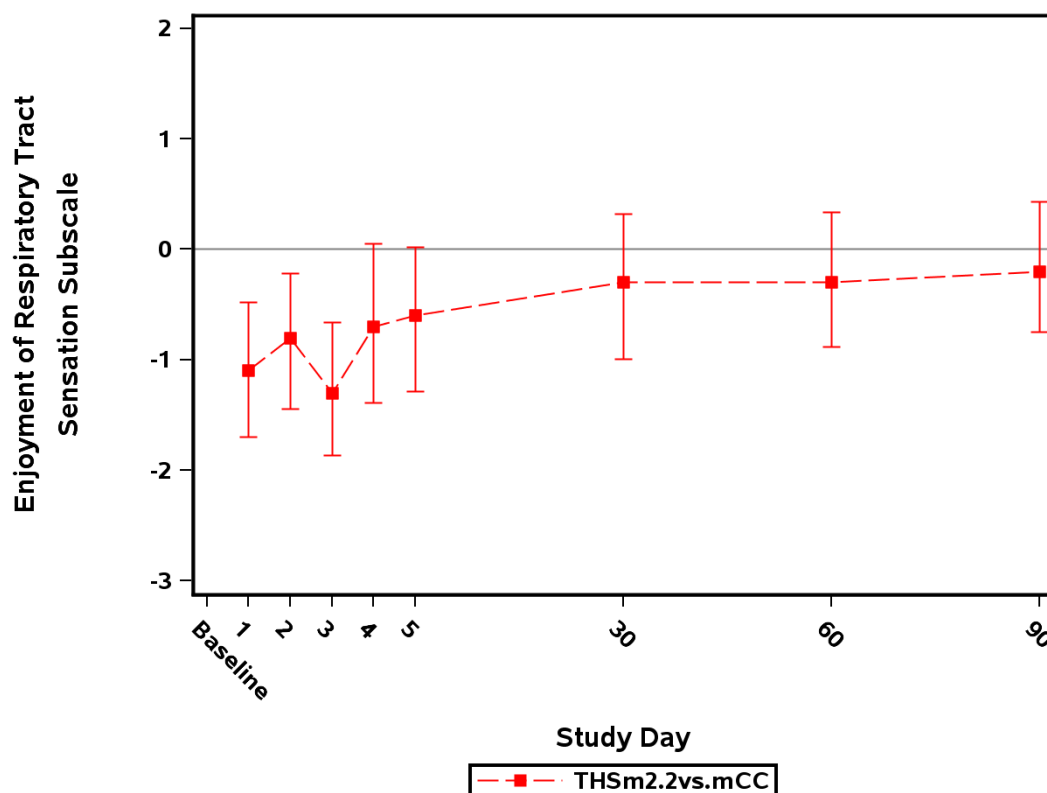
Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.1

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**Figure 15.1.2.7.1 MCEQ Subscales Least Squares Means Differences and 95% CI - PP Set**



Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

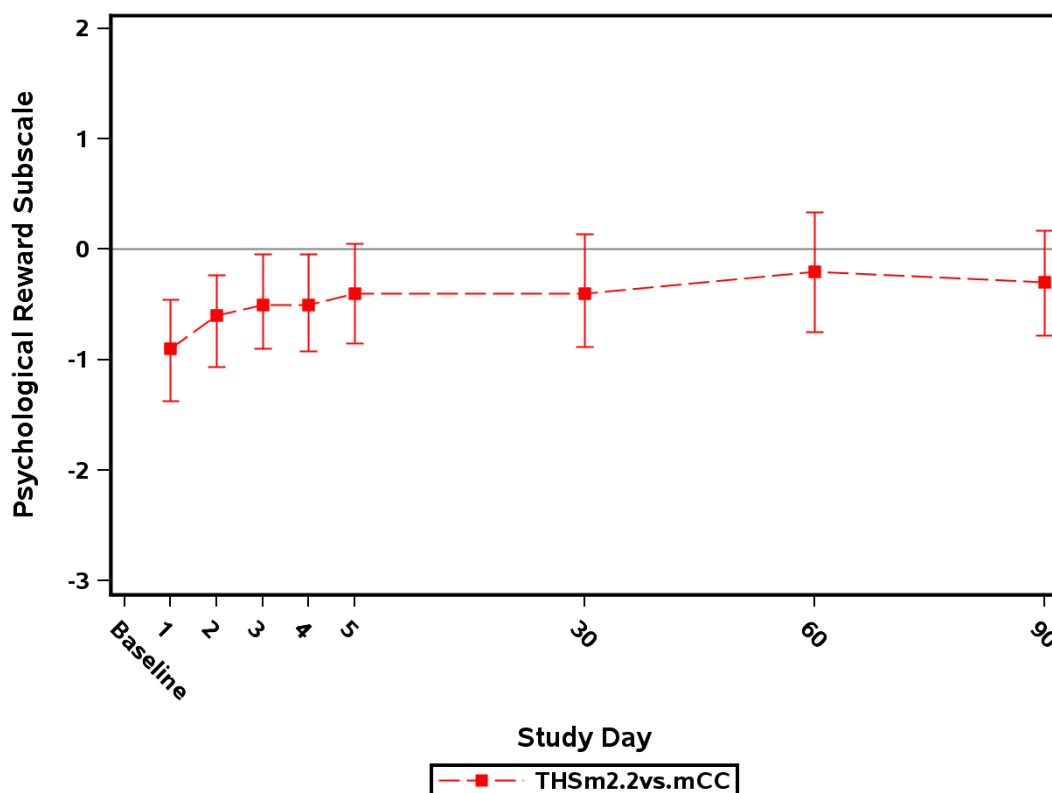
Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.1

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**Figure 15.1.2.7.1 MCEQ Subscales Least Squares Means Differences and 95% CI - PP Set**



Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

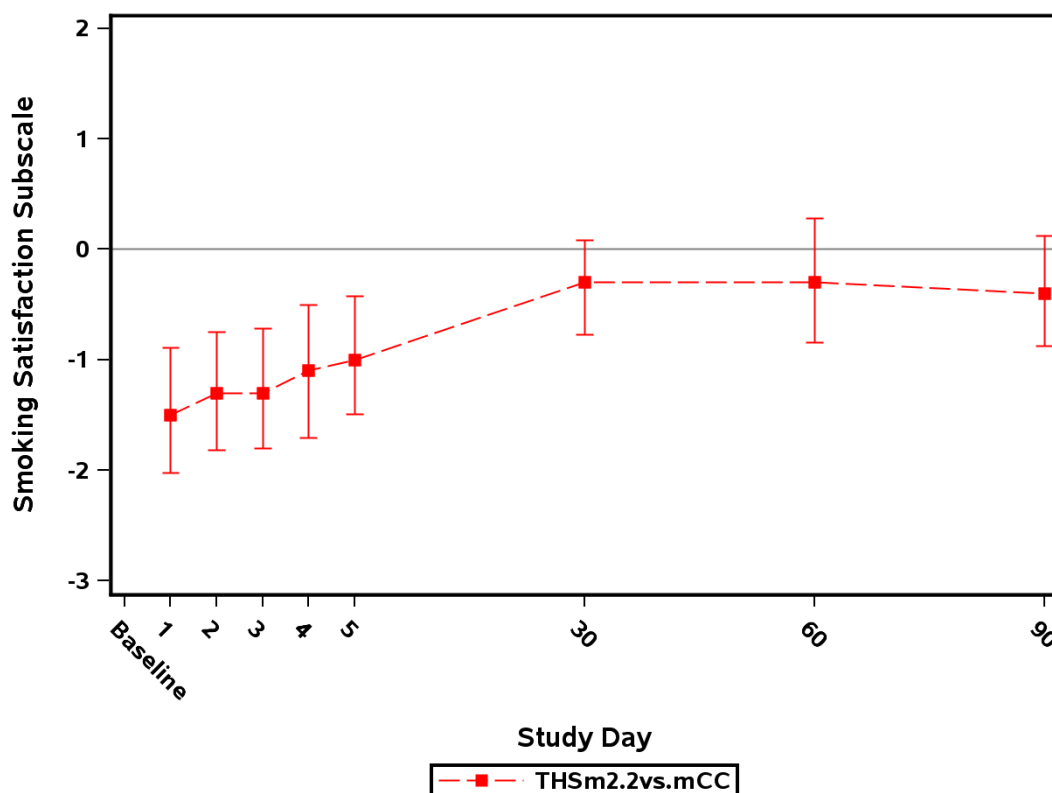
Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.1

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**Figure 15.1.2.7.1 MCEQ Subscales Least Squares Means Differences and 95% CI - PP Set**



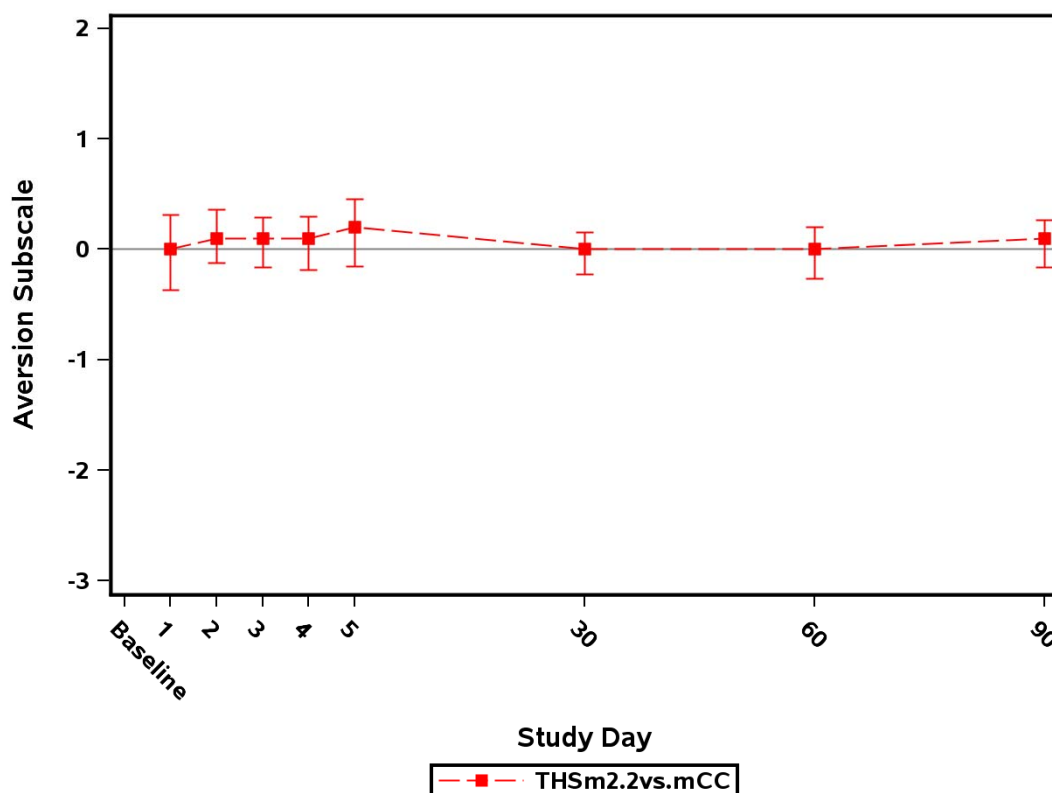
Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.1

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**Figure 15.1.2.7.2 MCEQ Subscales Least Squares Means Differences and 95% CI - FAS**

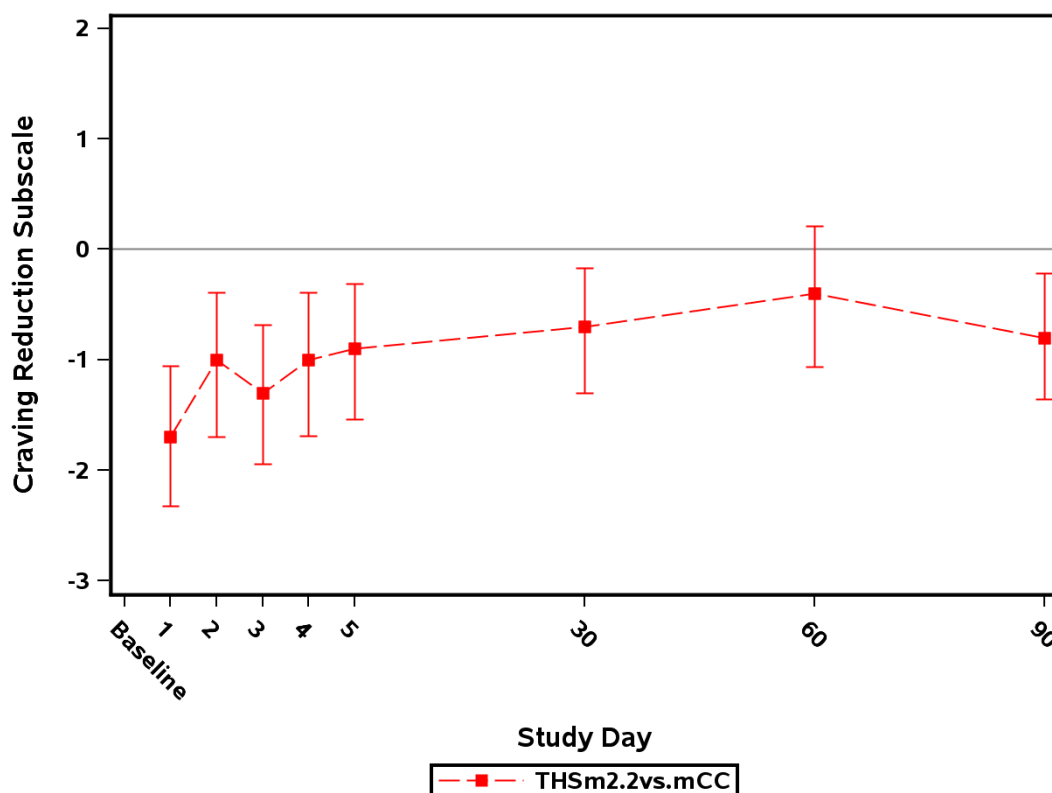
Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.2

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_ls\_fas.sas 21SEP15 Status: Final (Page 1 of 5)

**Figure 15.1.2.7.2 MCEQ Subscales Least Squares Means Differences and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

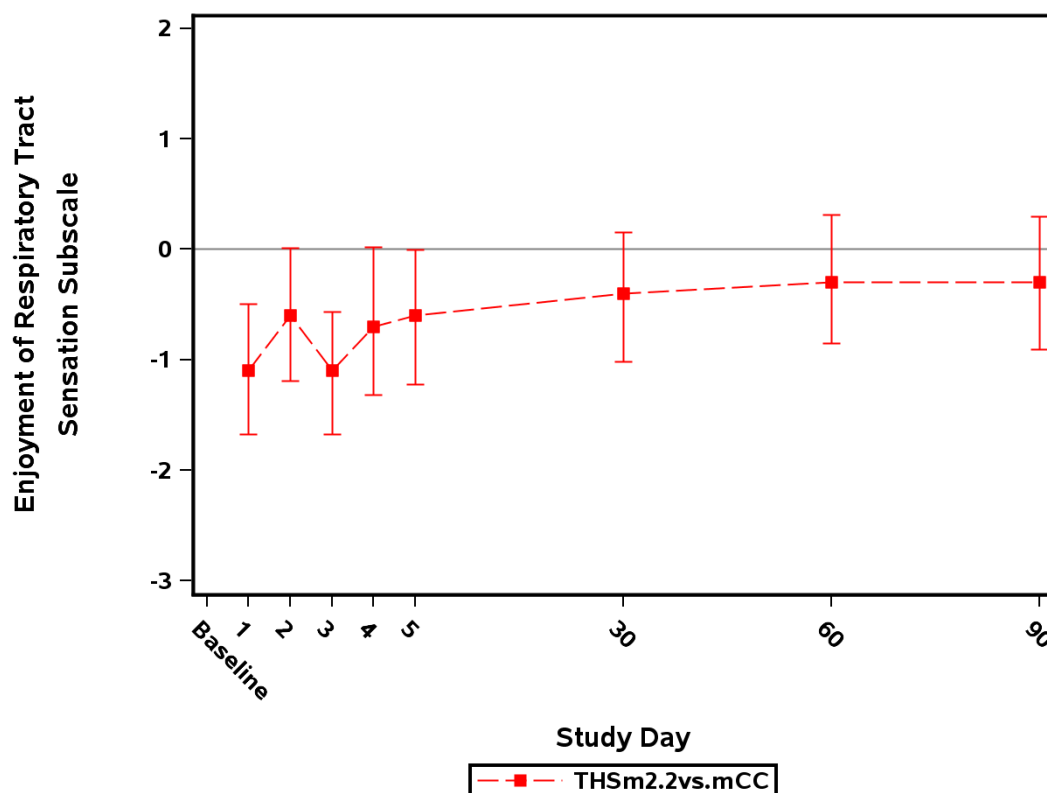
Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.2

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_ls\_fas.sas 21SEP15 Status: Final (Page 2 of 5)



**Figure 15.1.2.7.2 MCEQ Subscales Least Squares Means Differences and 95% CI - FAS**



Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

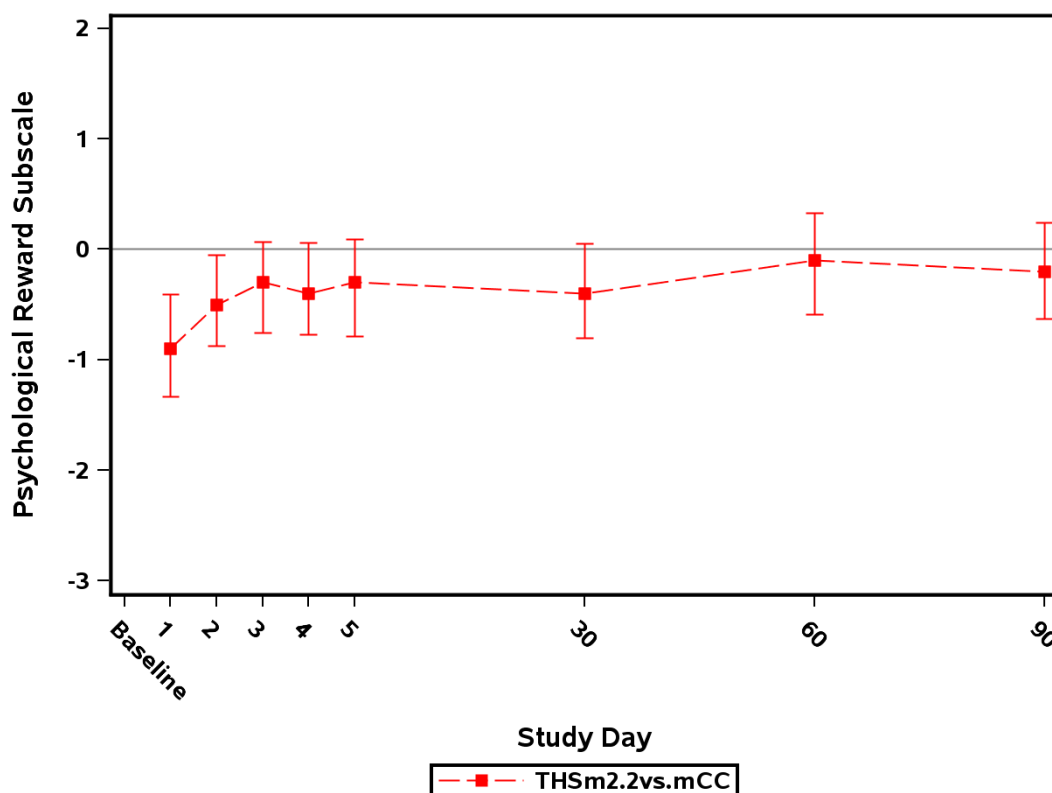
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.2

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**Figure 15.1.2.7.2 MCEQ Subscales Least Squares Means Differences and 95% CI - FAS**

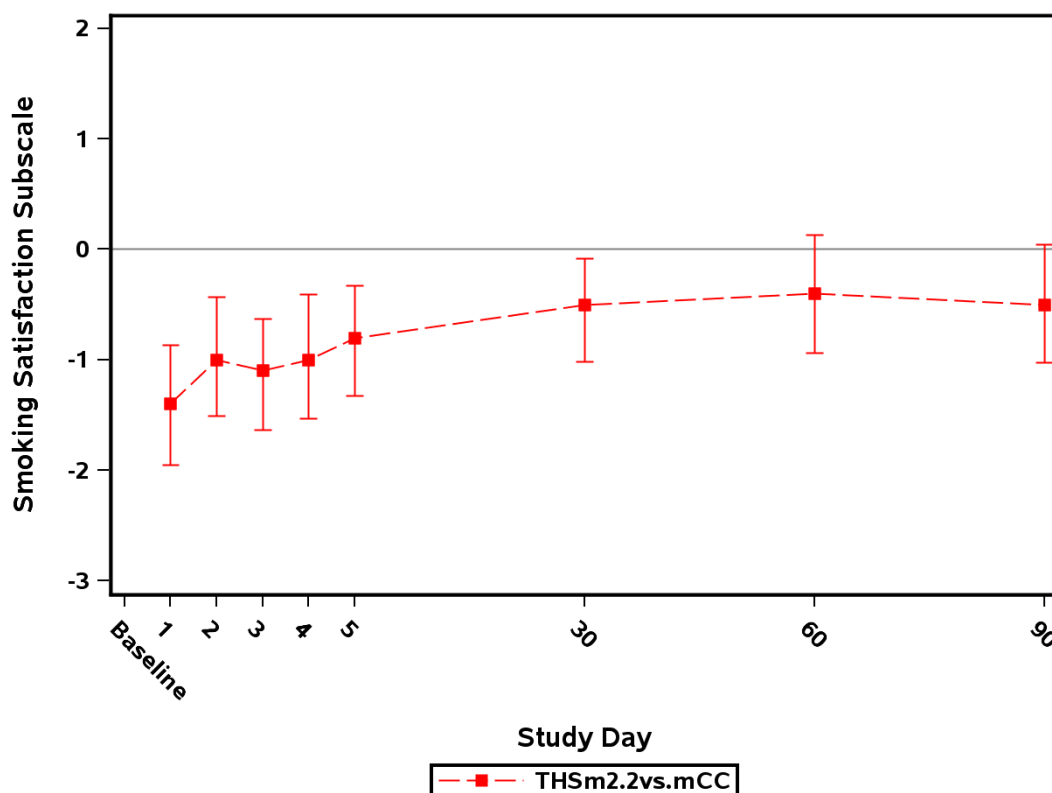
Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.2

Study ID: ZRHM-REXA-08-US Program: f\_mceq\_ls\_fas.sas 21SEP15 Status: Final (Page 4 of 5)

**Figure 15.1.2.7.2 MCEQ Subscales Least Squares Means Differences and 95% CI - FAS**

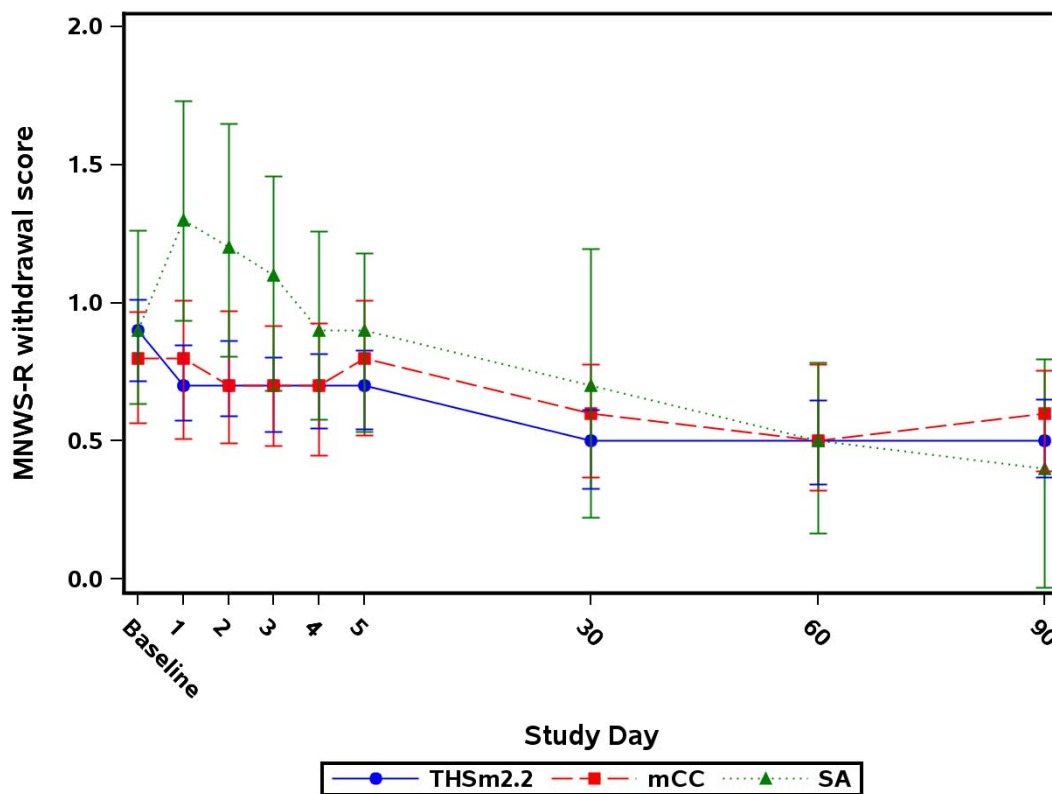
Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1.

Note: Scores of MCEQ subscales are reported on a 7-point scale. Higher scores indicate greater intensity on that scale.

Appendix 15.2.4.55.2

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**Figure 15.1.2.8.1 MNWS Total Score Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

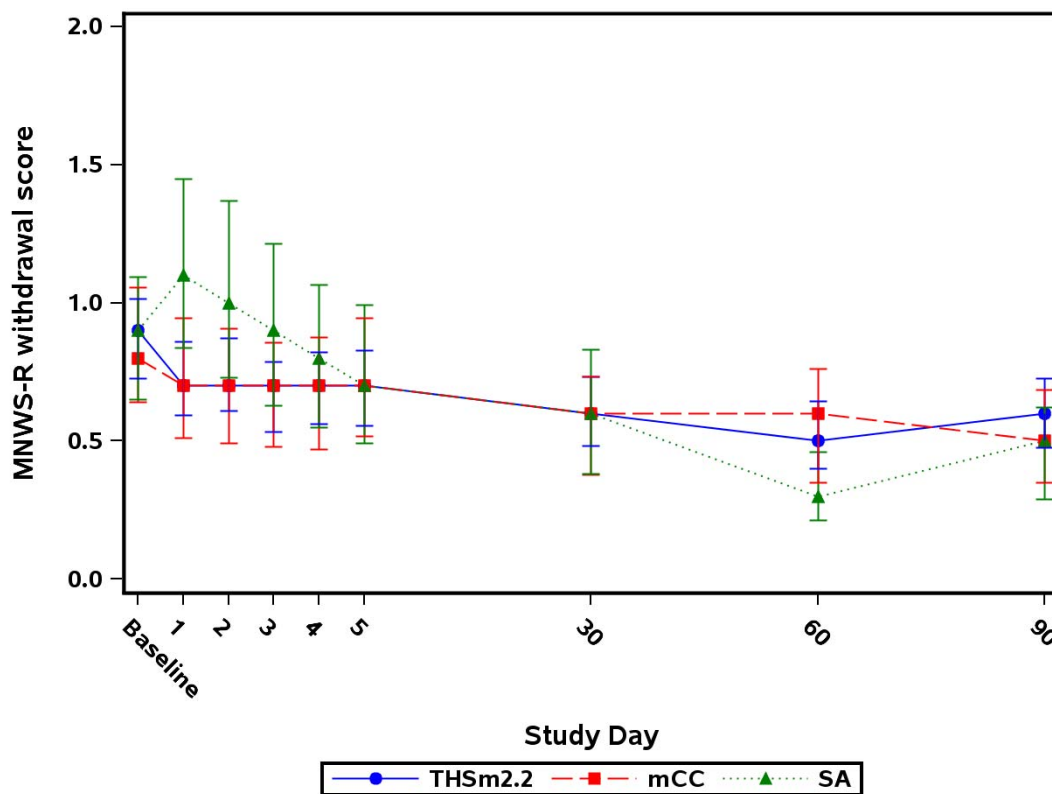
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: MNWS-R total score reported a scale of 0 to 4. Higher scores indicate greater intensity of withdrawal symptoms.

Appendix 15.2.4.56.1

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**Figure 15.1.2.8.2 MNWS Total Score Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

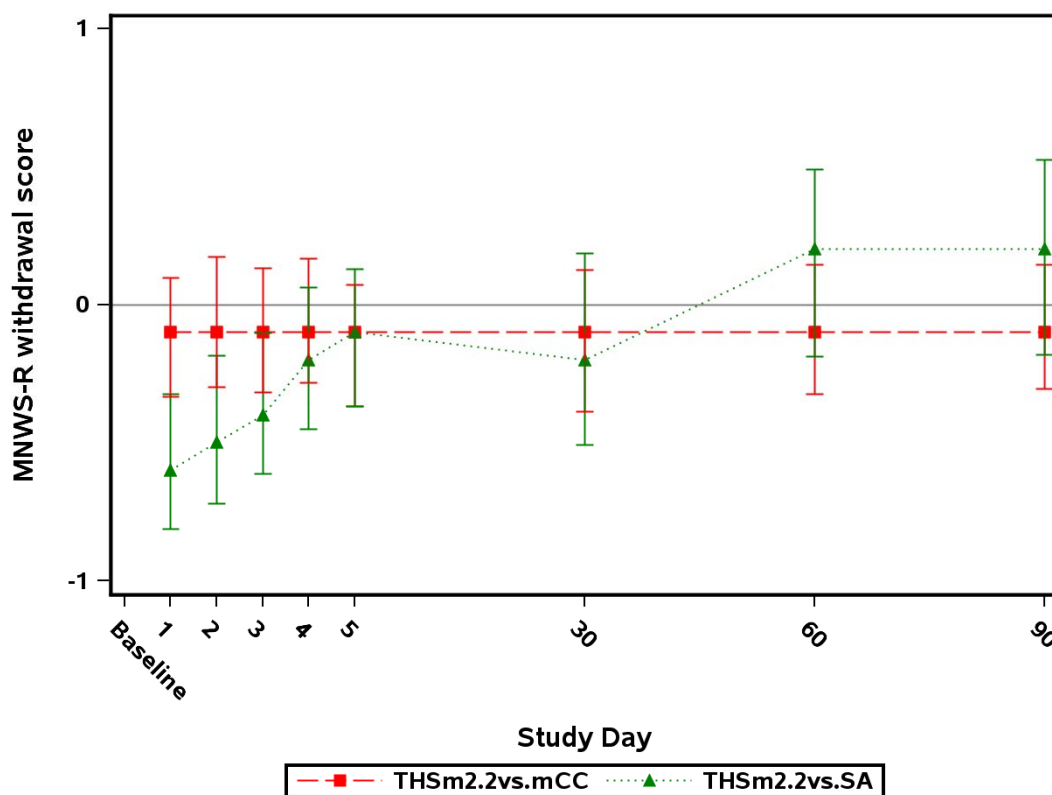
Note: MNWS-R total score reported a scale of 0 to 4. Higher scores indicate greater intensity of withdrawal symptoms.

Appendix 15.2.4.56.2

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**Figure 15.1.2.9.1 MNWS Total Score Least Squares Means Differences and 95% CI - PP Set**



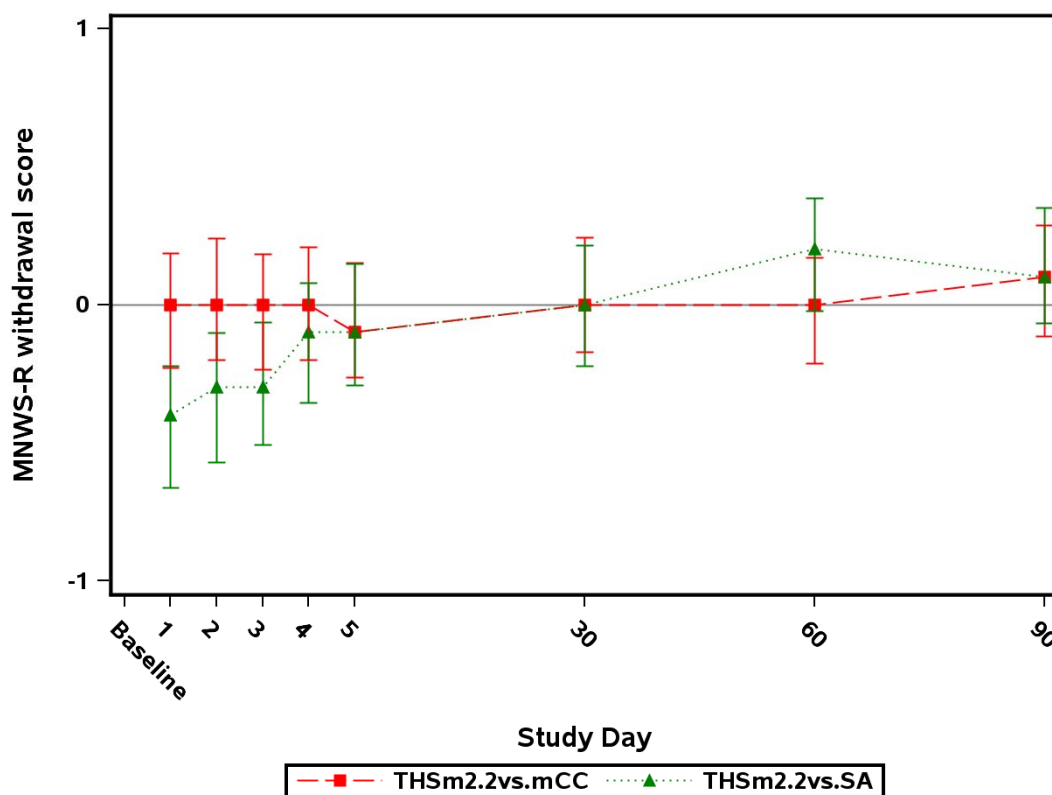
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: MNWS-R total score reported a scale of 0 to 4. Higher scores indicate greater intensity of withdrawal symptoms.

Appendix 15.2.4.57.1

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**Figure 15.1.2.9.2 MNWS Total Score Least Squares Means Differences and 95% CI – FAS**

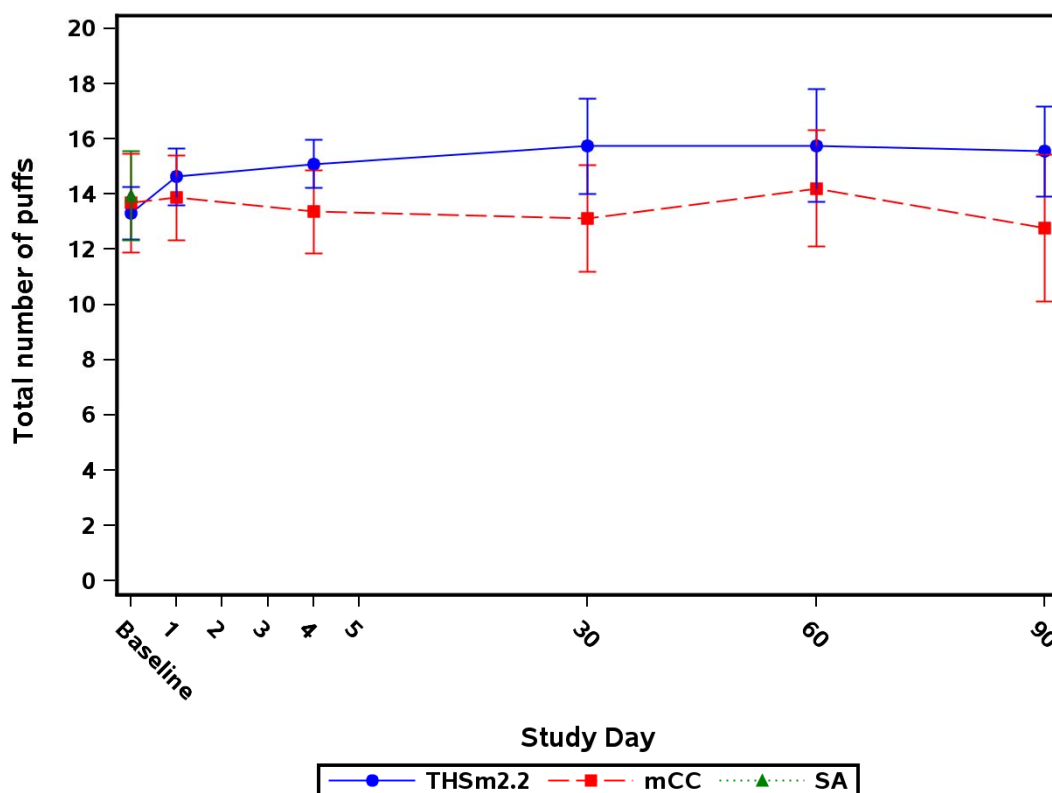
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: MNWS-R total score reported a scale of 0 to 4. Higher scores indicate greater intensity of withdrawal symptoms.

Appendix 15.2.4.57.2

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

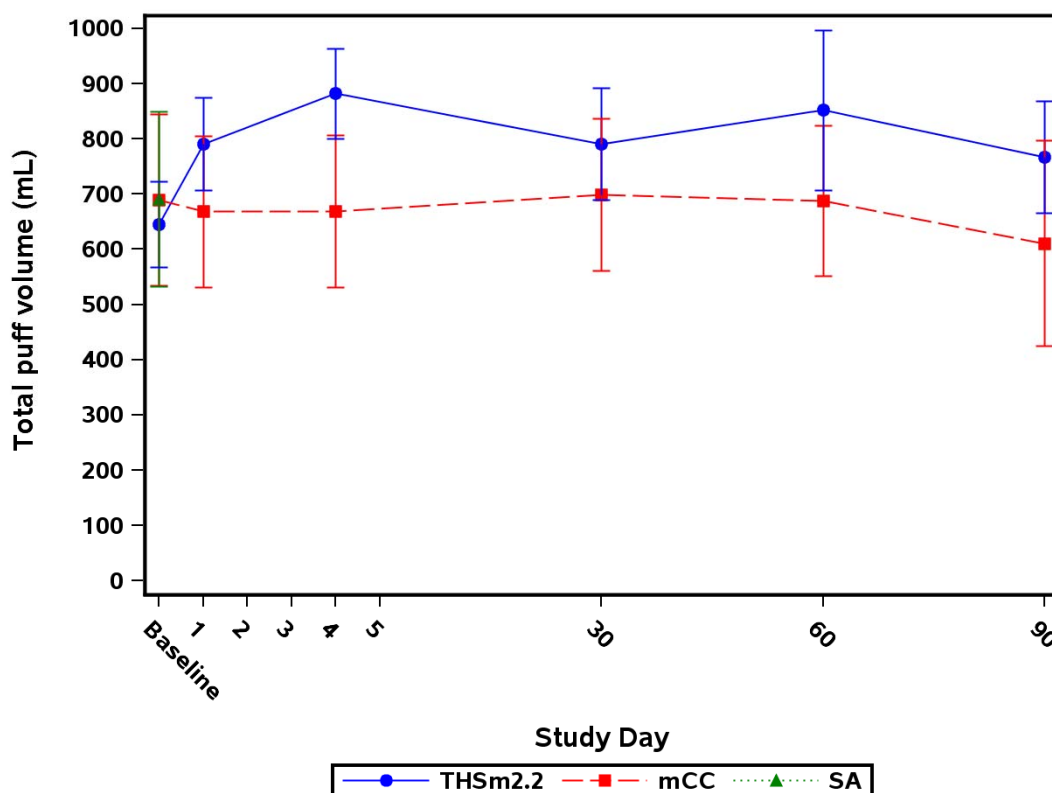
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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Study ID: ZRHM-REXA-08-US Program: f\_hst\_pp.sas 21SEP15 Status: Final (Page 1 of 17)

**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

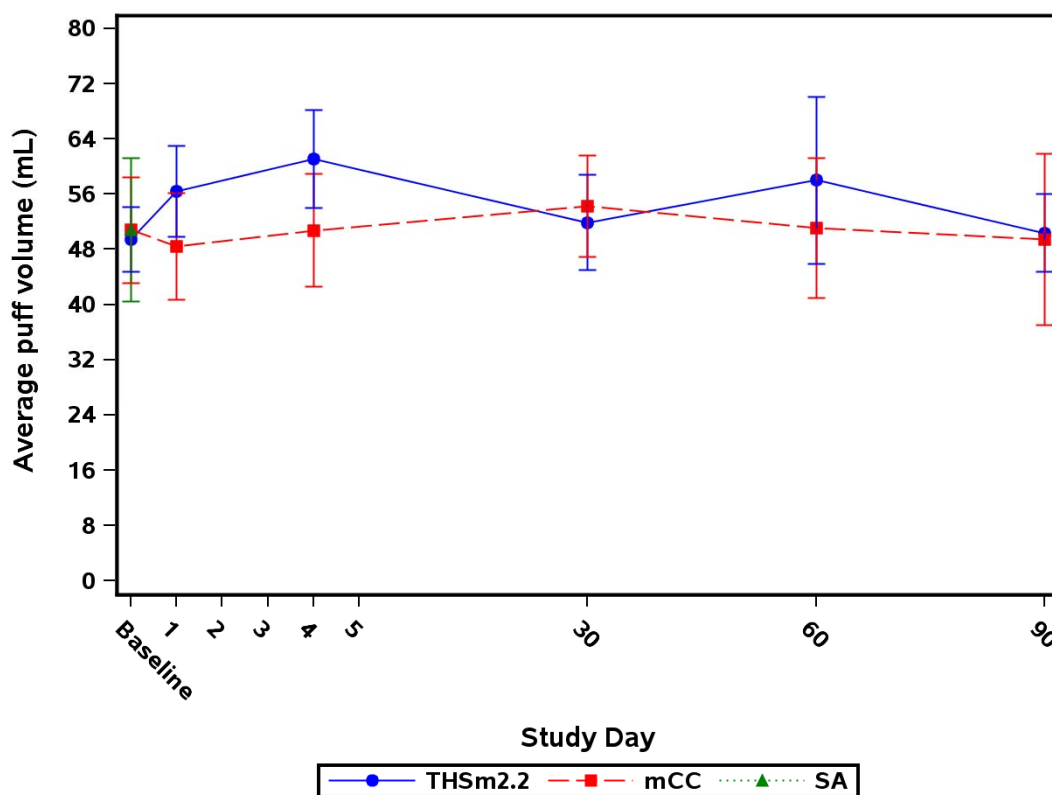
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.60

Study ID: ZRHM-REXA-08-US Program: f\_hst\_pp.sas 21SEP15 Status: Final (Page 2 of 17)



**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

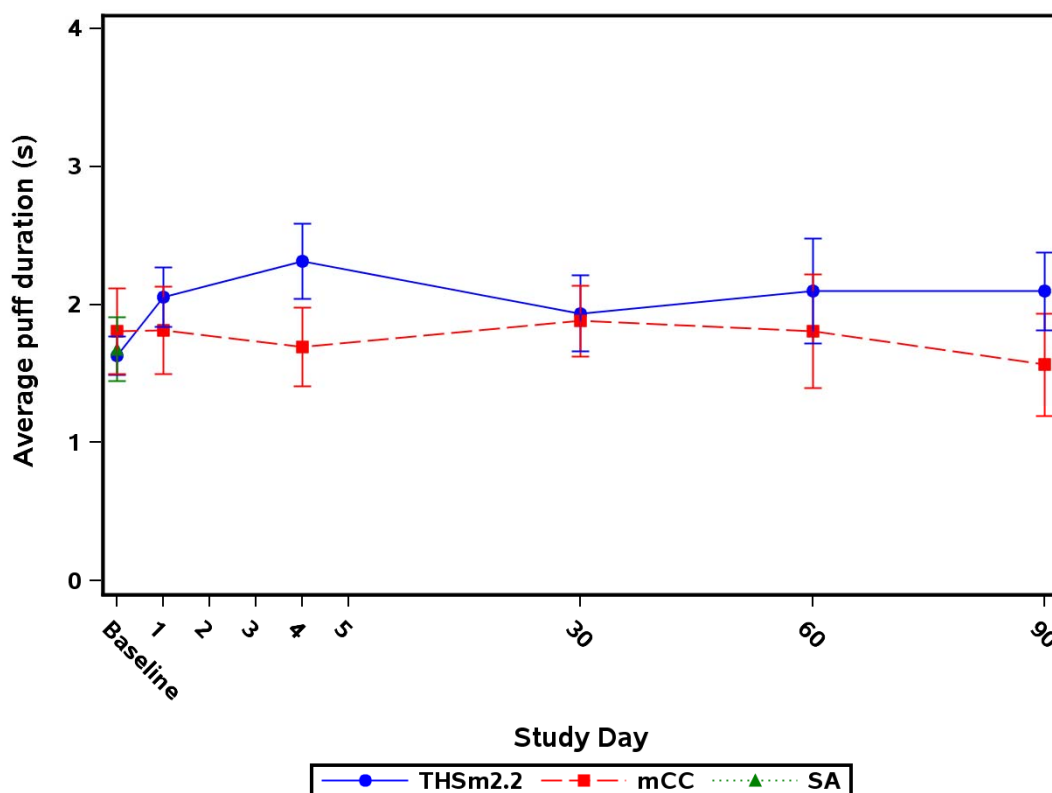
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**



Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

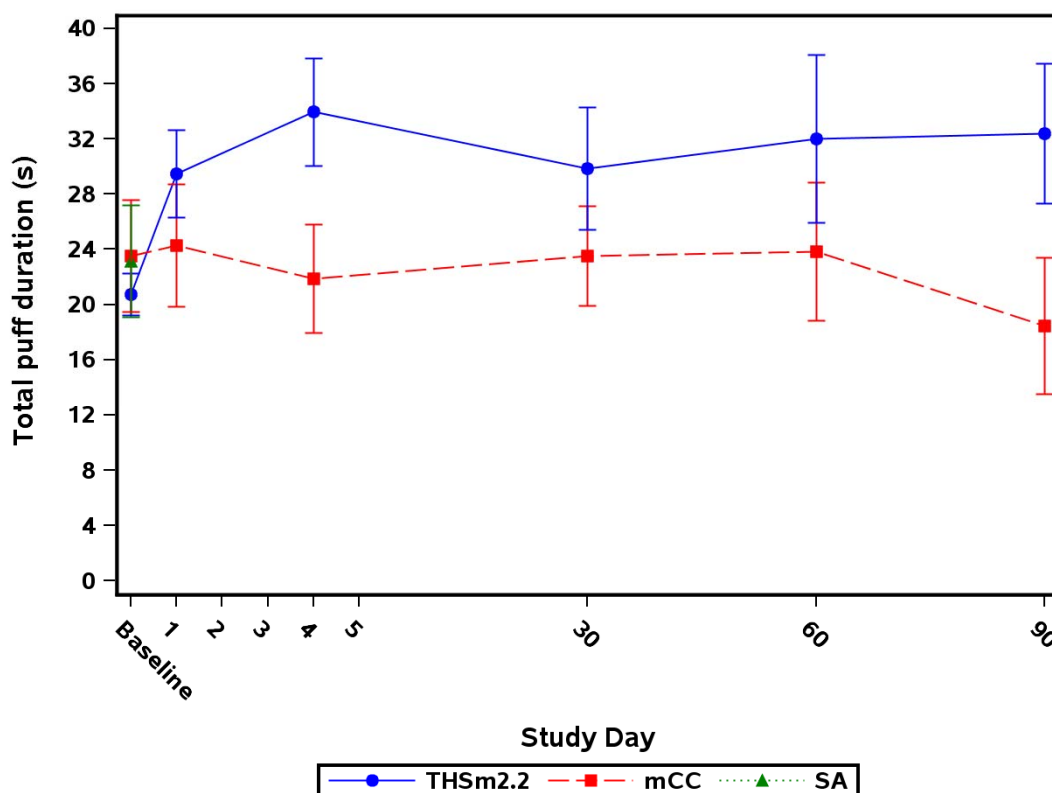
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**



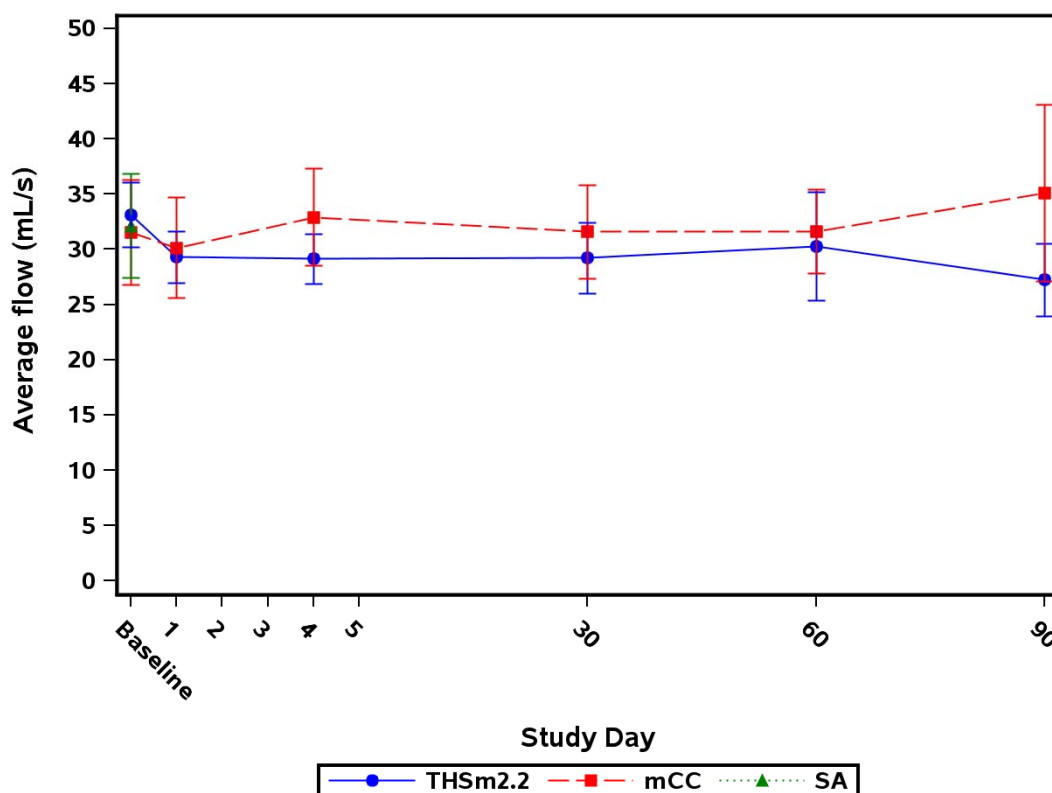
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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Study ID: ZRHM-REXA-08-US Program: f\_hst\_pp.sas 21SEP15 Status: Final (Page 5 of 17)

**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

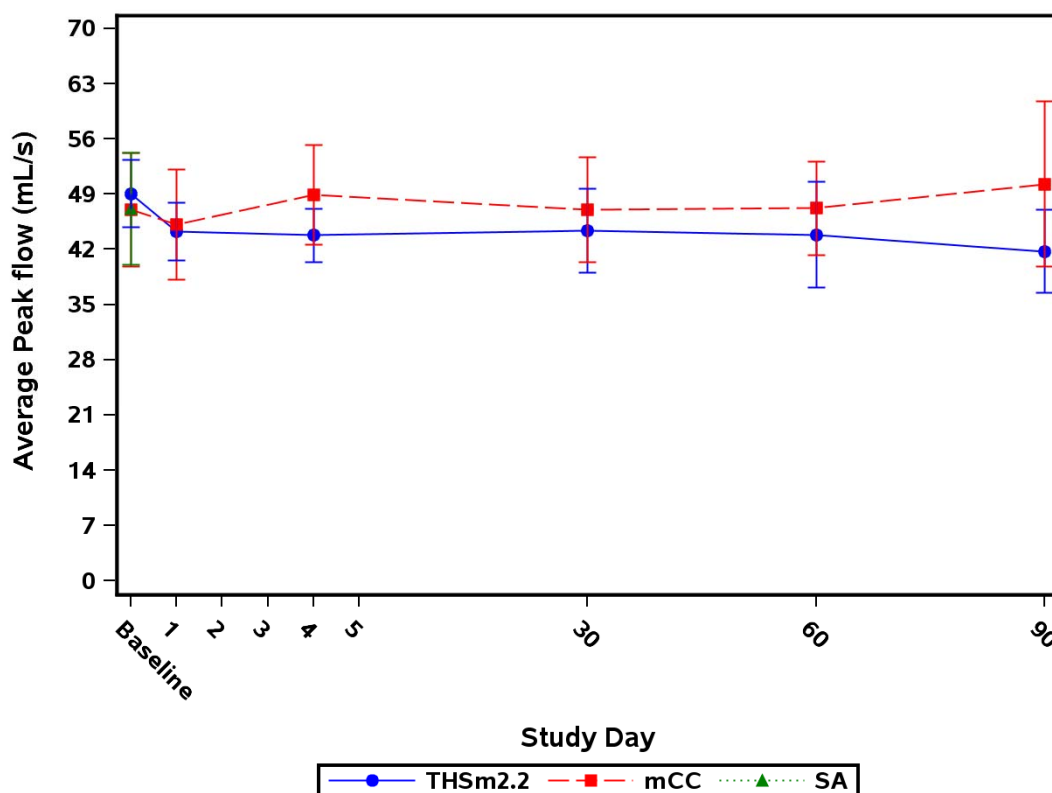
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

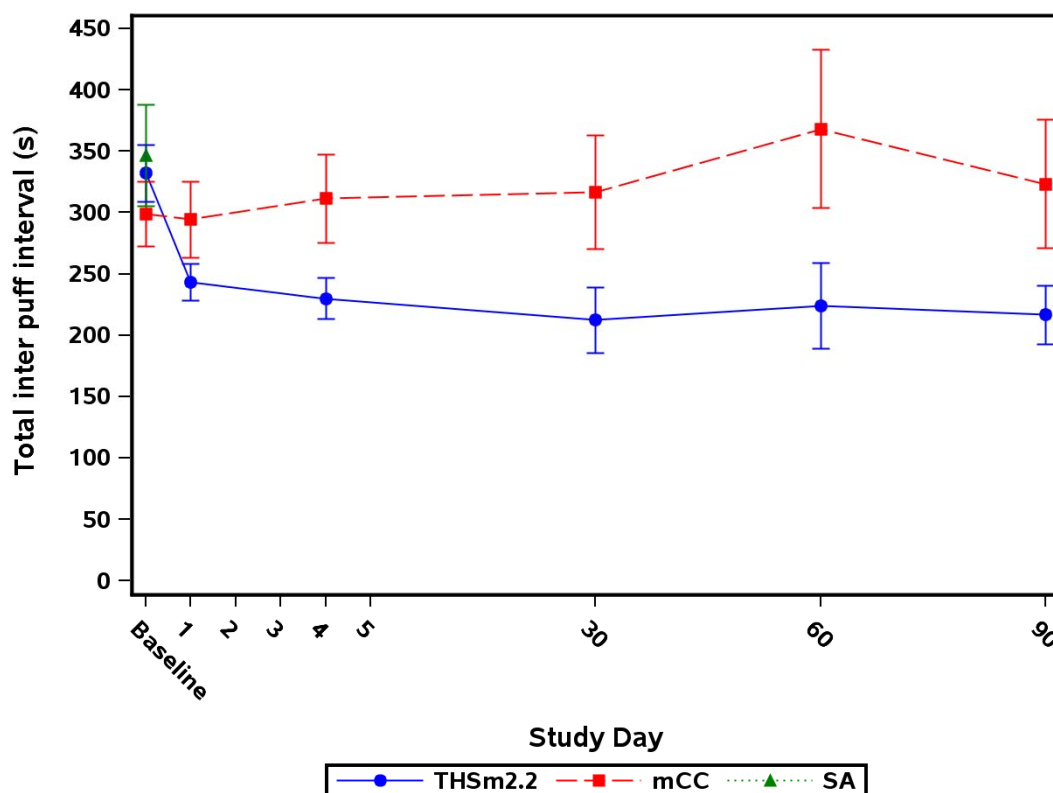
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**



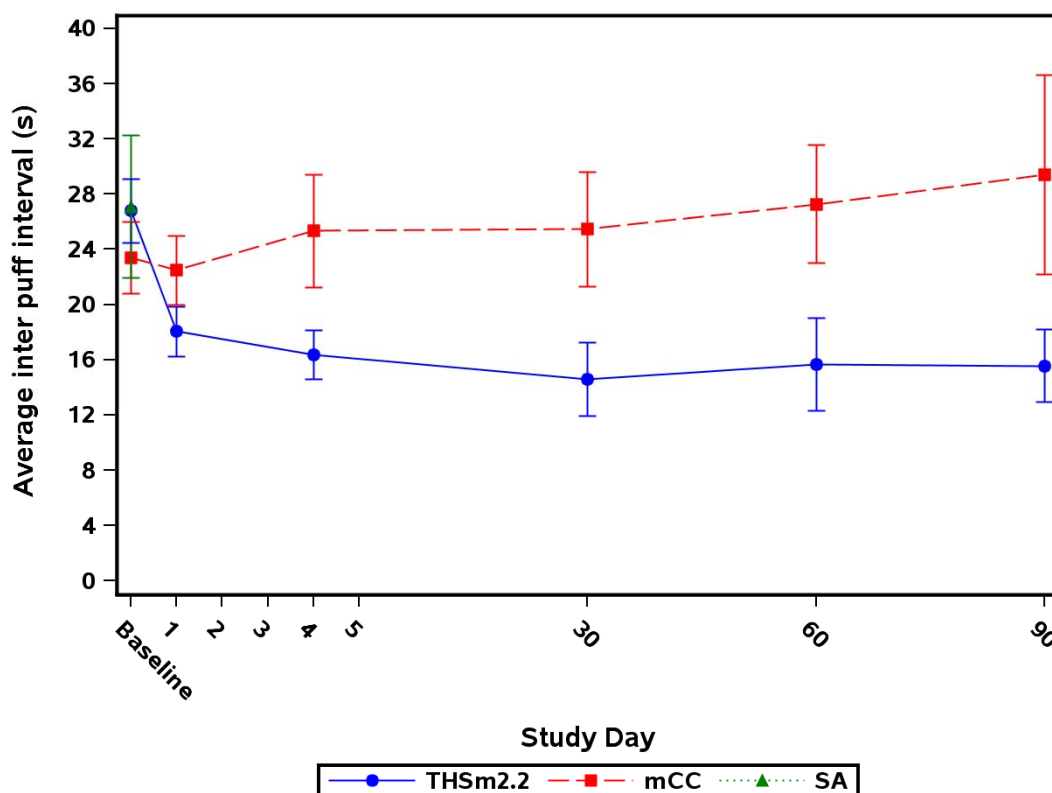
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

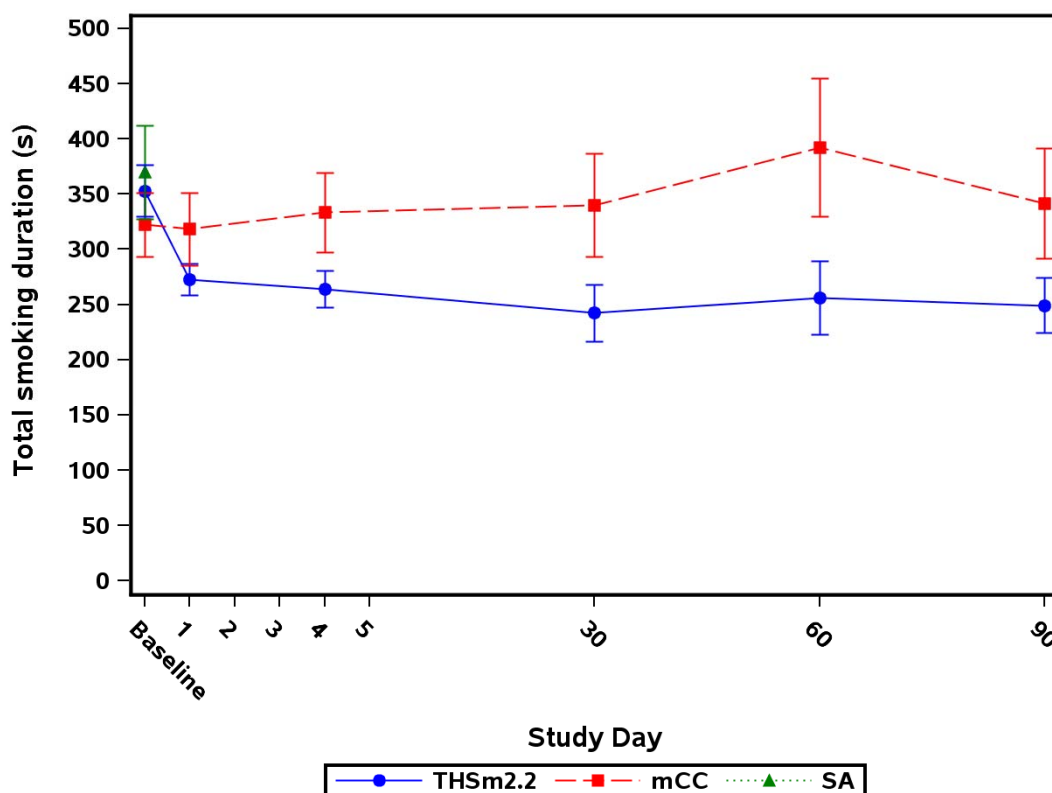
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

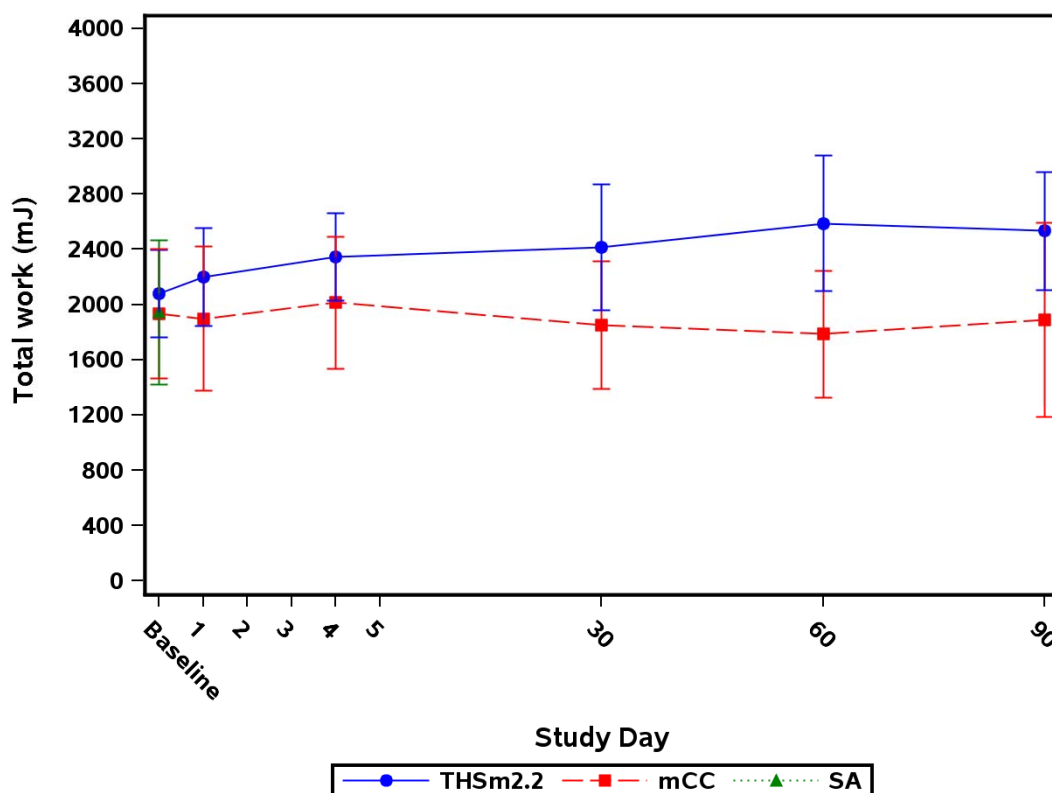
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

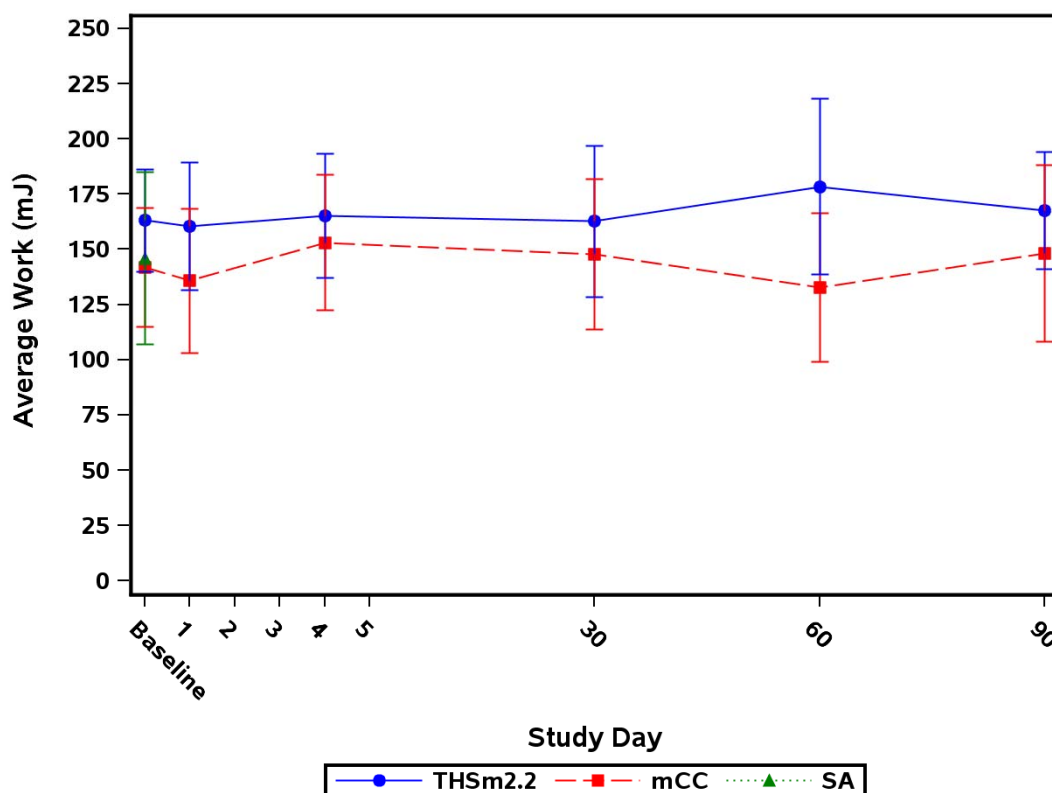
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

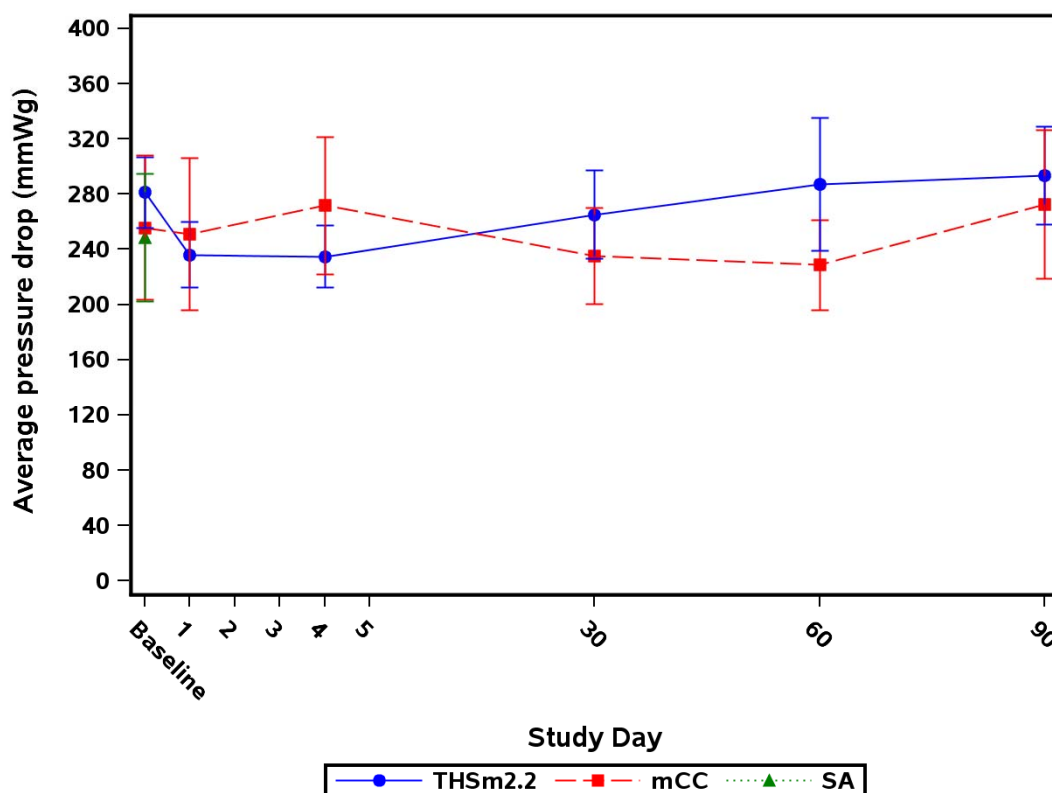
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.60

Study ID: ZRHM-REXA-08-US Program: f\_hst\_pp.sas 21SEP15 Status: Final (Page 12 of 17)



**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**



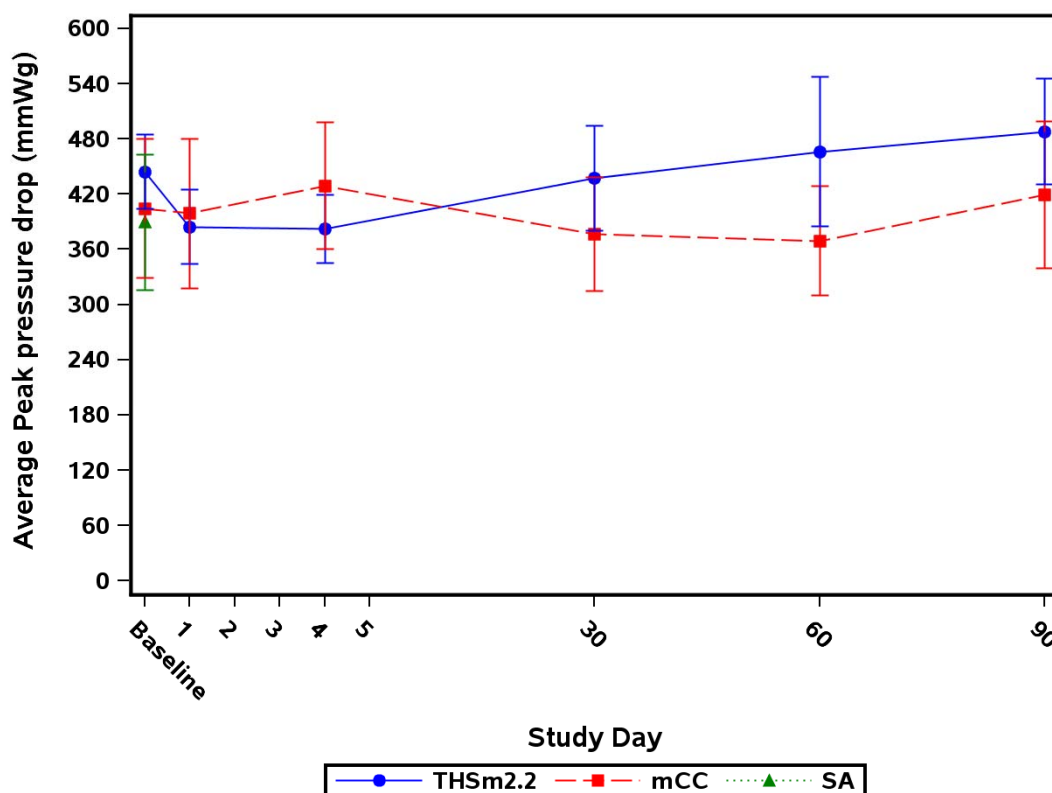
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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Study ID: ZRHM-REXA-08-US Program: f\_hst\_pp.sas 21SEP15 Status: Final (Page 13 of 17)

**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

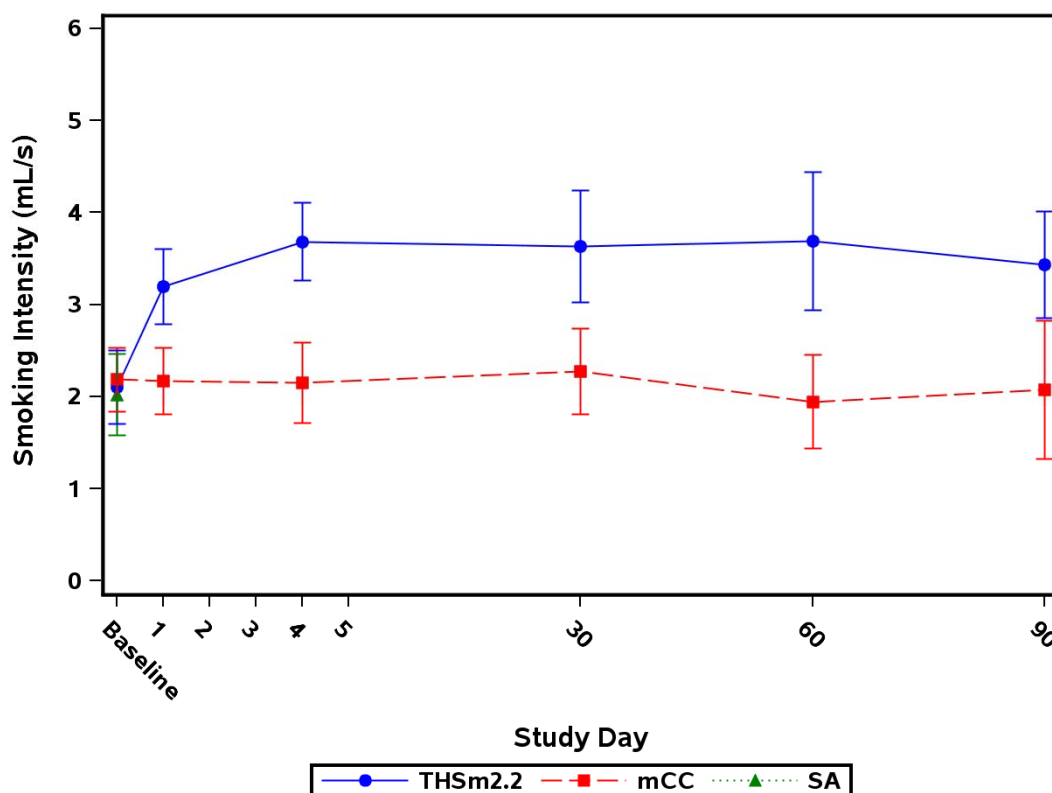
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**



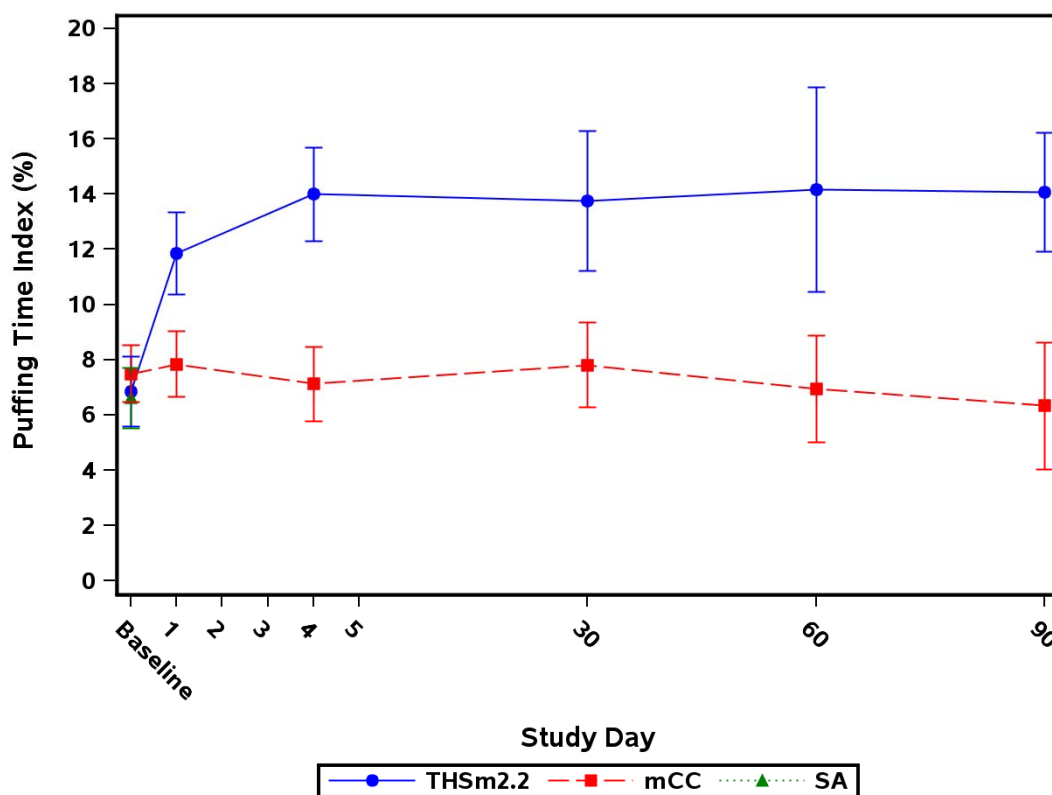
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

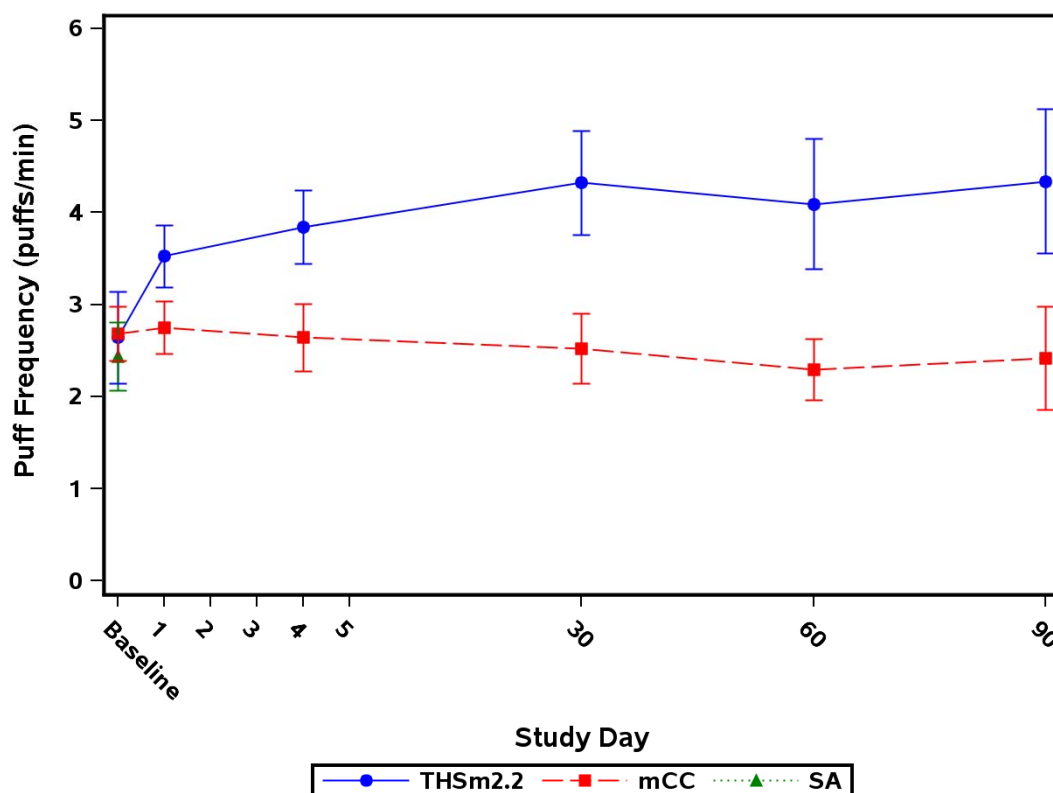
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.10 HST Parameters Averaged Over the Visit Arithmetic Mean and 95% CI – PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

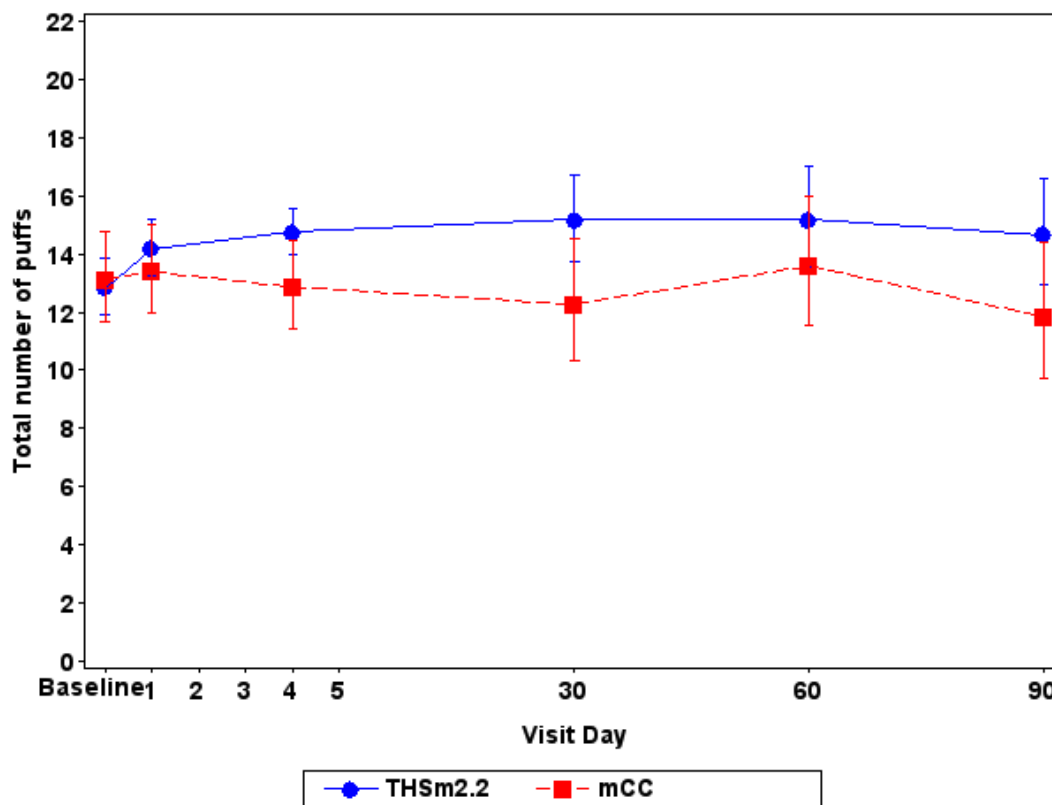
Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.60

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in CC/THS 2.2 arms on Day 1 or last assessment prior to 06:29 AM in SA arm on Day 1.

Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

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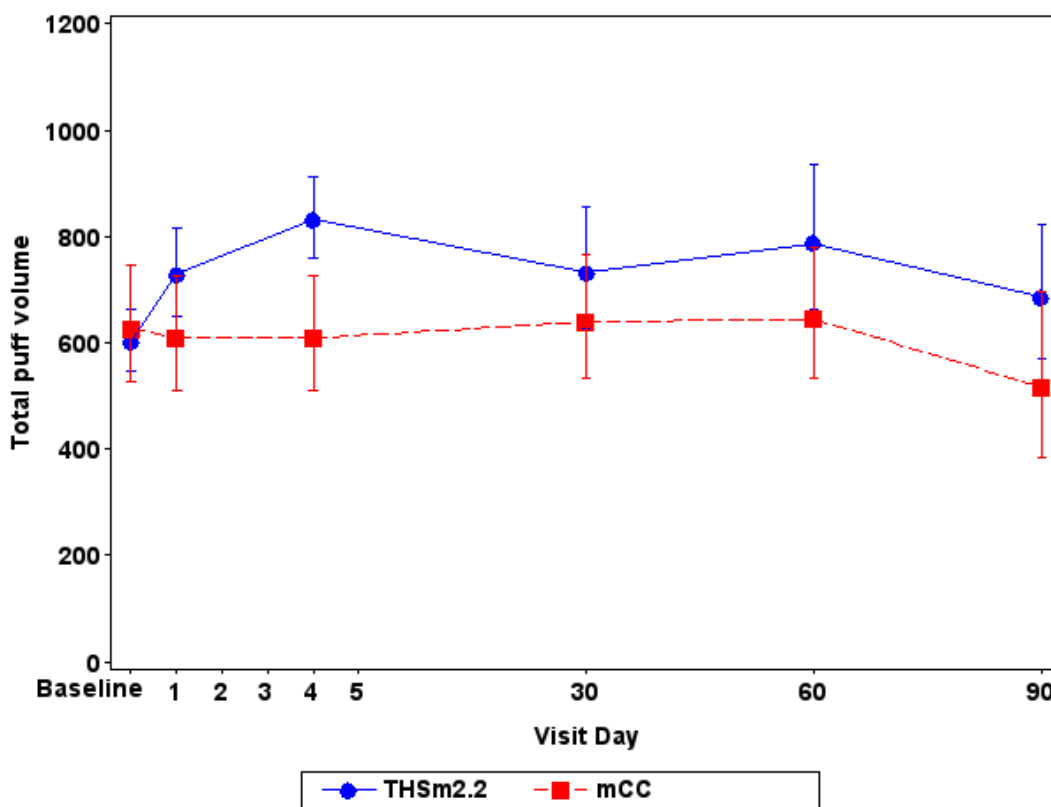
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in CC/THS 2.2 arms on Day 1 or last assessment prior to 06:29 AM in SA arm on Day 1.

Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

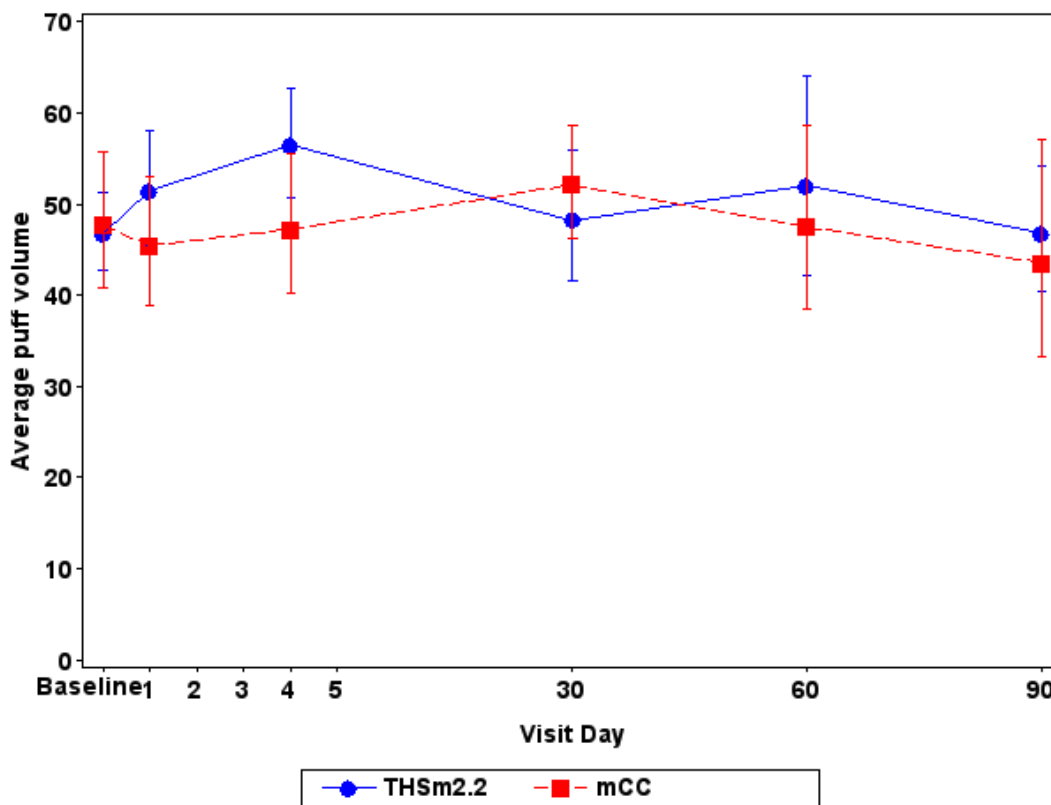
Appendix: 15.2.4.42.1

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in CC/THS 2.2 arms on Day 1 or last assessment prior to 06:29 AM in SA arm on Day 1.

Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

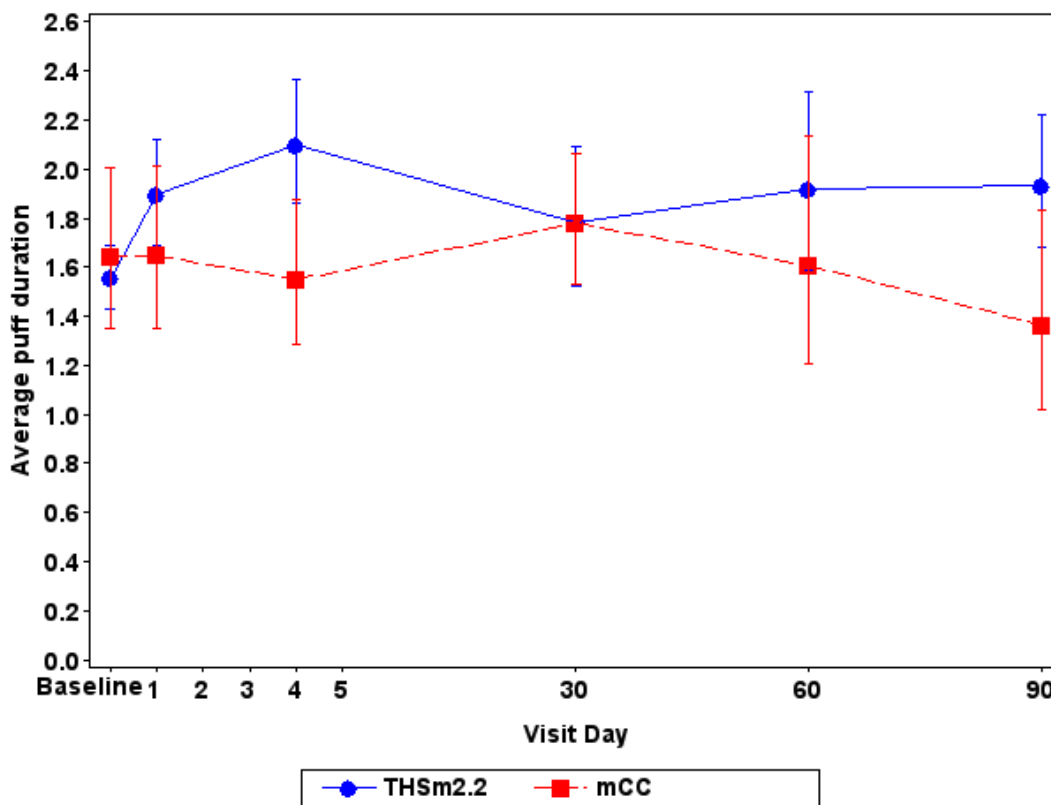
Appendix: 15.2.4.42.1

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

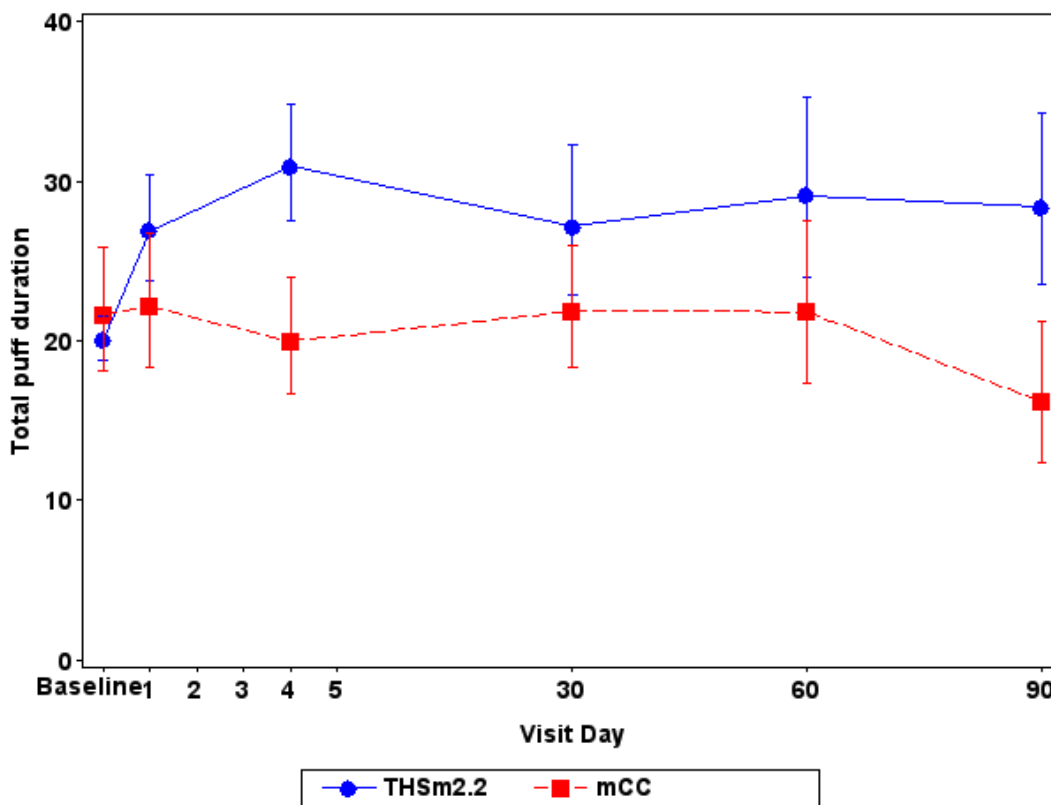
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

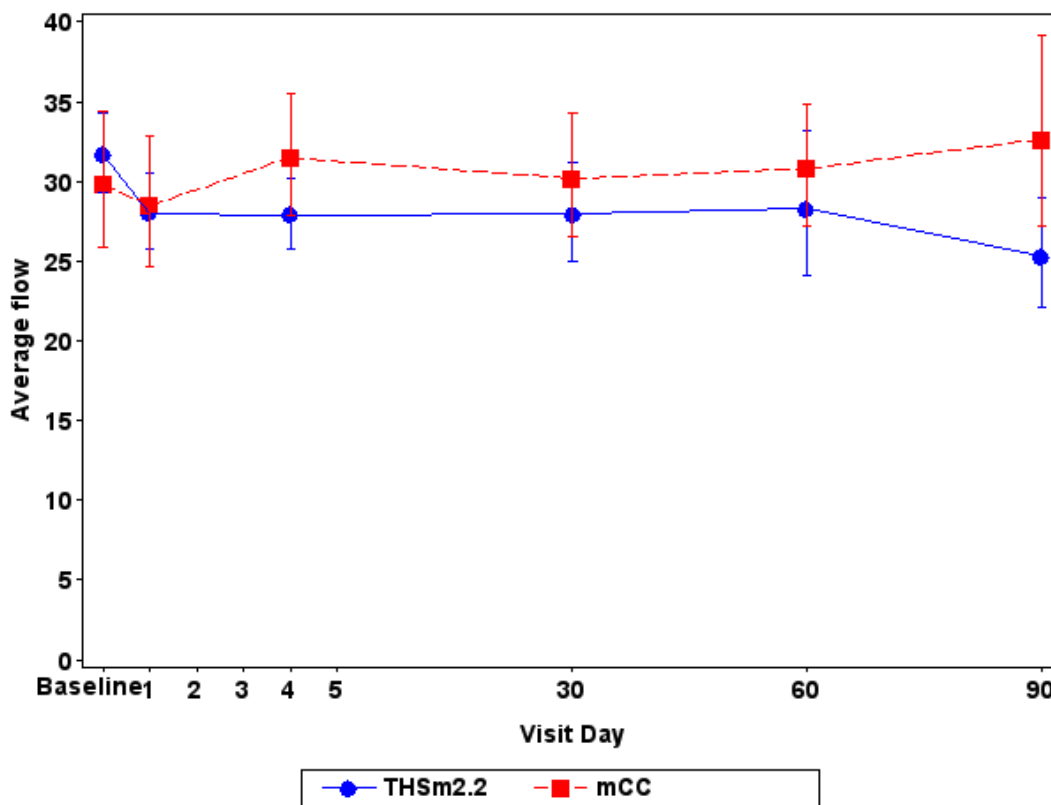
Appendix: 15.2.4.42.1

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

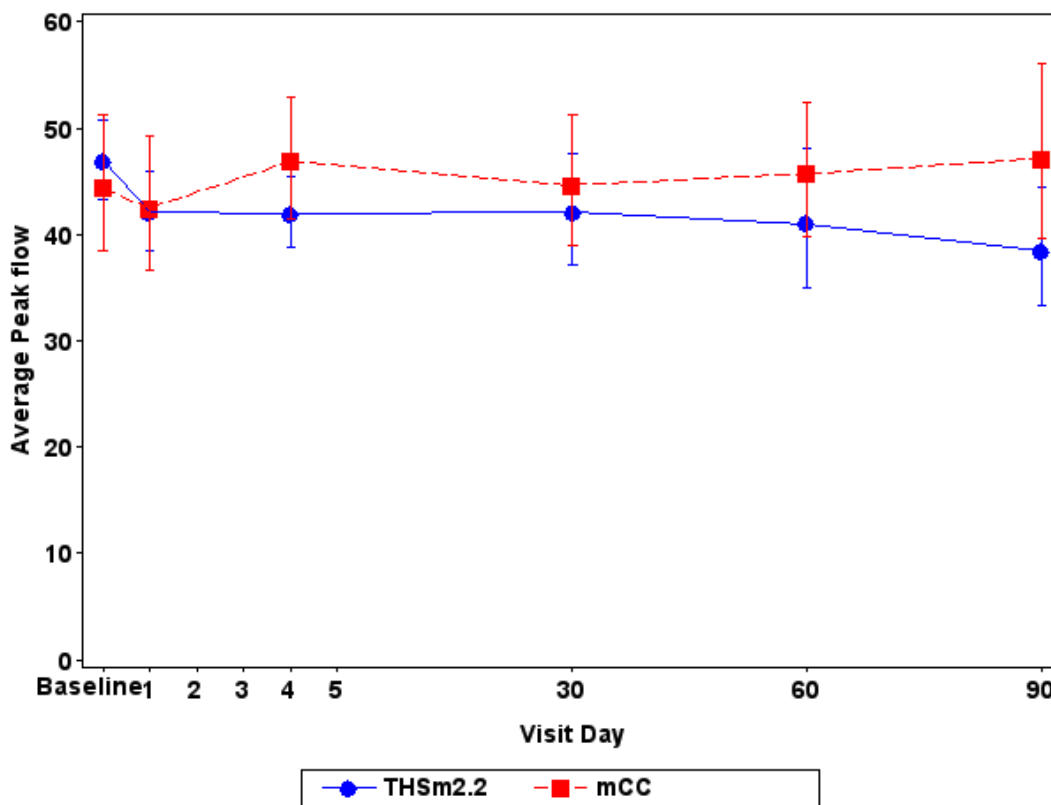
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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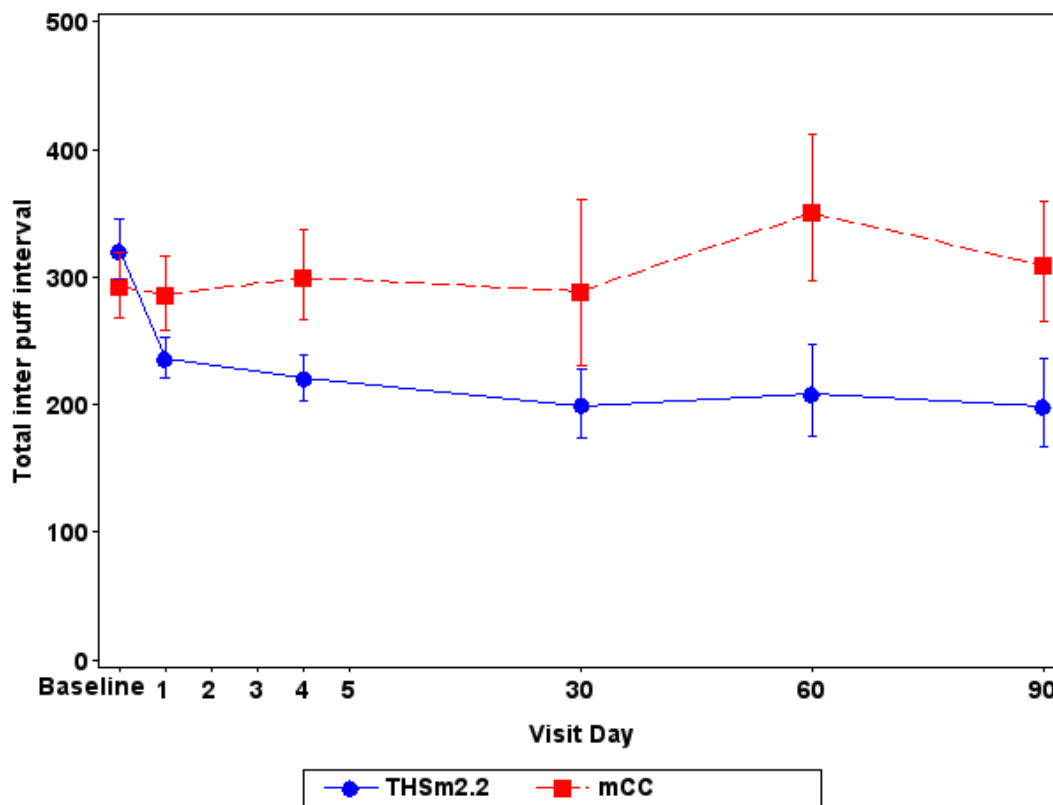
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Note: HST parameters are averaged over the visit day.

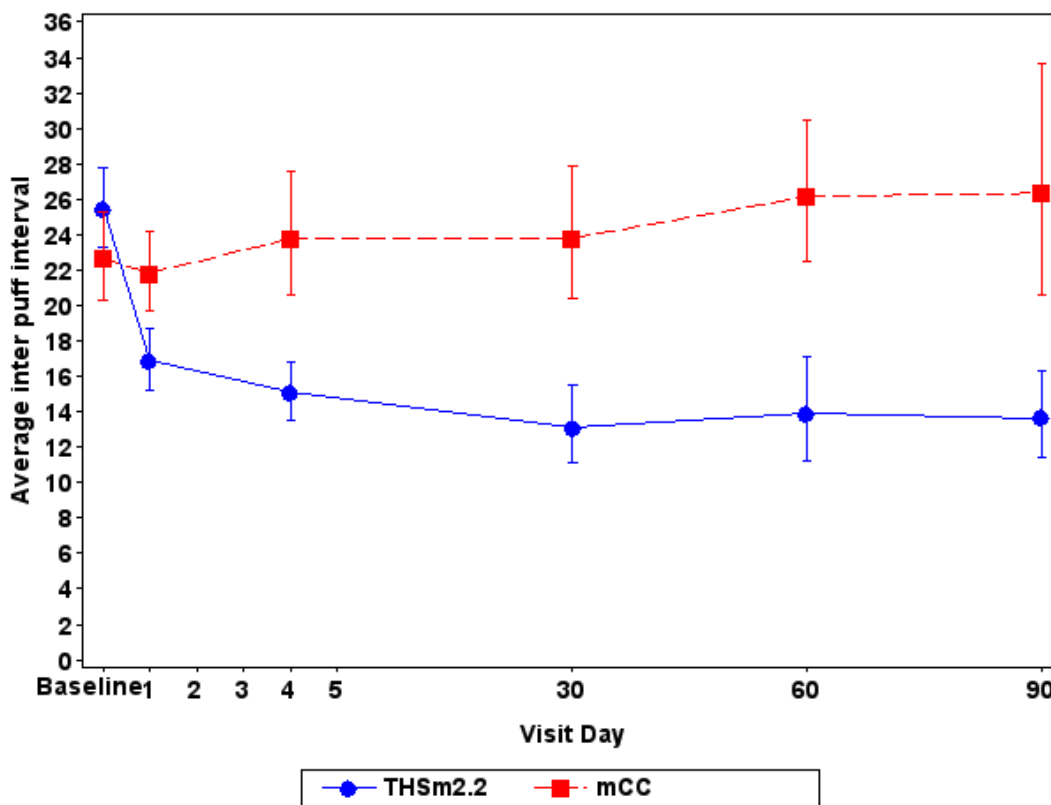
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Appendix: 15.2.4.42.1

Study ID: ZRHM-REXA-08-US

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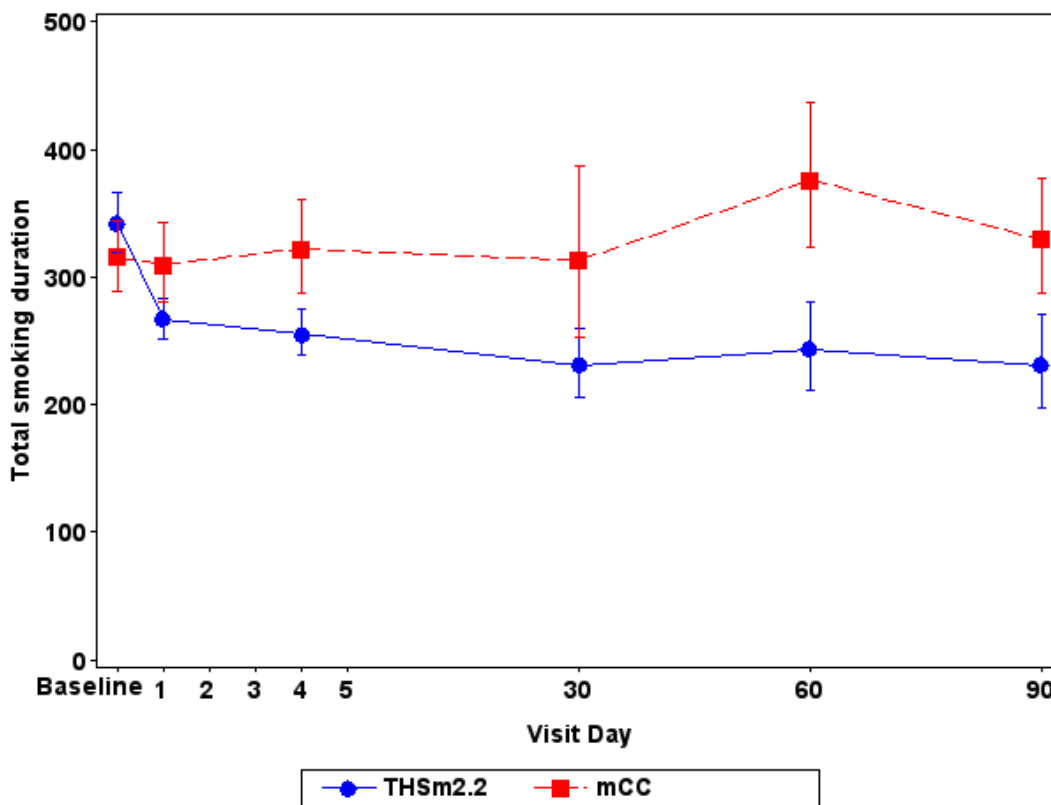
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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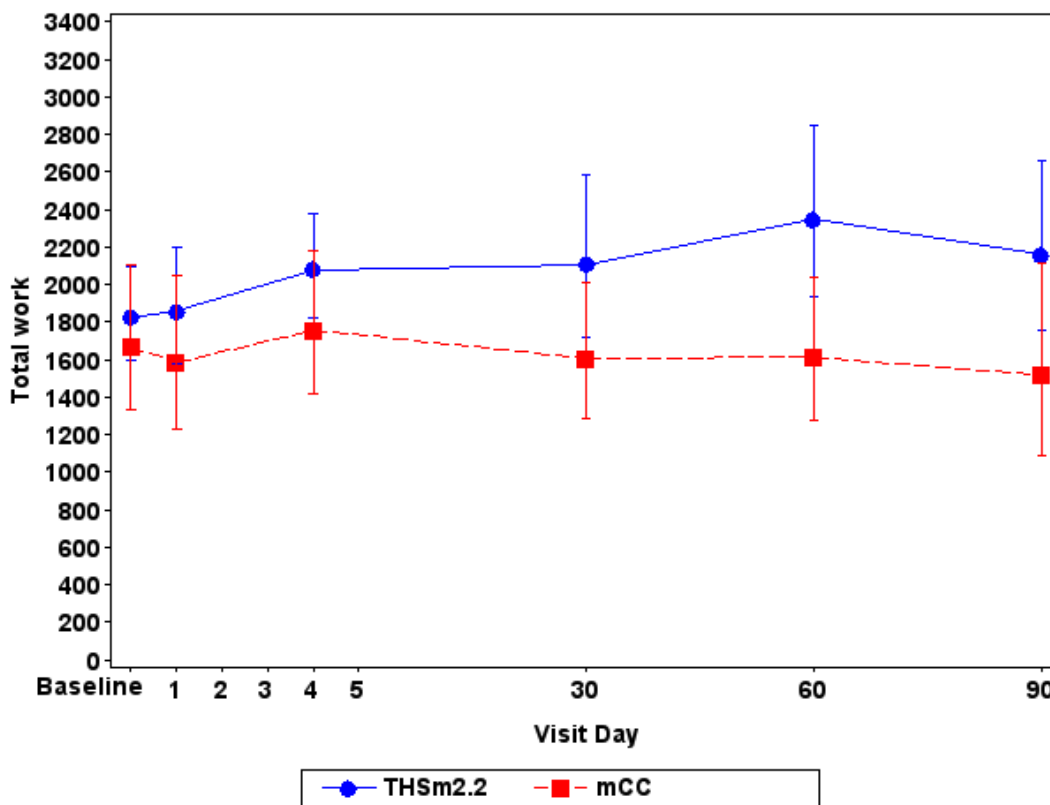
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Note: HST parameters are averaged over the visit day.

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Study ID: ZRHM-REXA-08-US

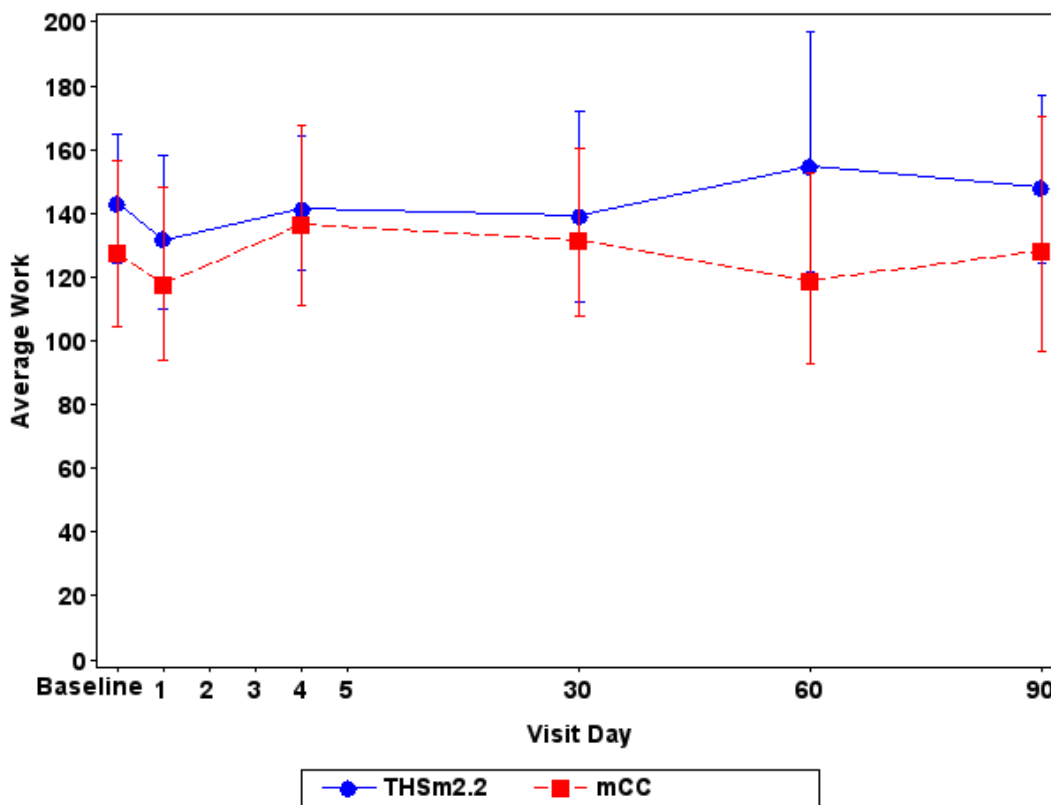
Program: f1501021001\_ZRHM-REXA-08\_US\_v1\_PMI.sas

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

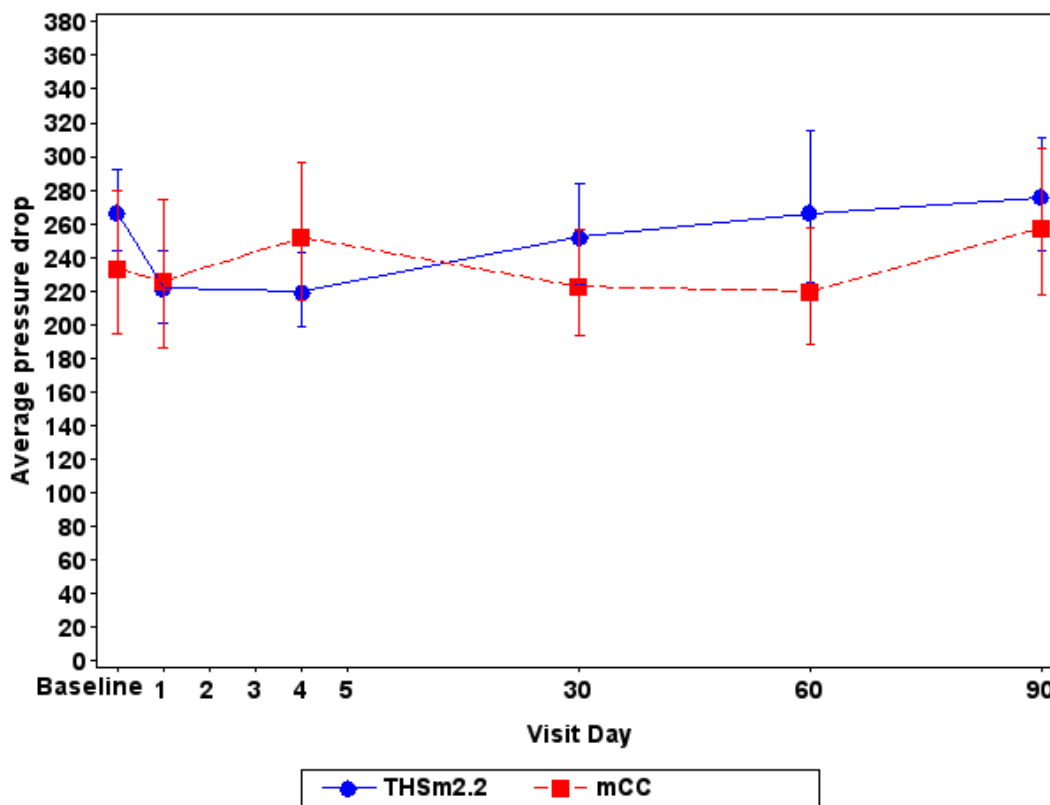
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

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Study ID: ZRHM-REXA-08-US

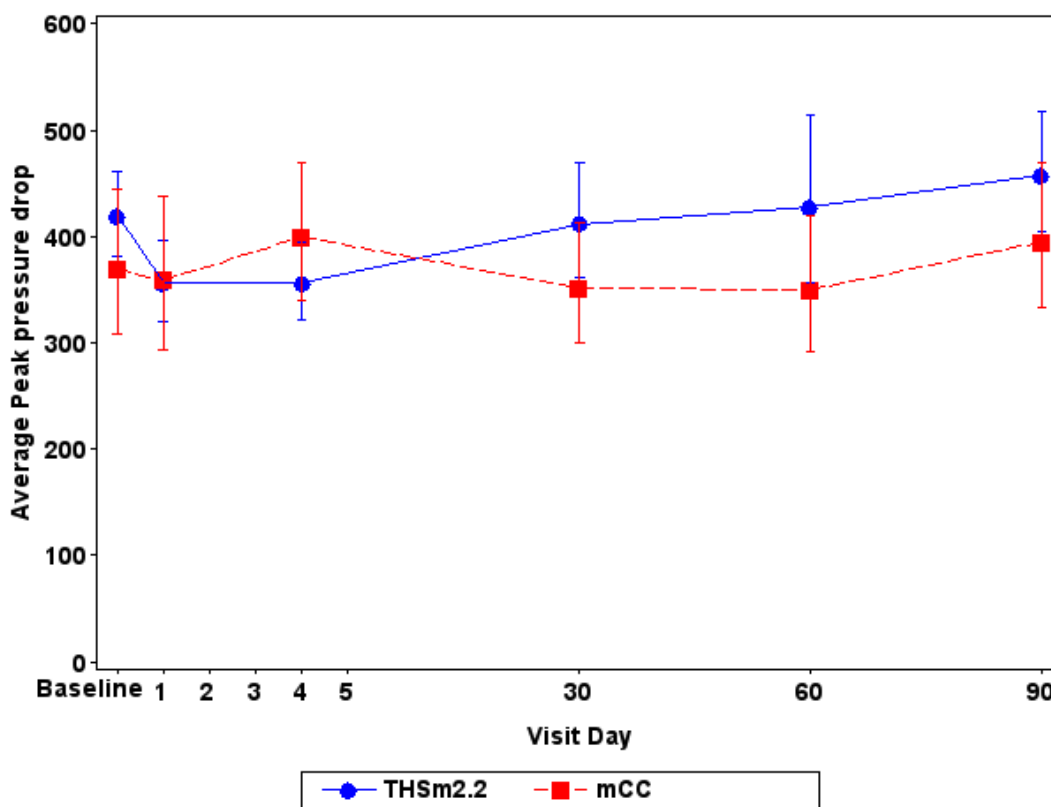
Program: f1501021001\_ZRHM-REXA-08\_US\_v1\_PMI.sas

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

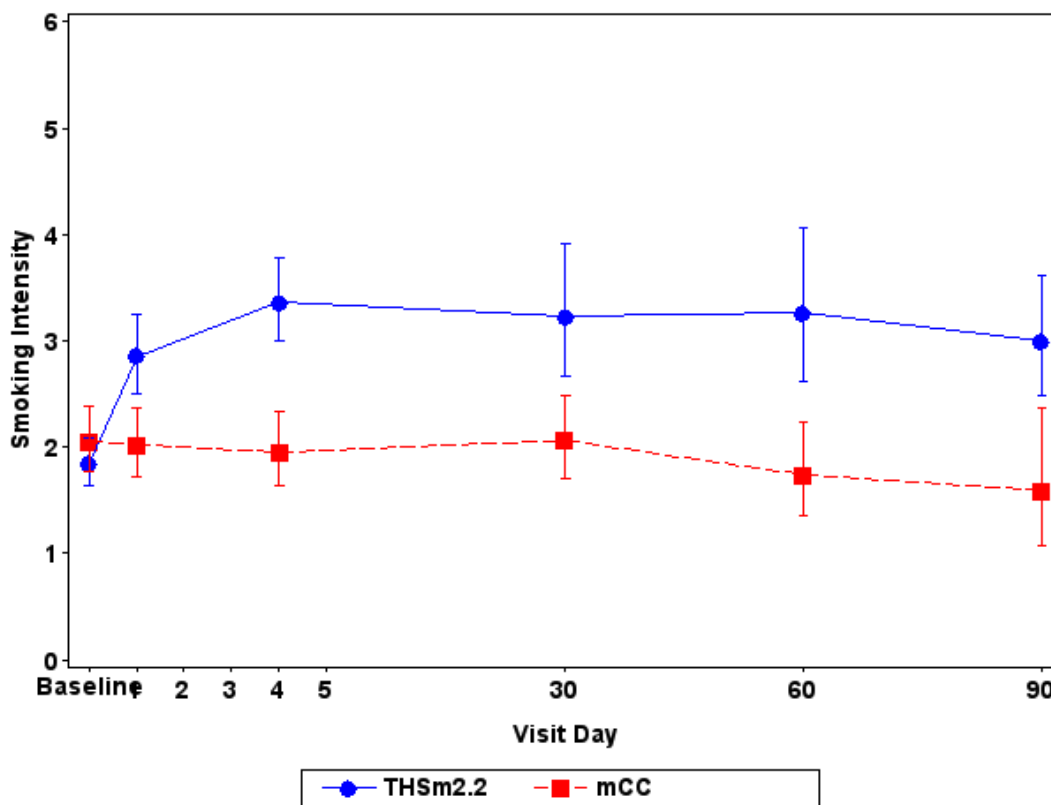
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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: HST parameters are averaged over the visit day.

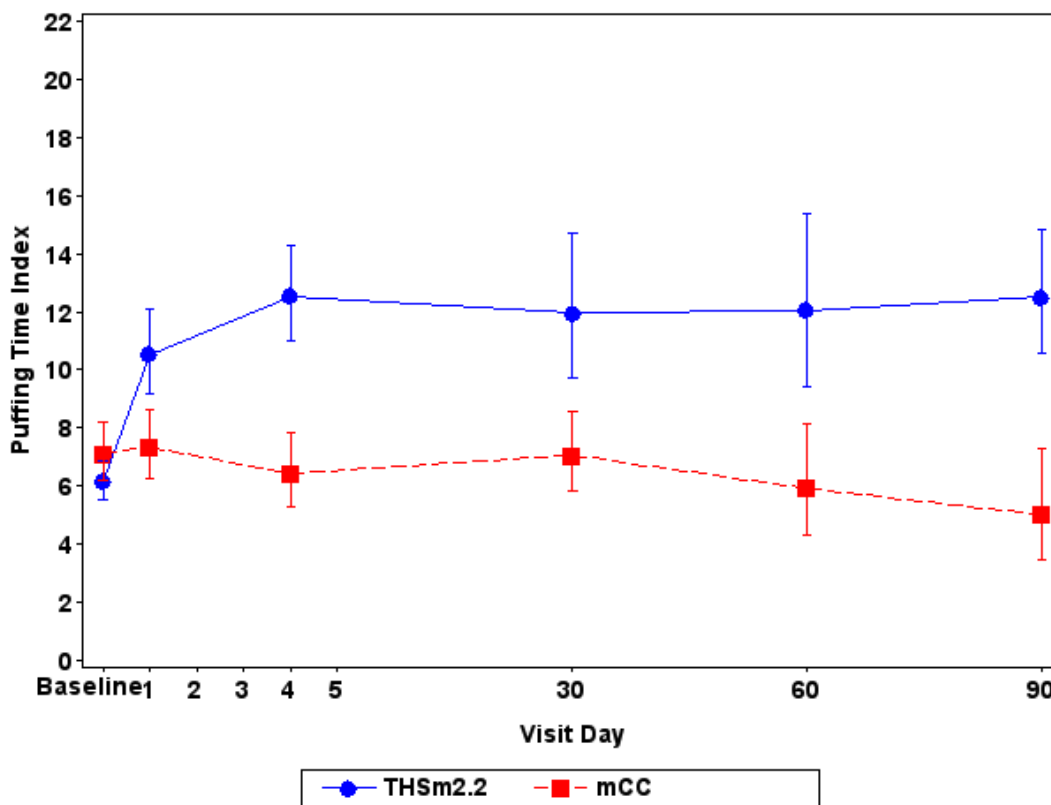
Appendix: 15.2.4.42.1

Study ID: ZRHM-REXA-08-US

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in CC/THS 2.2 arms on Day 1 or last assessment prior to 06:29 AM in SA arm on Day 1.

Baseline is summarized using the baseline data from the PP Set for Period 1.

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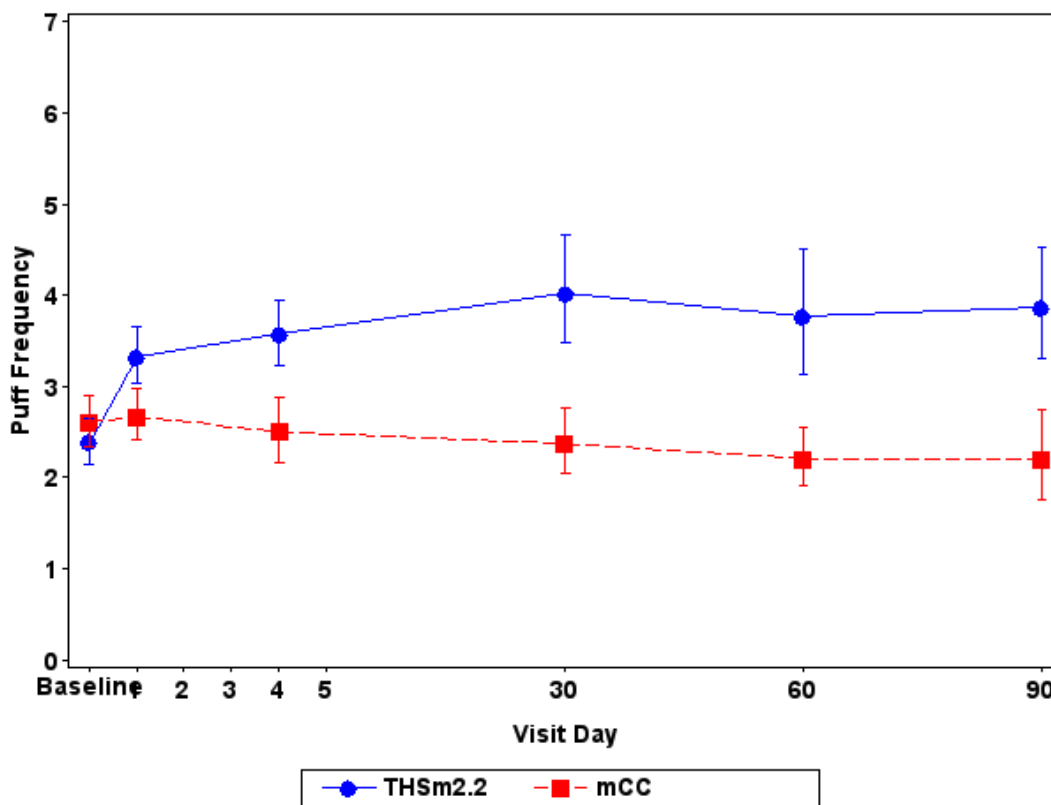
Appendix: 15.2.4.42.1

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**Figure 15.1.2.10.1 HST Parameters Averaged Over the Visit Geometric Mean and 95% CI - PP Set**



Note: mCC = Conventional menthol cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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Baseline is summarized using the baseline data from the PP Set for Period 1.

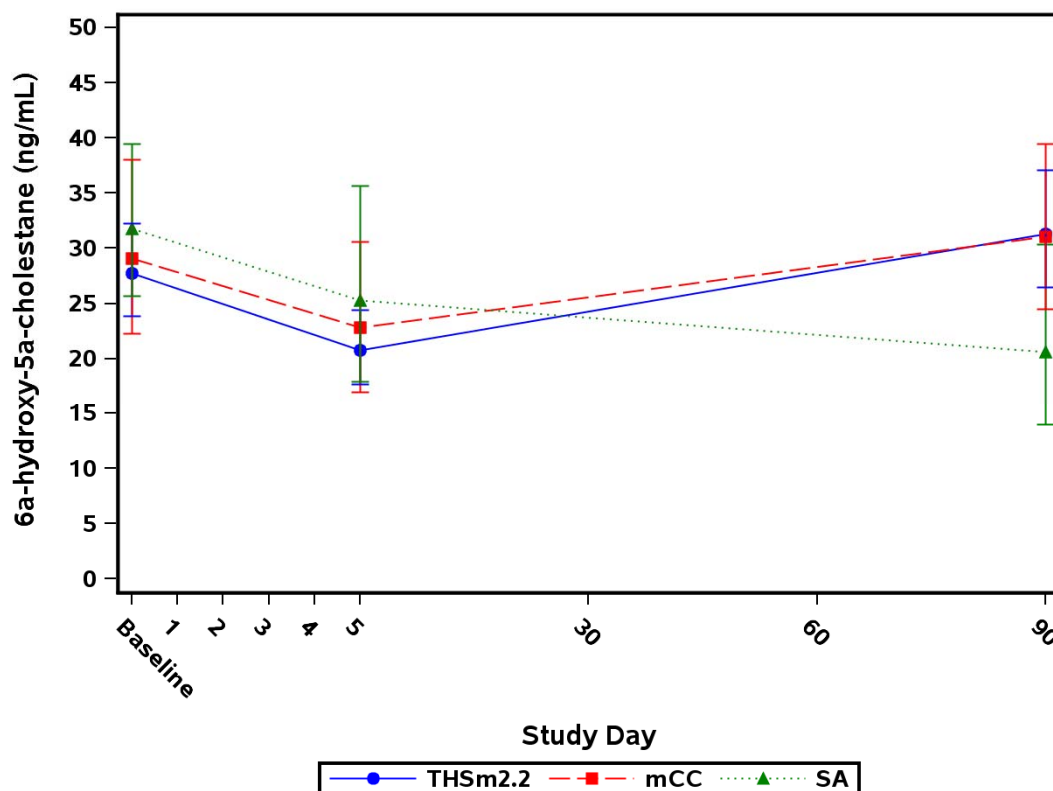
Note: HST parameters are averaged over the visit day.

Appendix: 15.2.4.42.1

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**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

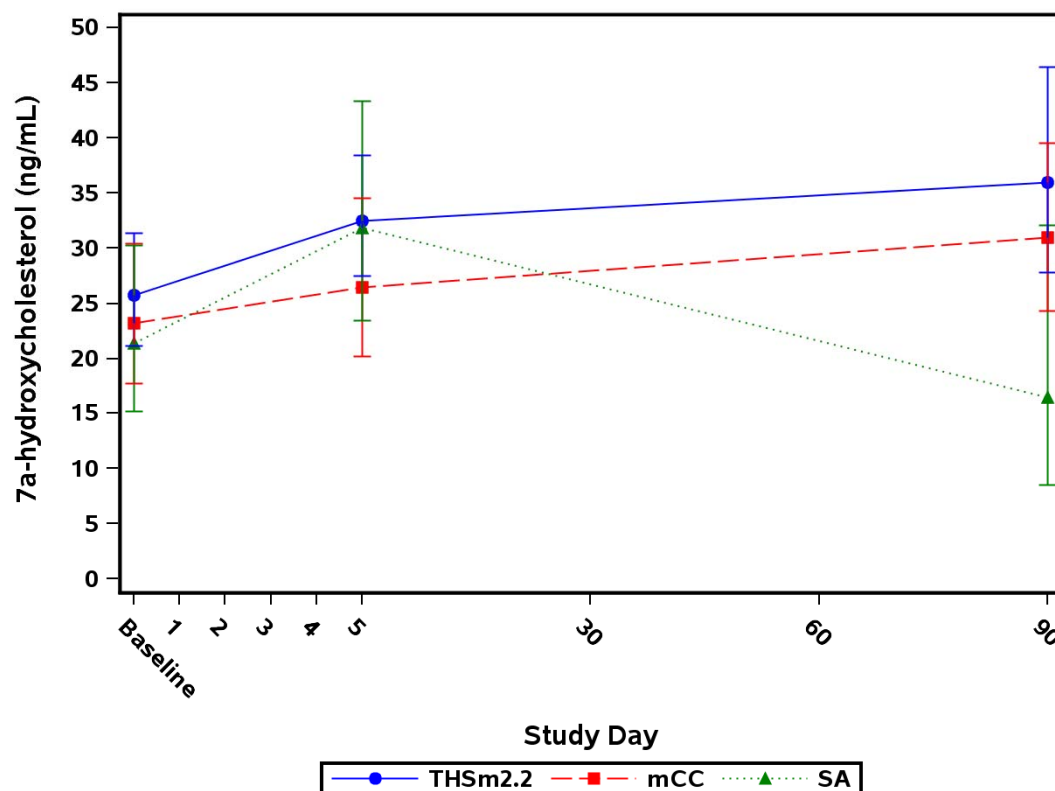
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

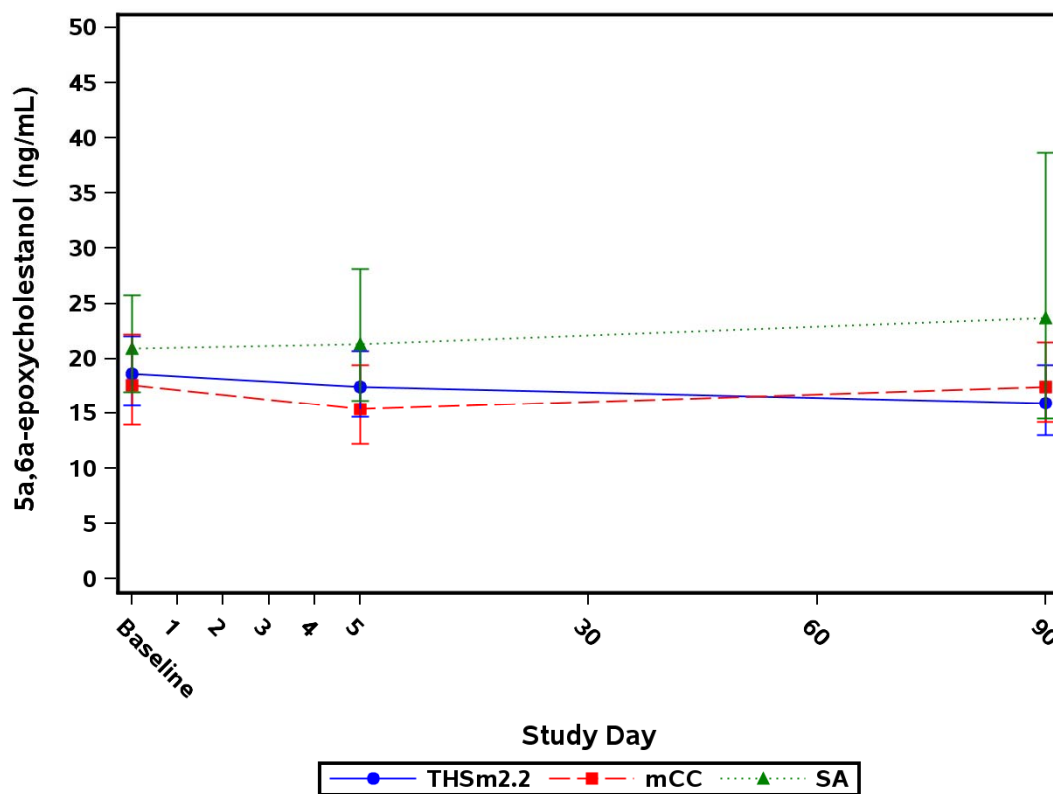
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

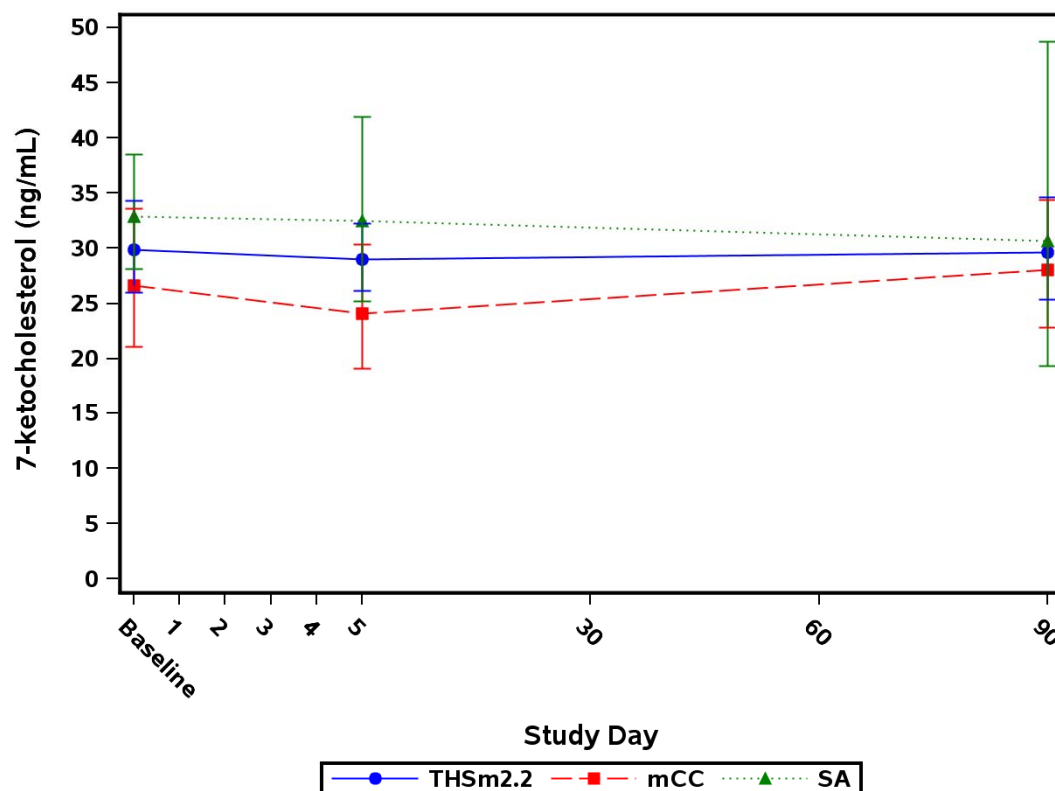
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

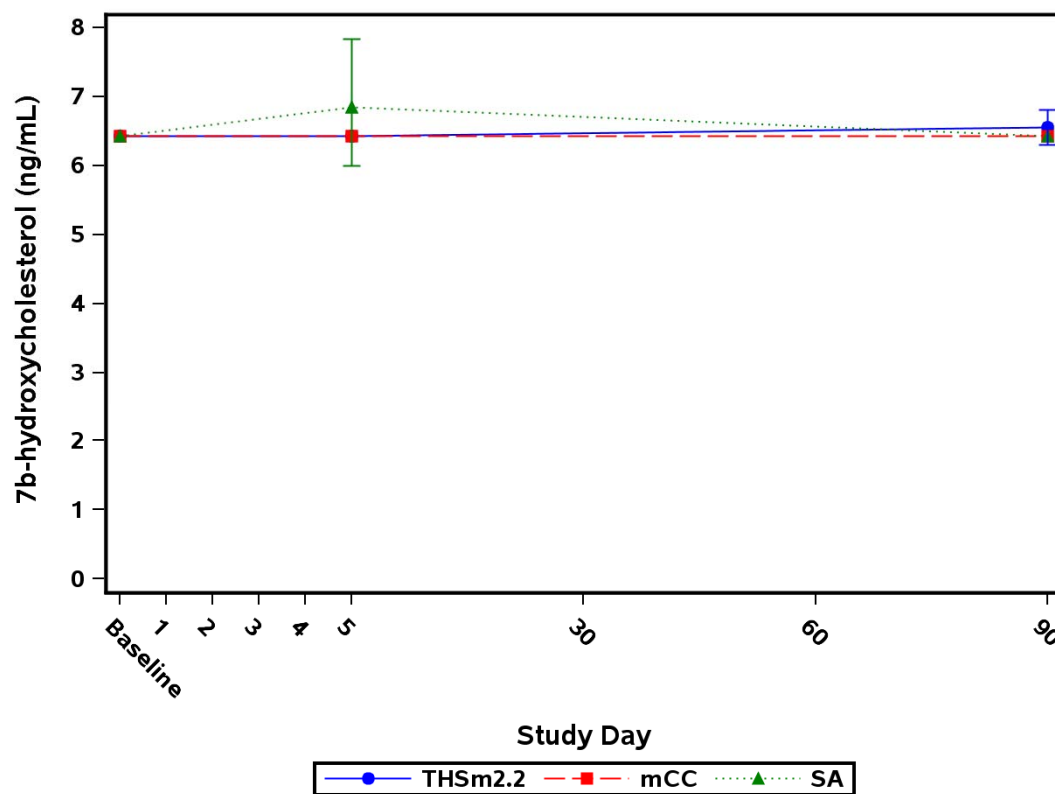
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

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**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

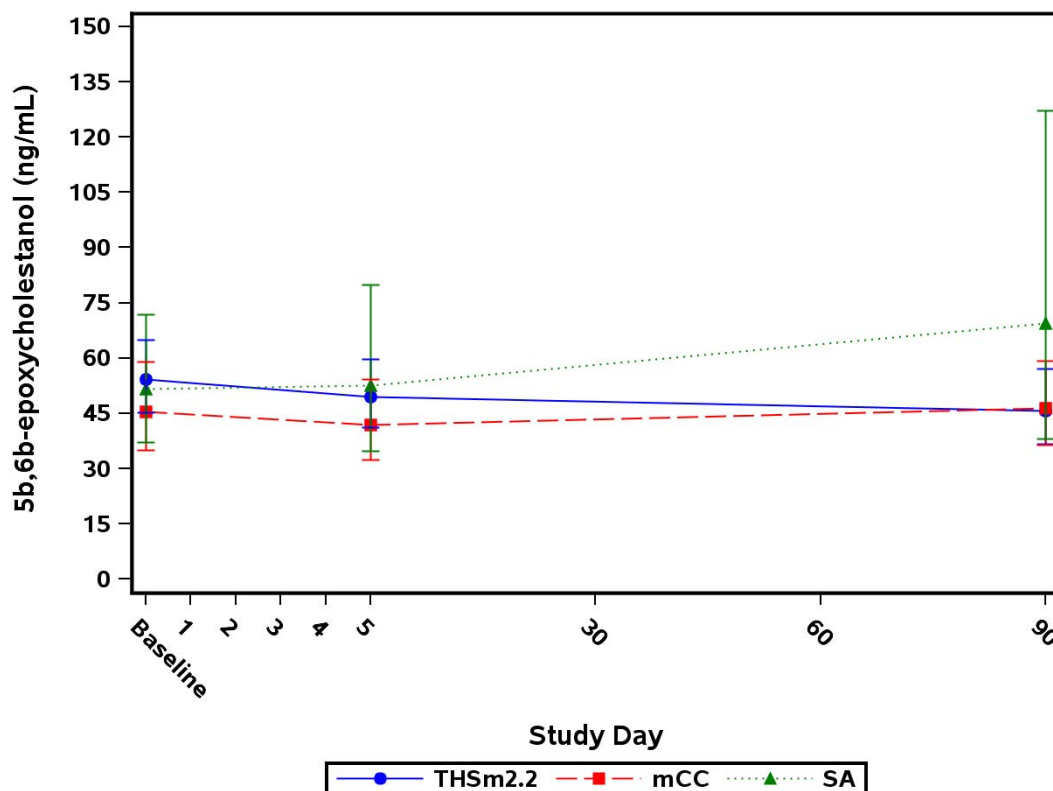
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

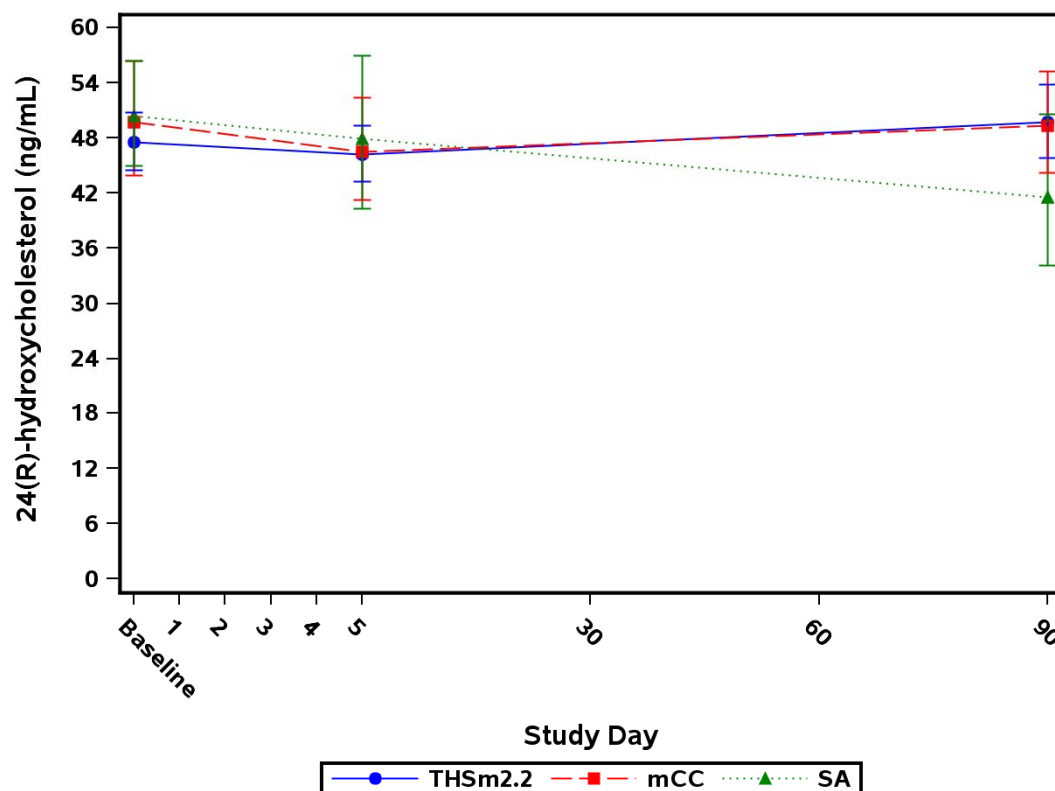
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 6 of 12)

**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

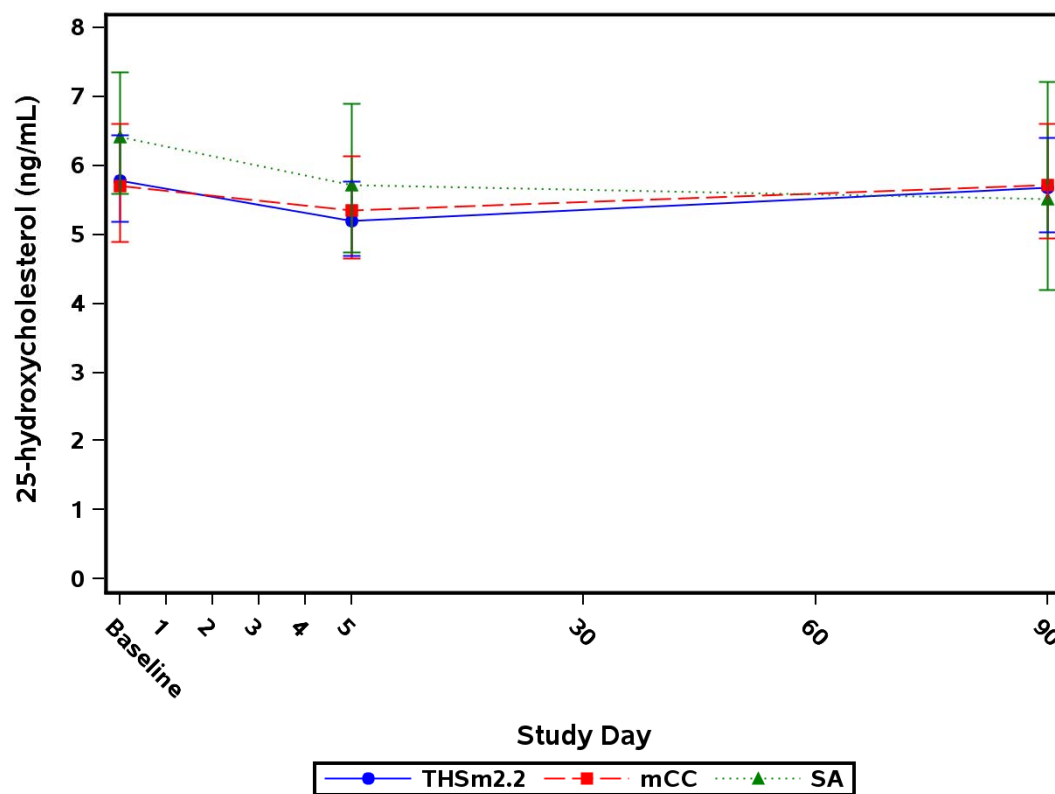
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 7 of 12)

**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

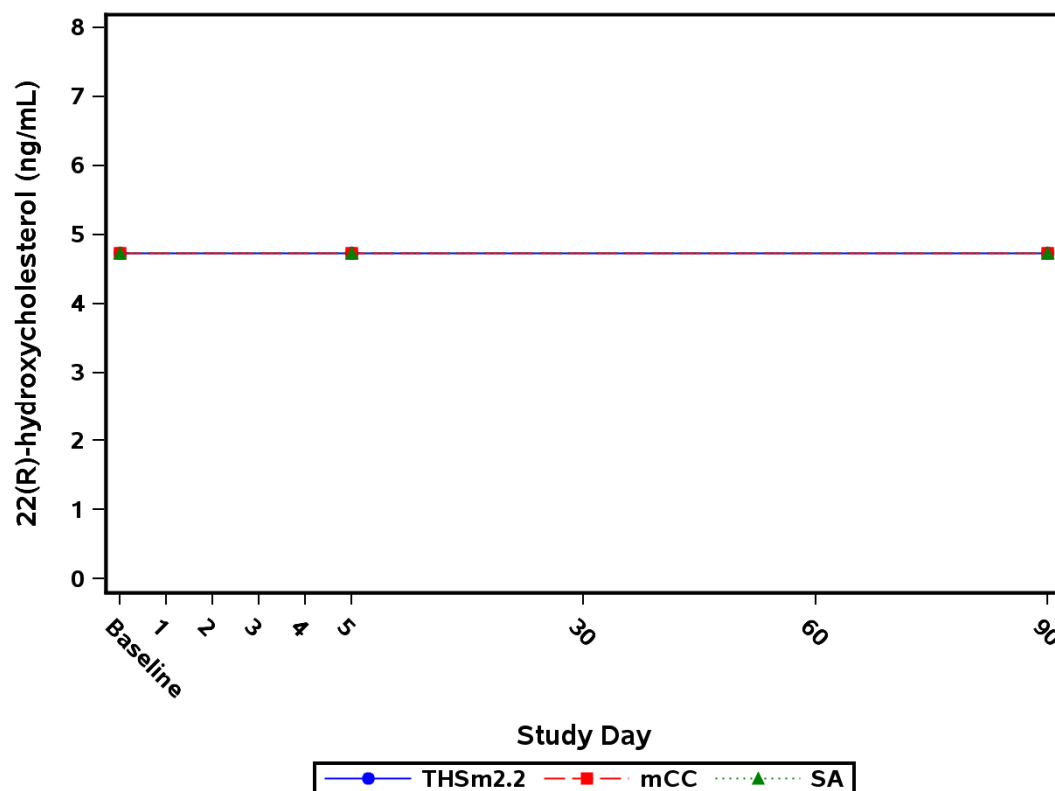
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 8 of 12)



**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

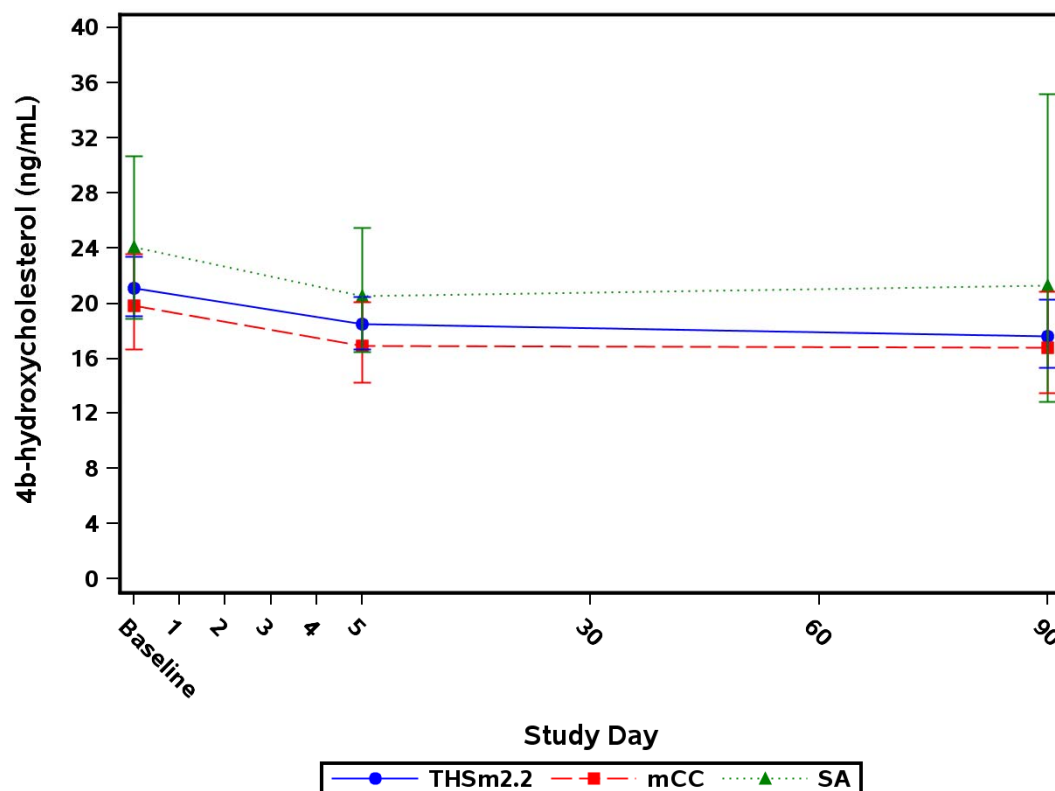
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 9 of 12)

**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

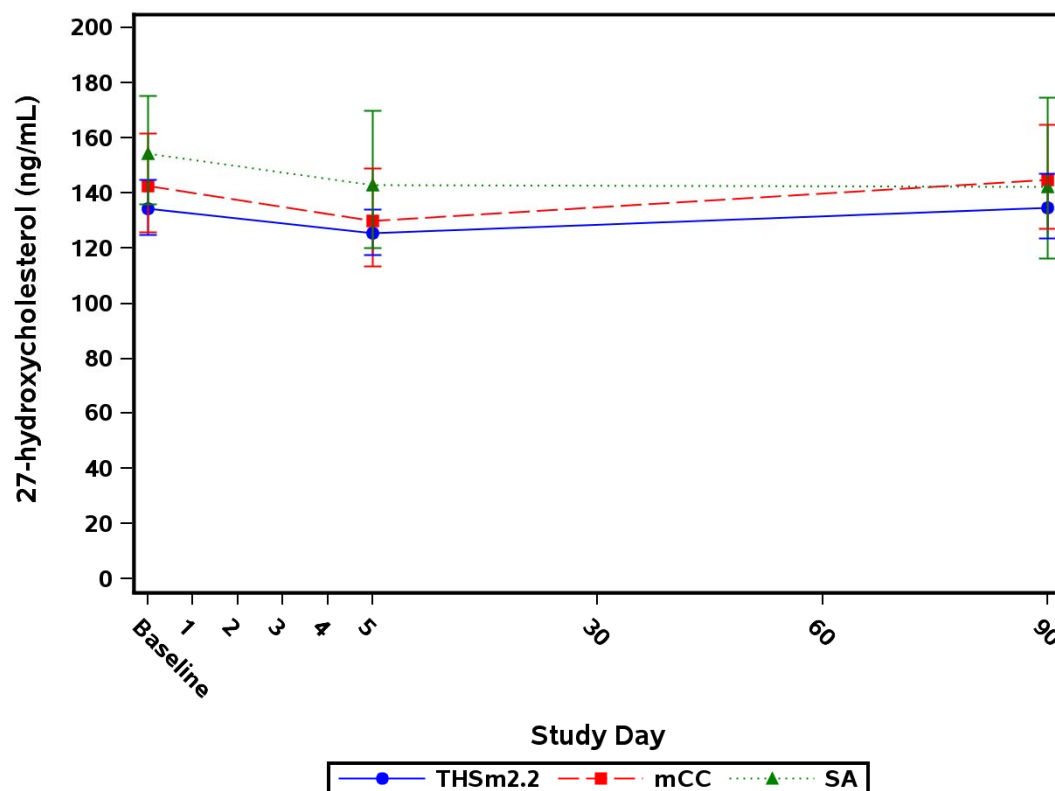
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 10 of 12)

**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

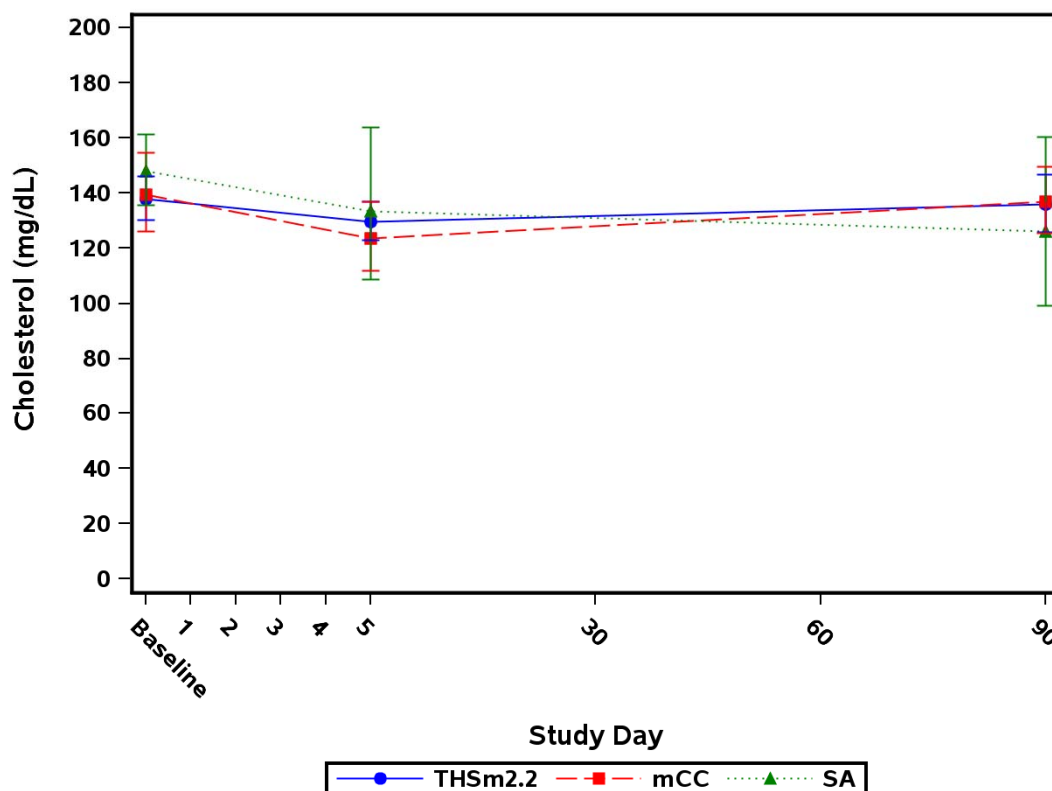
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 11 of 12)

**Figure 15.1.2.11.1 Oxysterol Parameters Arithmetic Mean and 95% CI - PP Set**

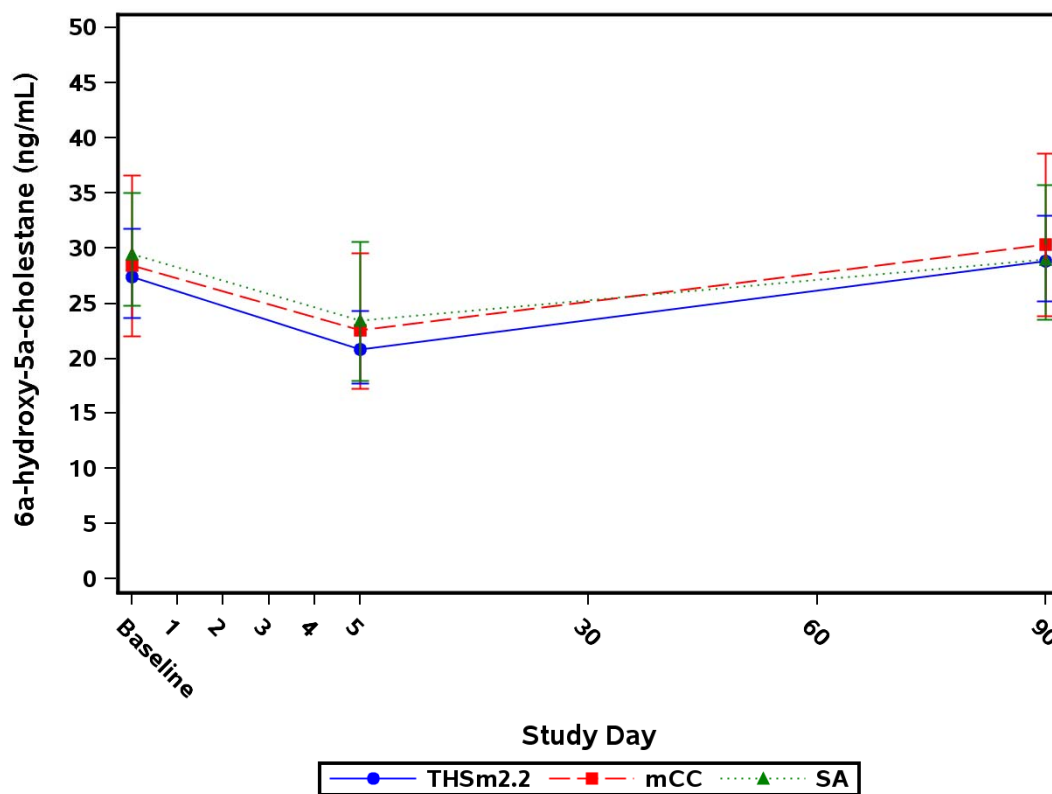
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.1

Study ID:REXA-08 Program: f\_oxy\_pp.sas 21SEP15 Status: Final (Page 12 of 12)

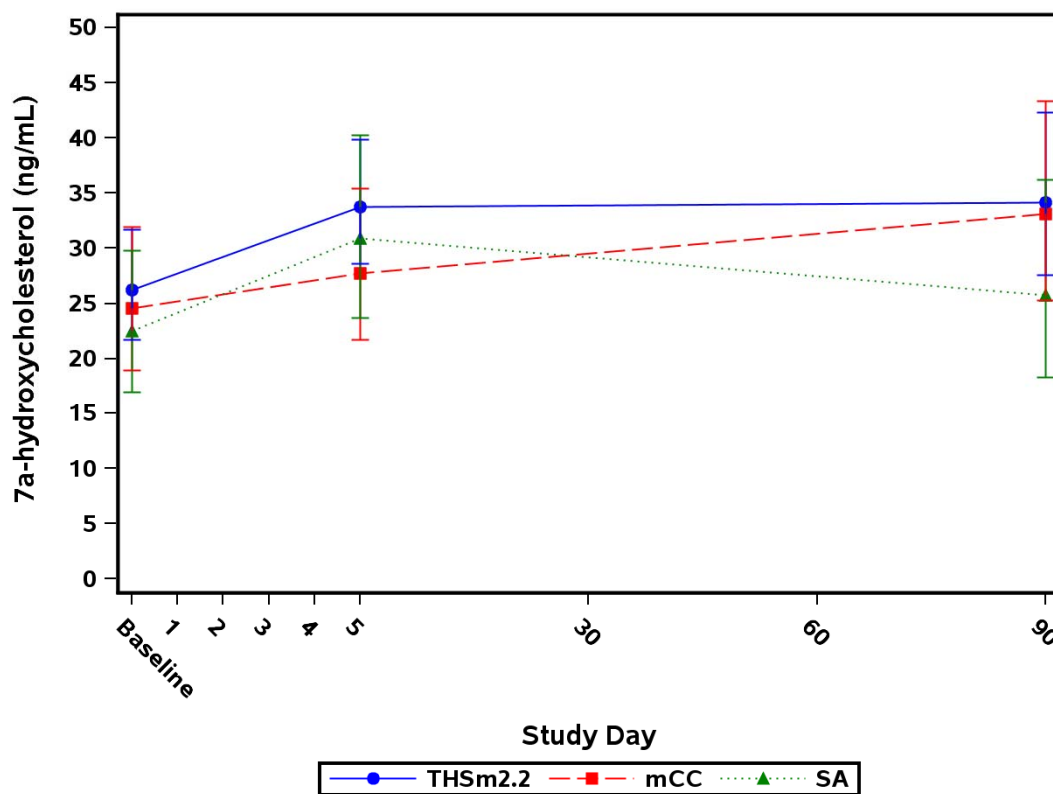
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 1 of 12)

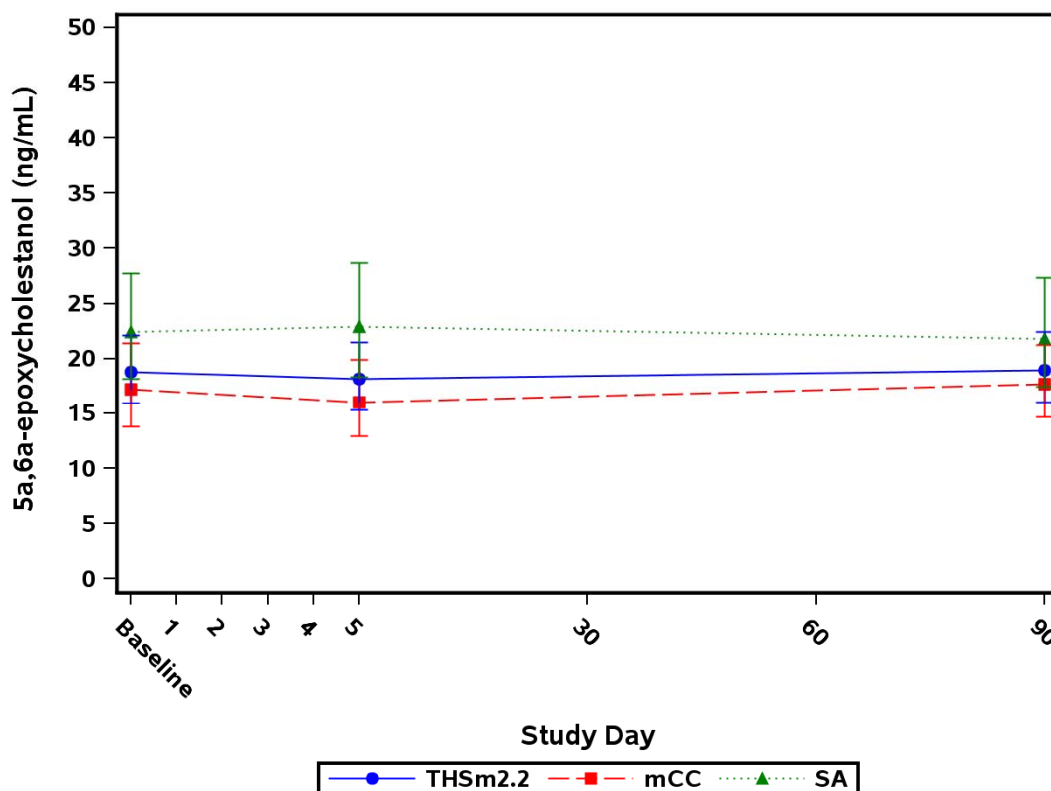
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 2 of 12)

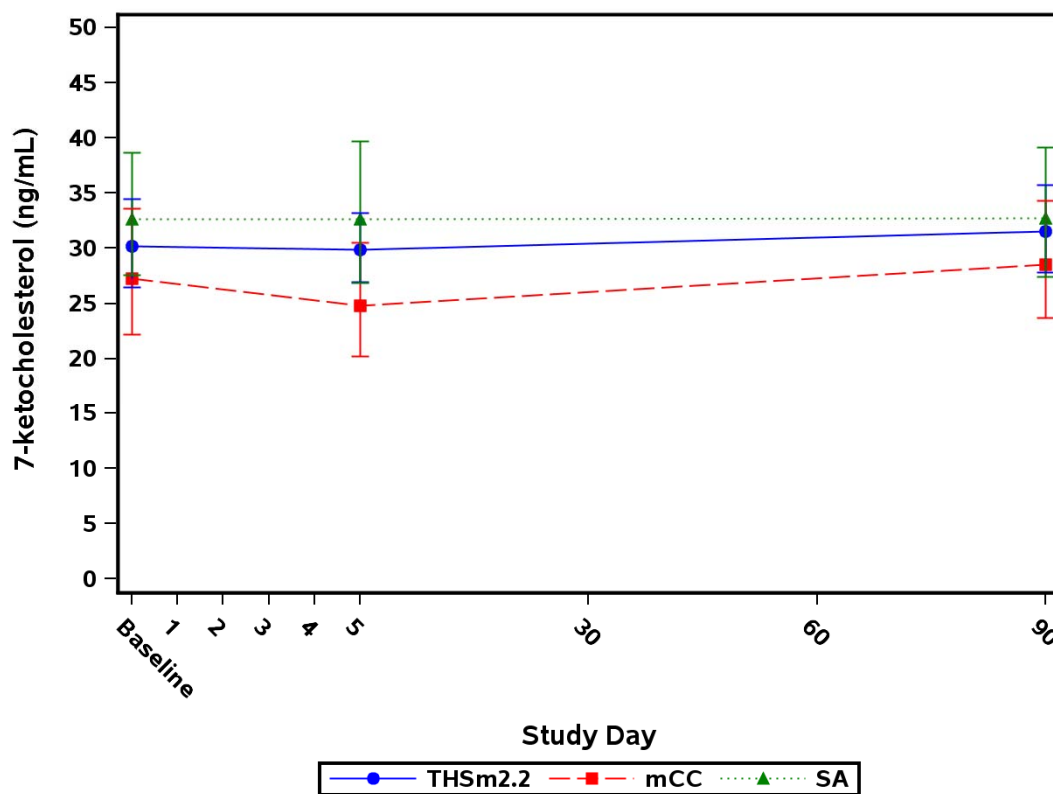
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 3 of 12)

**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

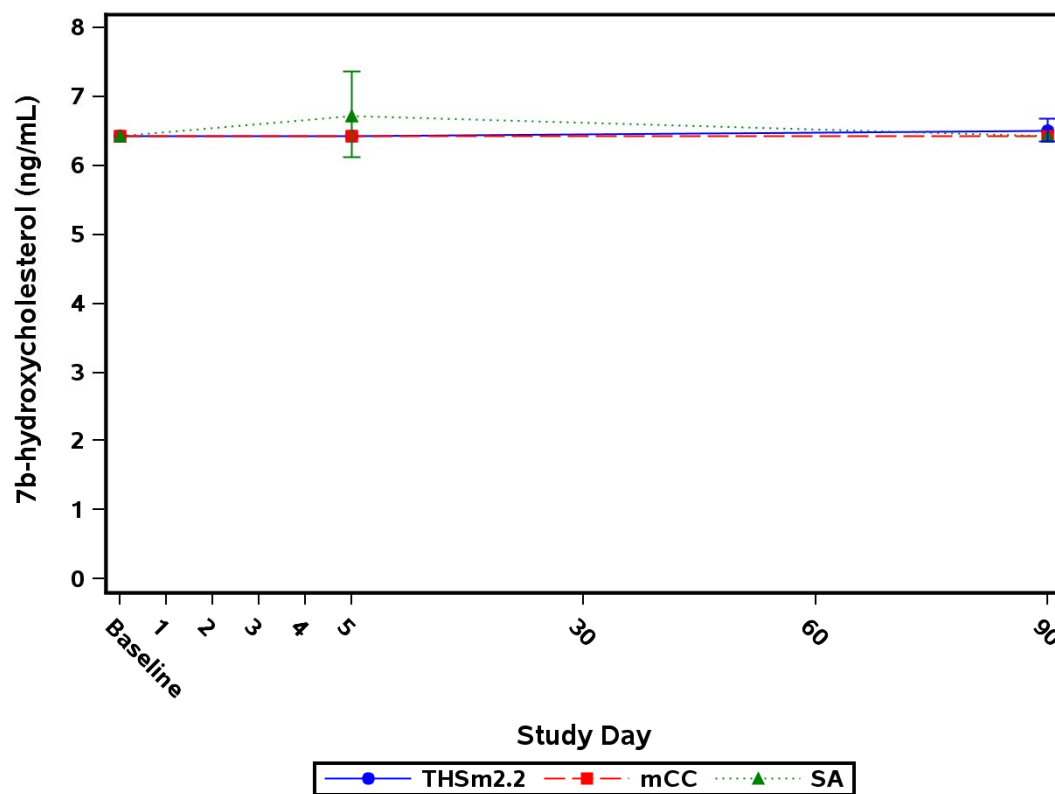
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 4 of 12)



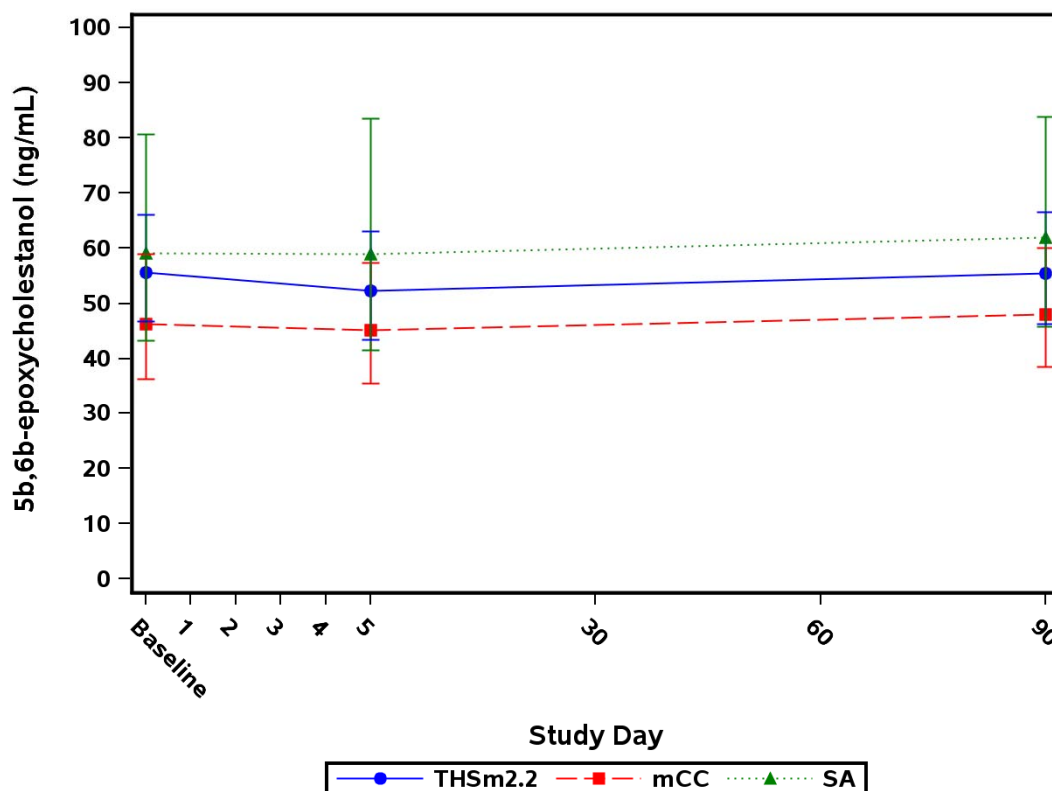
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 5 of 12)

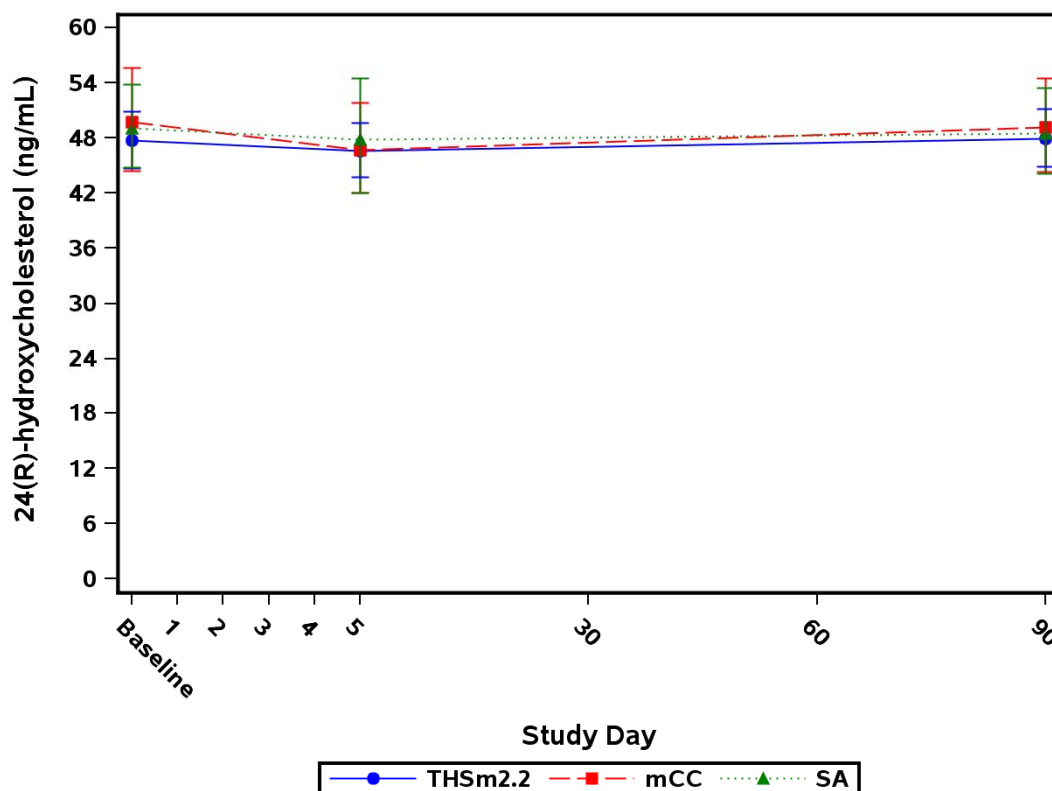
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 6 of 12)

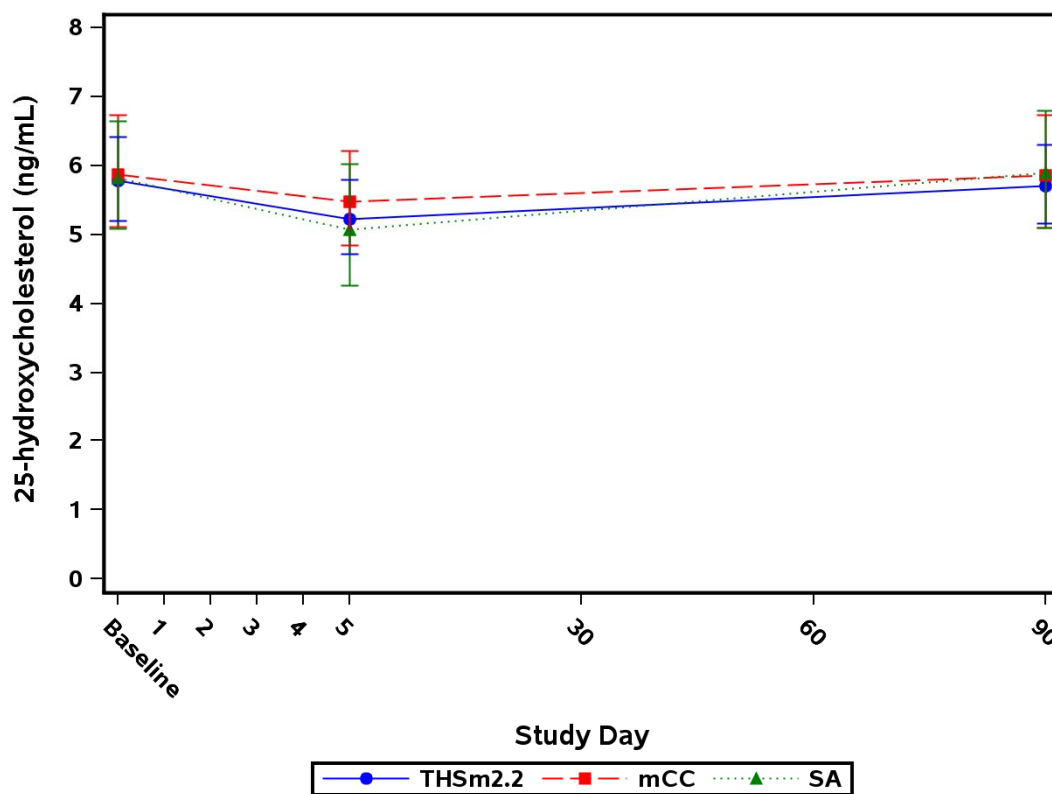
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 7 of 12)

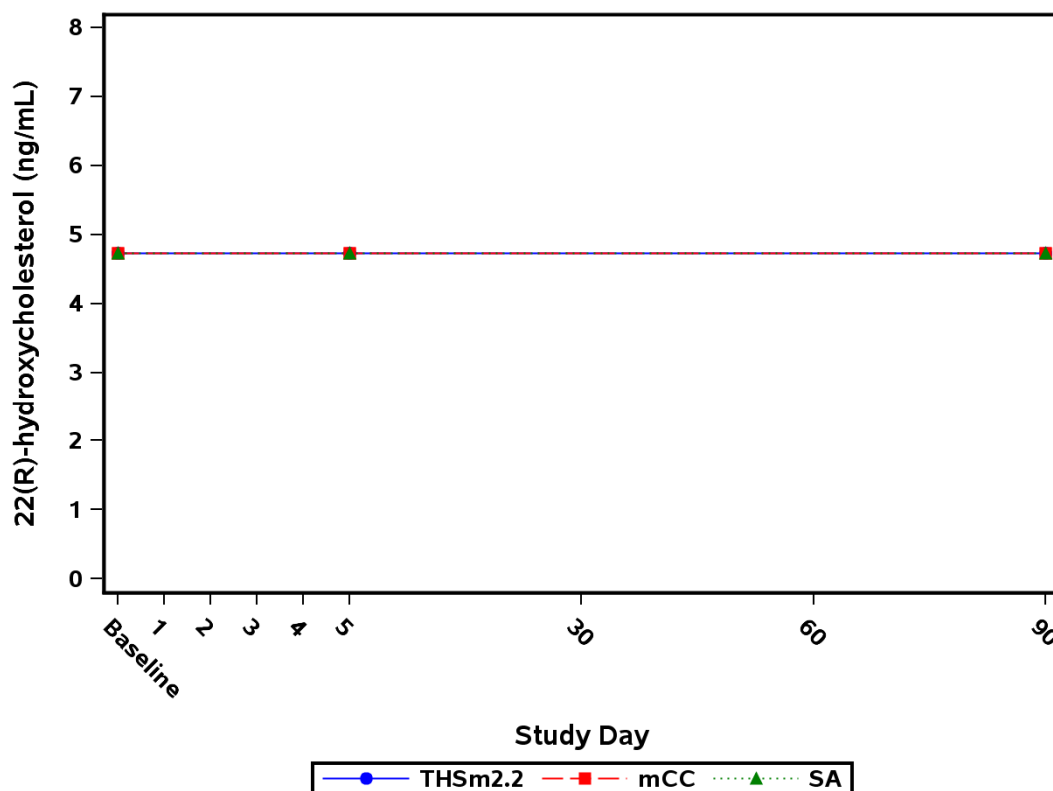
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 8 of 12)

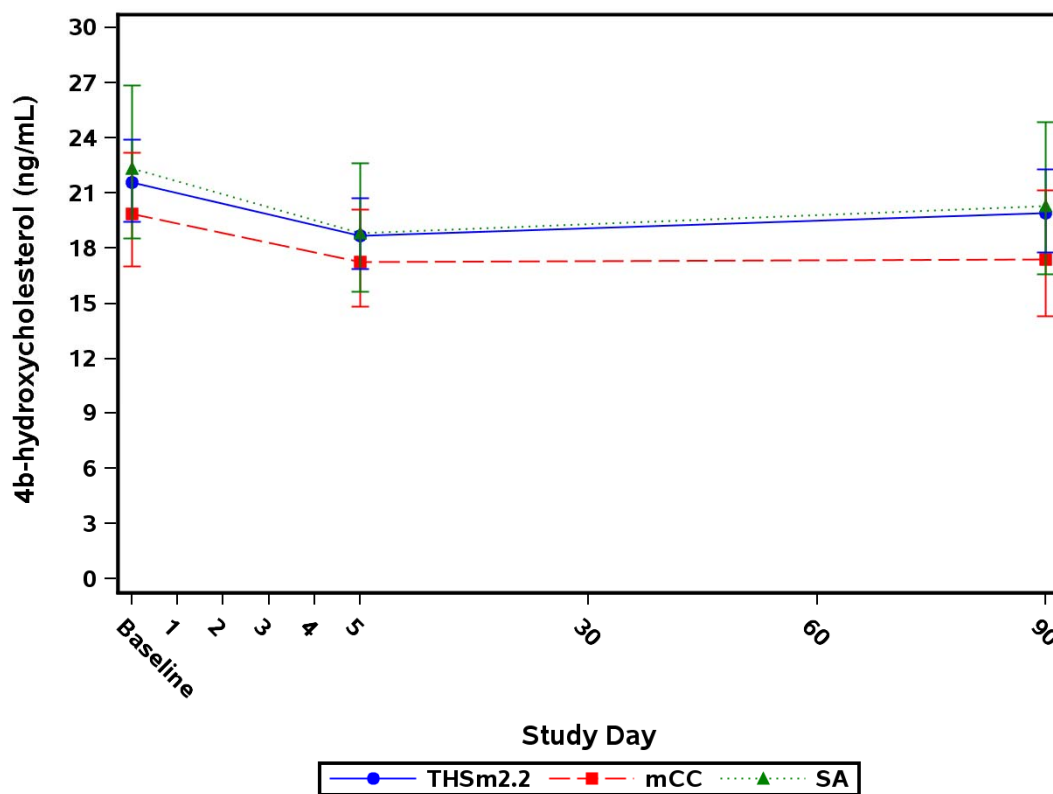
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 9 of 12)

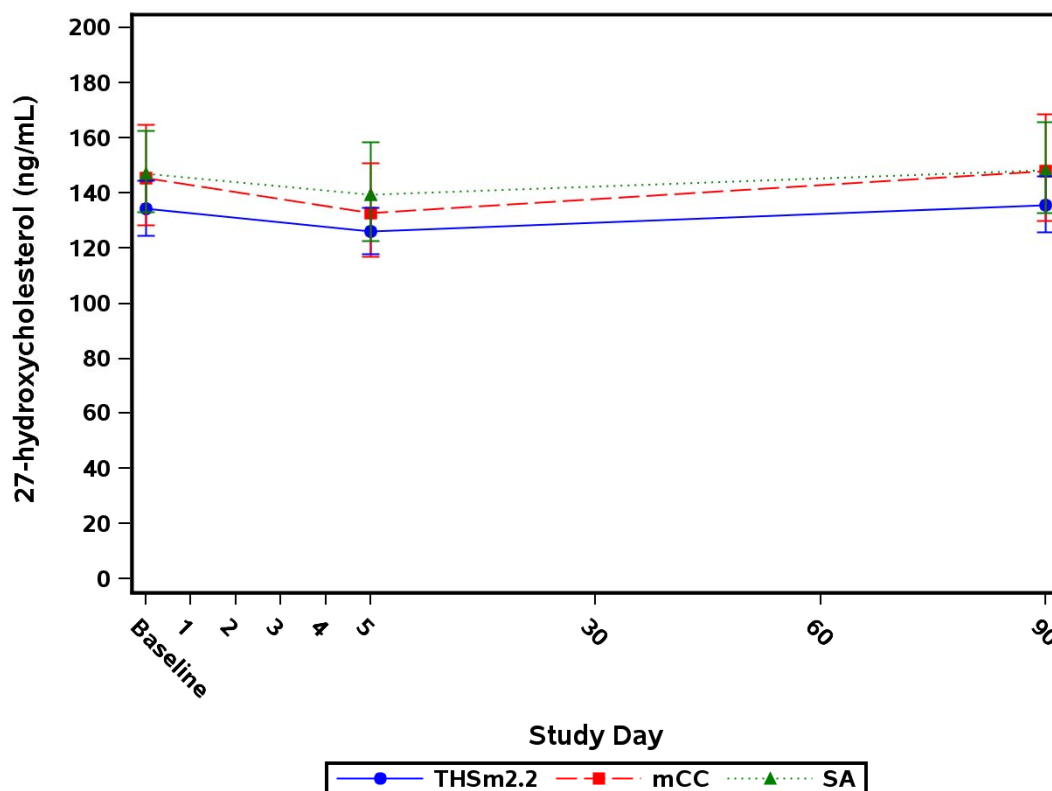
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 10 of 12)

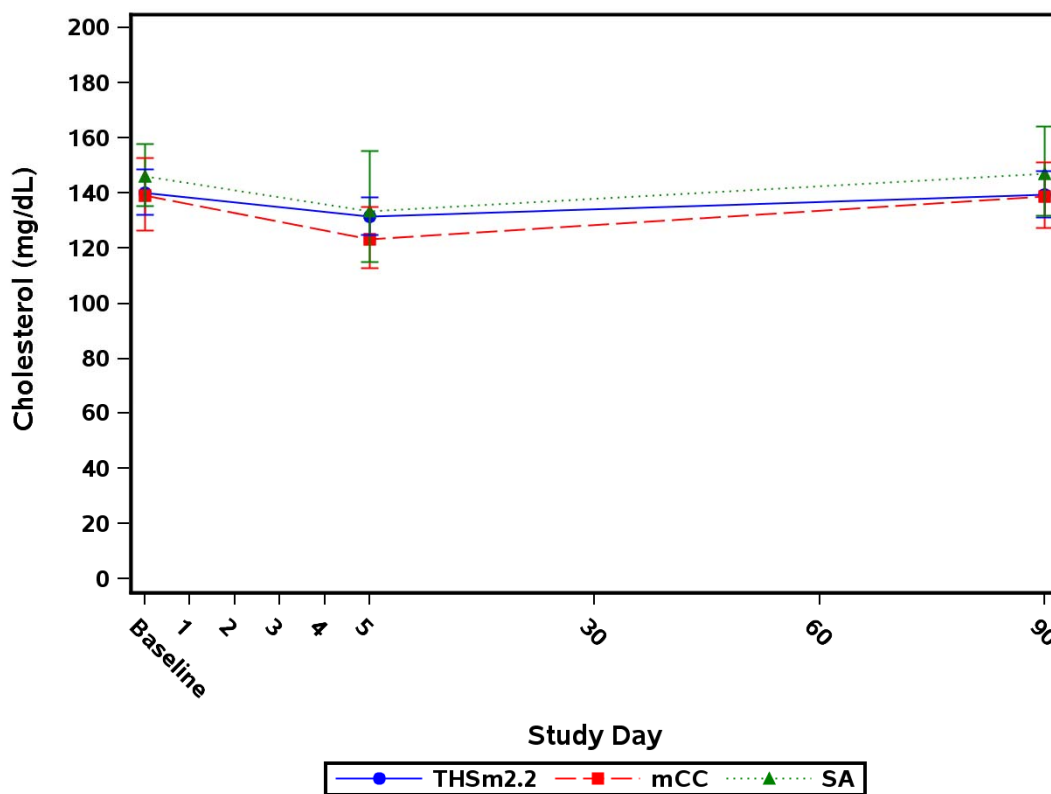
**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 11 of 12)

**Figure 15.1.2.11.2 Oxysterol Parameters Arithmetic Mean and 95% CI - FAS**

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

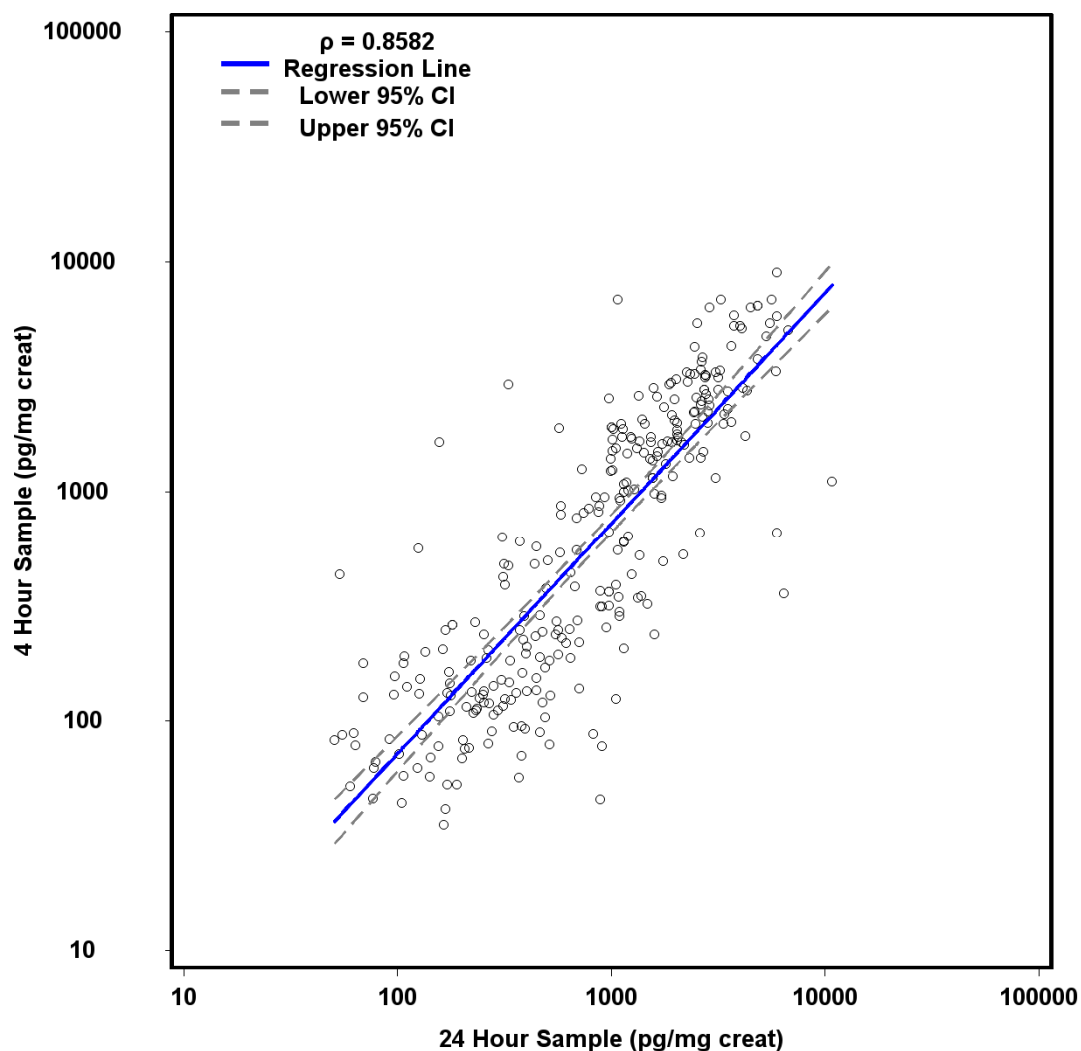
Appendix 15.2.4.66.2

Study ID:REXA-08 Program: f\_oxy\_fas.sas 21SEP15 Status: Final (Page 12 of 12)





**Figure 15.1.2.12.1 Scatter Plot of Urinary MHBMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

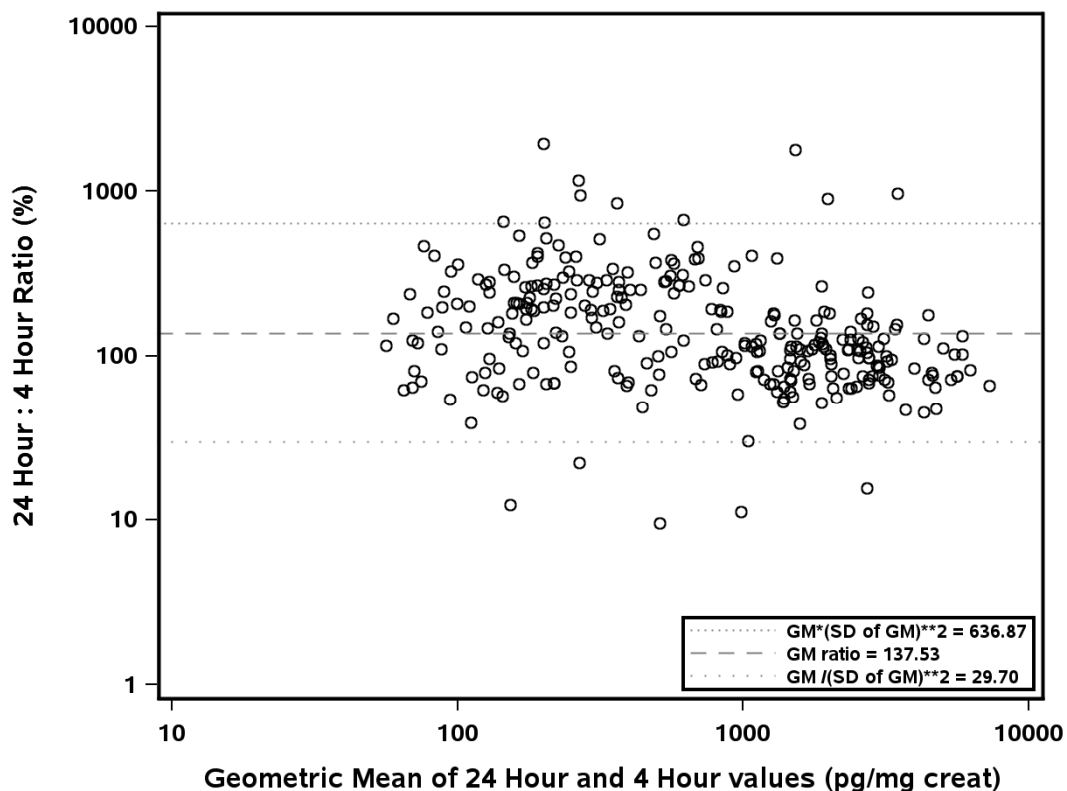
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_mhbma.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.12.2 Bland-Altman Plot for Concordance of Urinary MHBMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

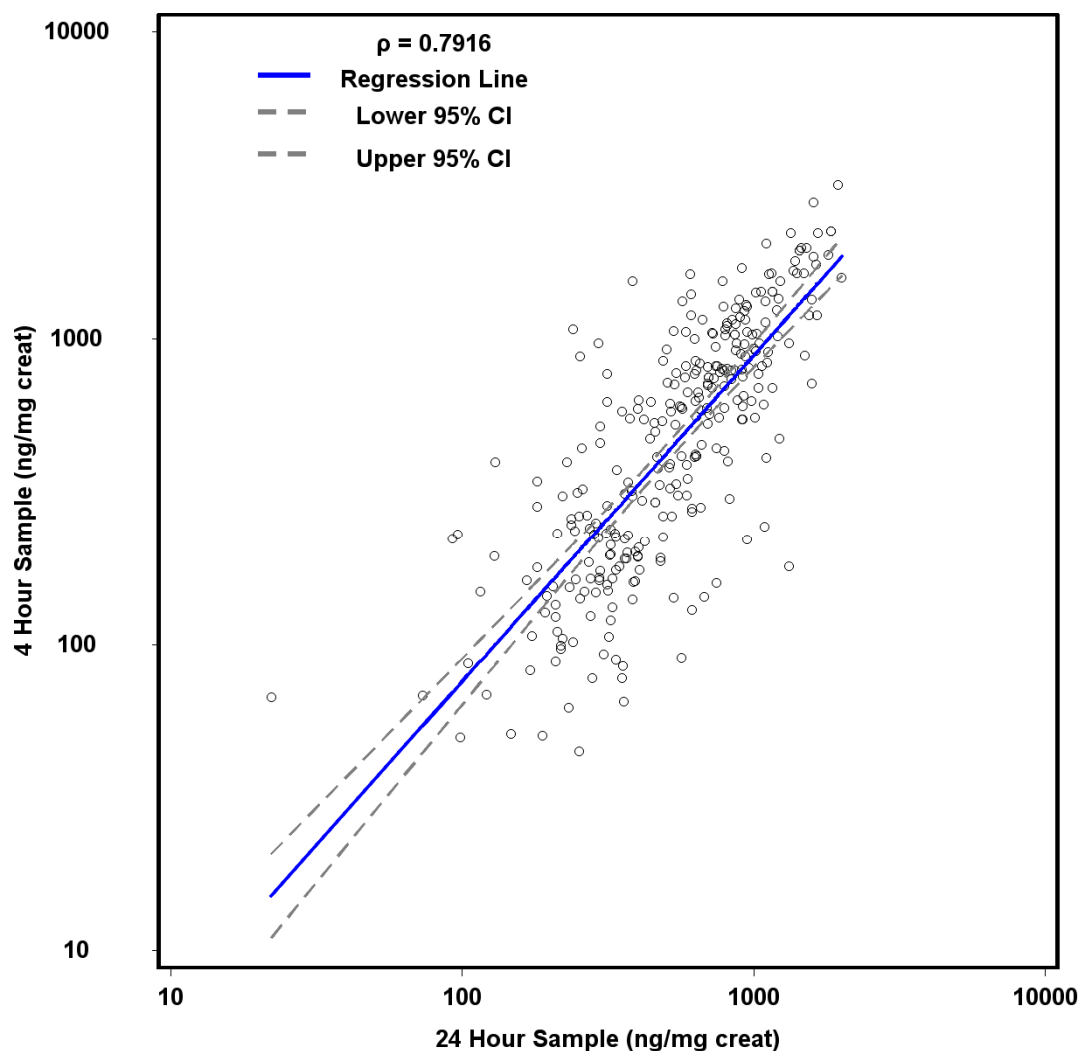
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_mhbma.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.13.1 Scatter Plot of Urinary 3-HMPA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

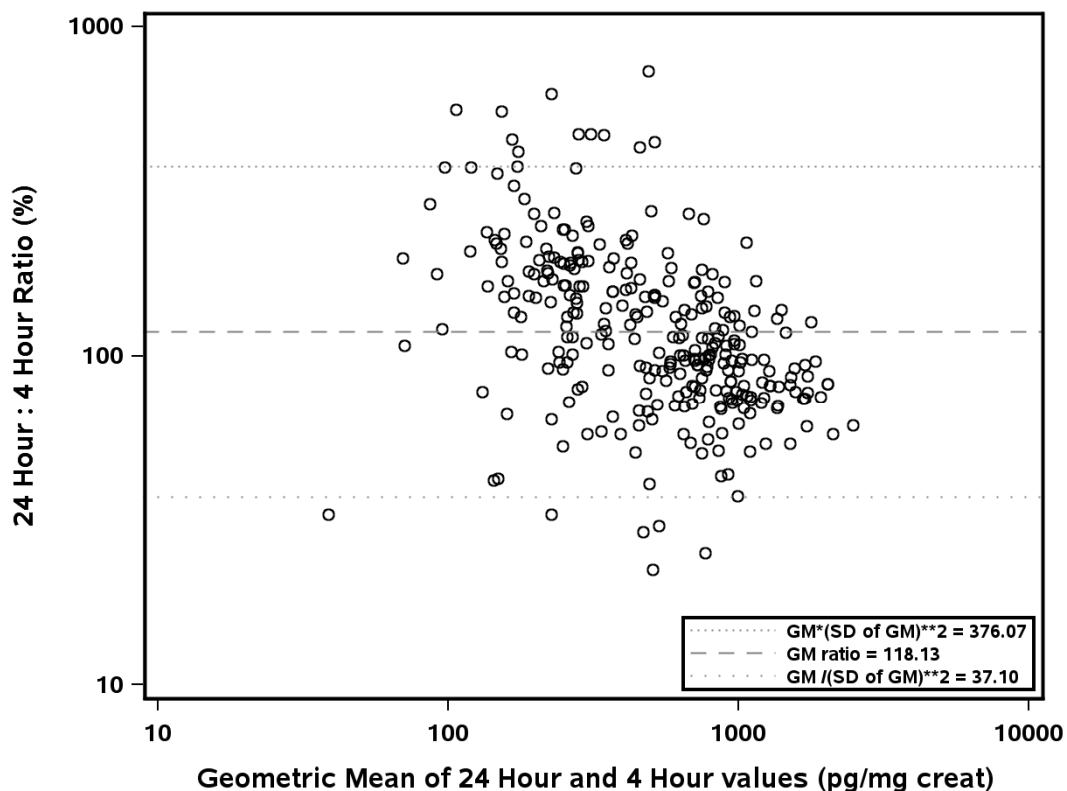
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_3hpm.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.13.2 Bland-Altman Plot for Concordance of Urinary 3-HMPA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

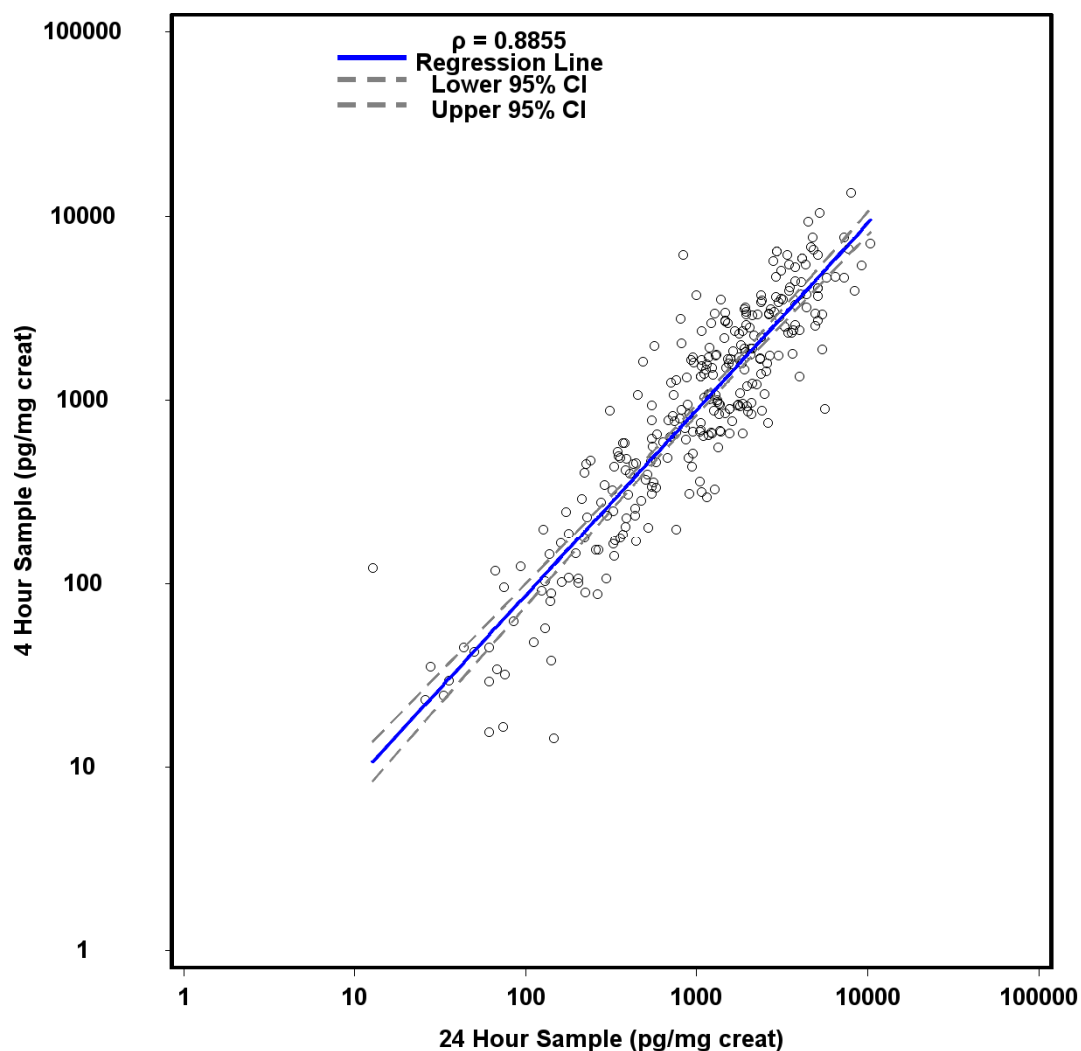
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_3hpma.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.14.1 Scatter Plot of Urinary S-PMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

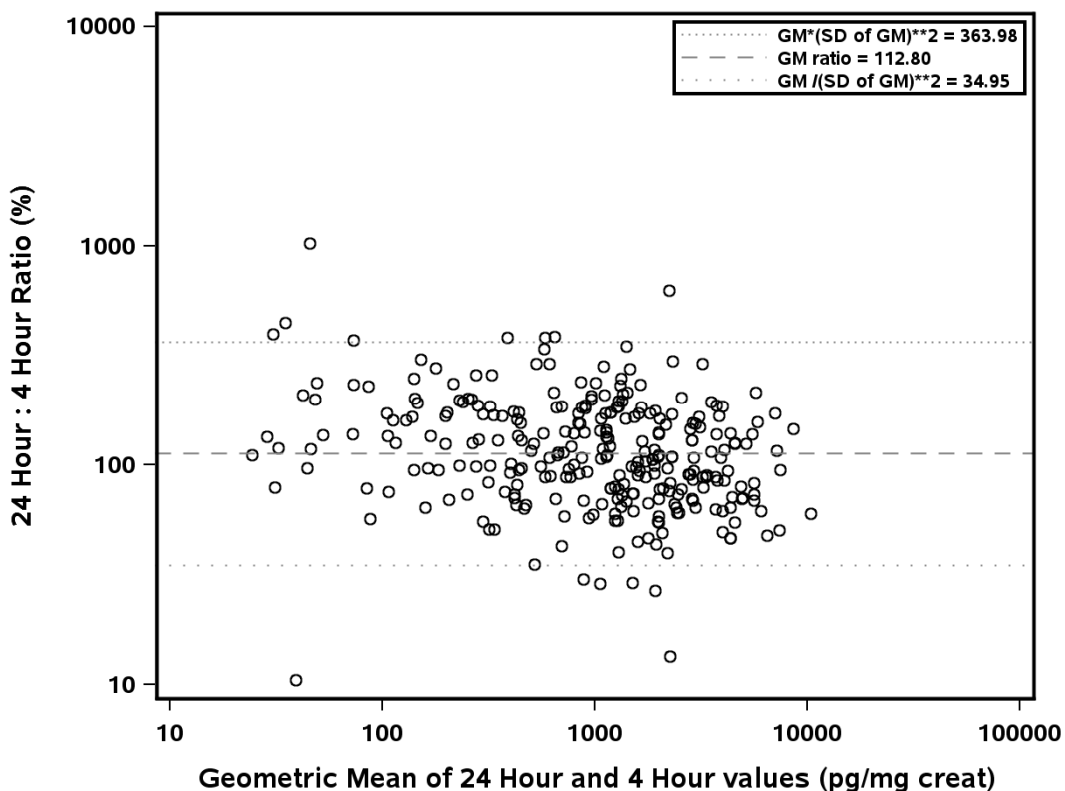
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_spma.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.14.2 Bland-Altman Plot for Concordance of Urinary S-PMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

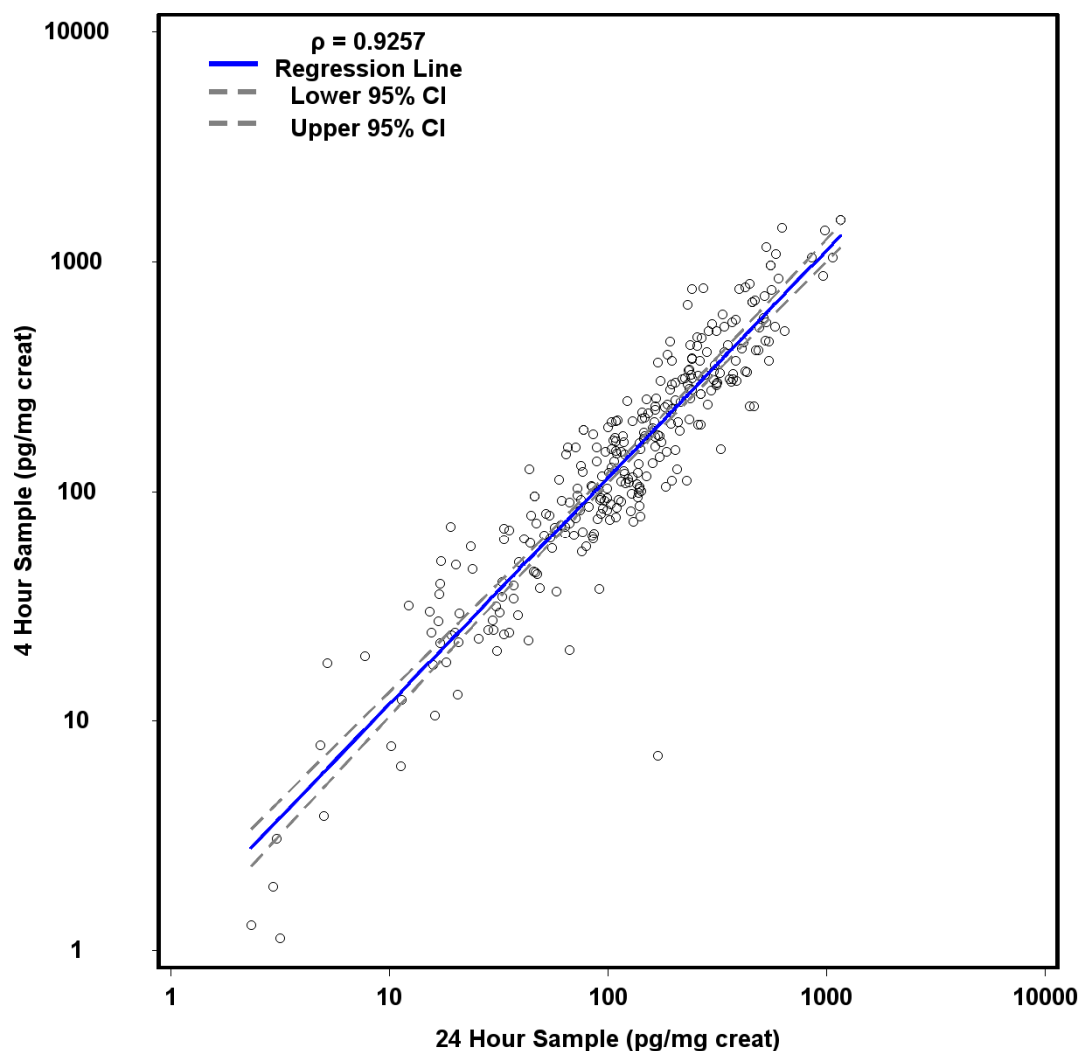
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_spma.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.15.1 Scatter Plot of Urinary Total NNAL Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

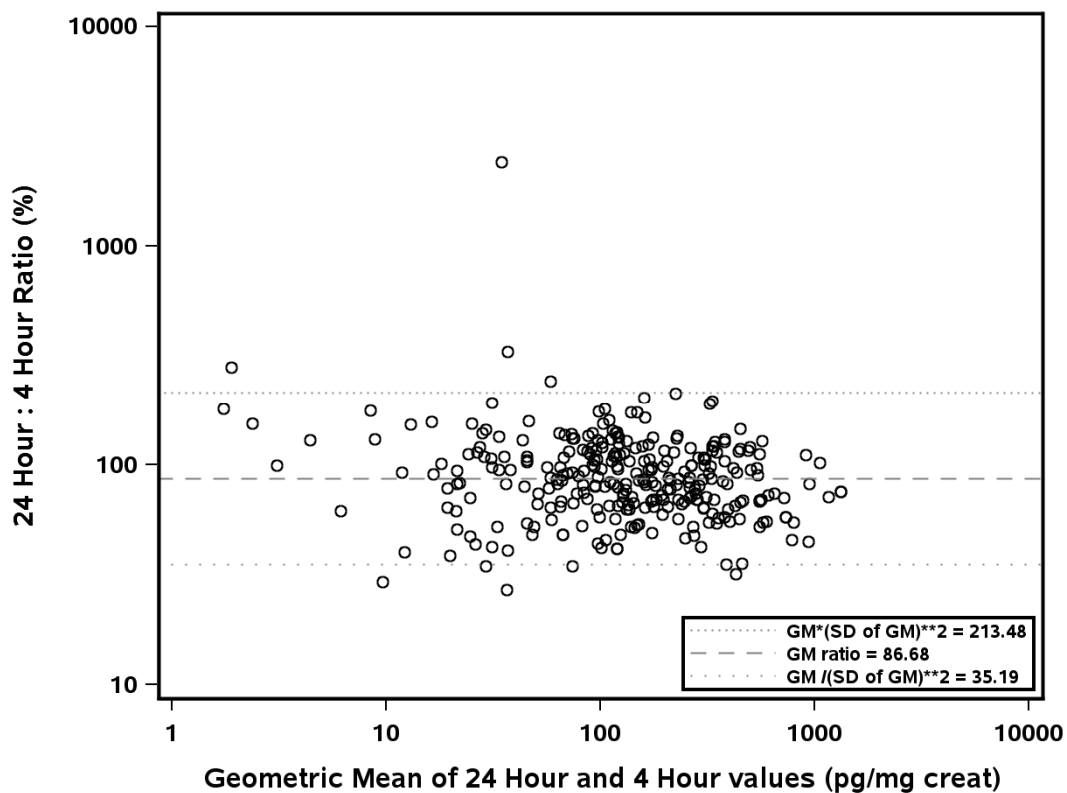
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_nnal.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.15.2 Bland-Altman Plot for Concordance of Urinary Total NNAL Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Data from all 3 randomized groups are presented.

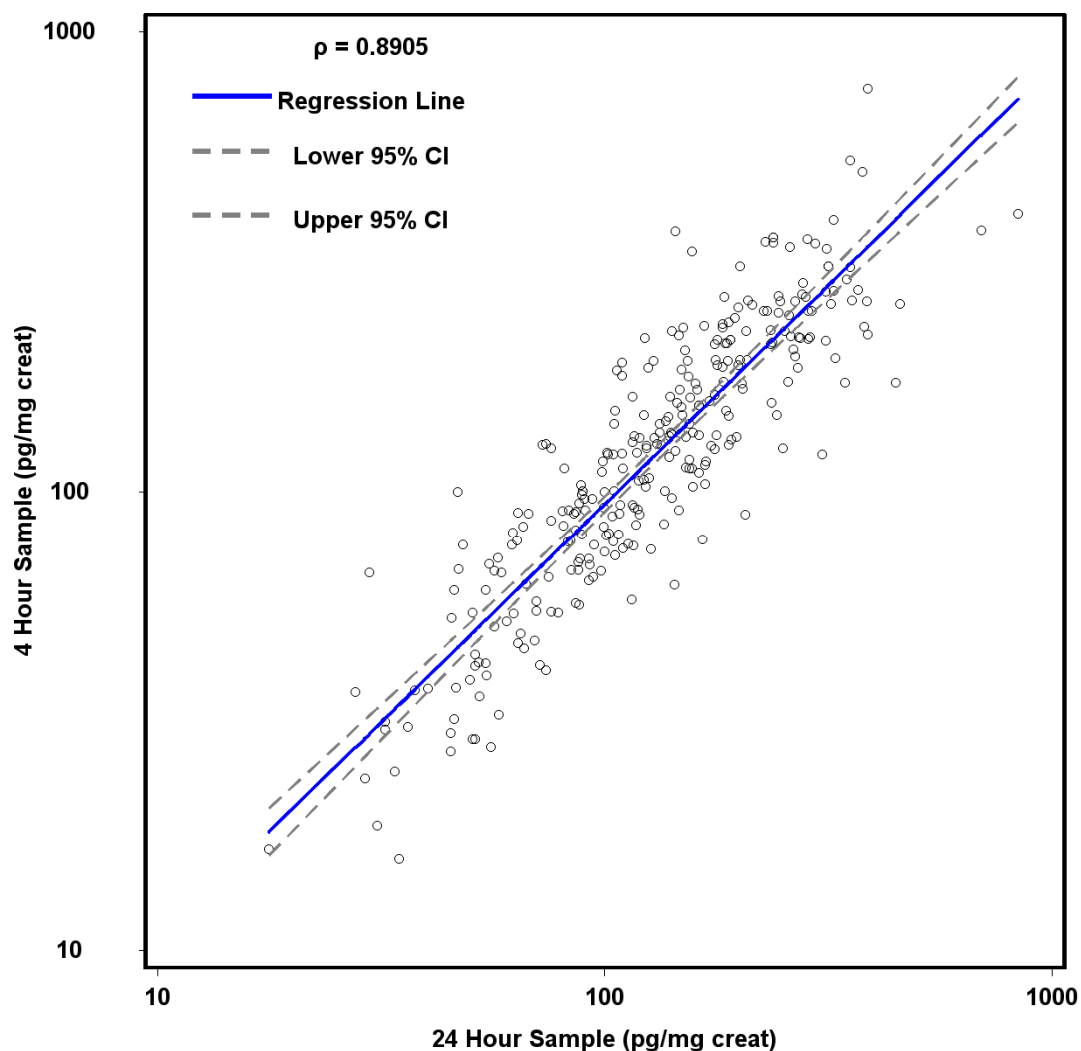
Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_nnal.sas 01DEC15 Status: Final (Page 1 of 1)





**Figure 15.1.2.16.1 Scatter Plot of Urinary Total 1-OHP Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

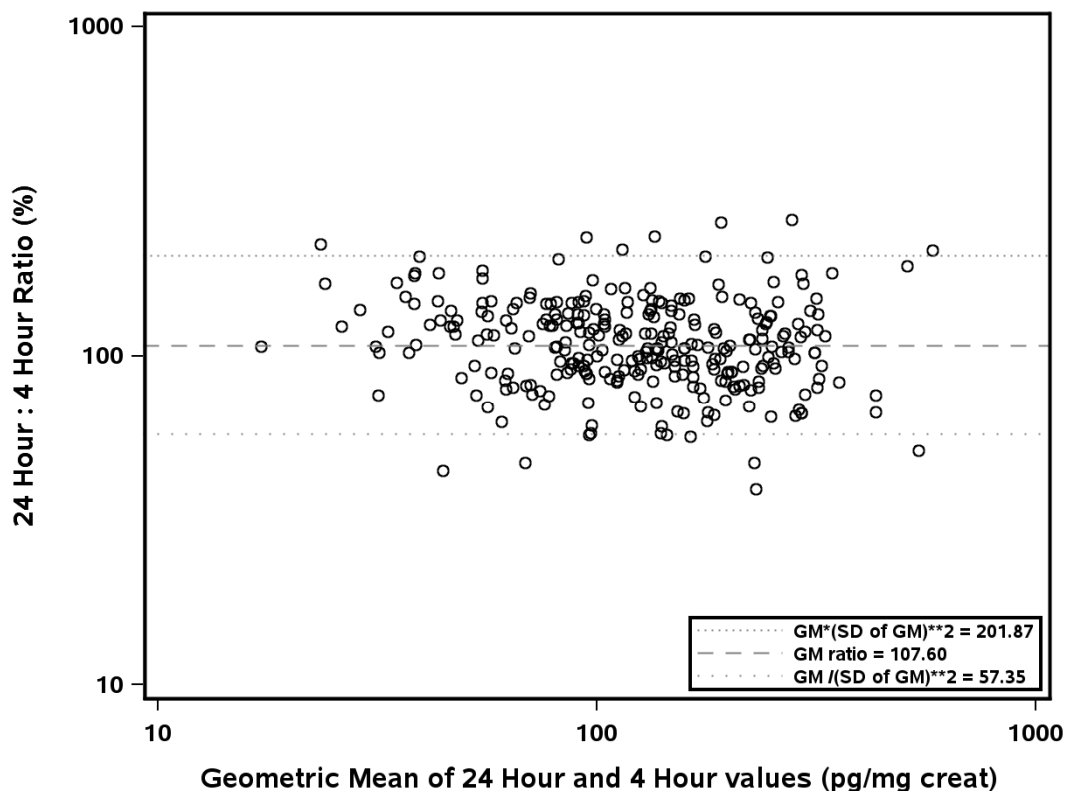
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_1ohp.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.16.2 Bland-Altman Plot for Concordance of Urinary Total 1-OHP Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

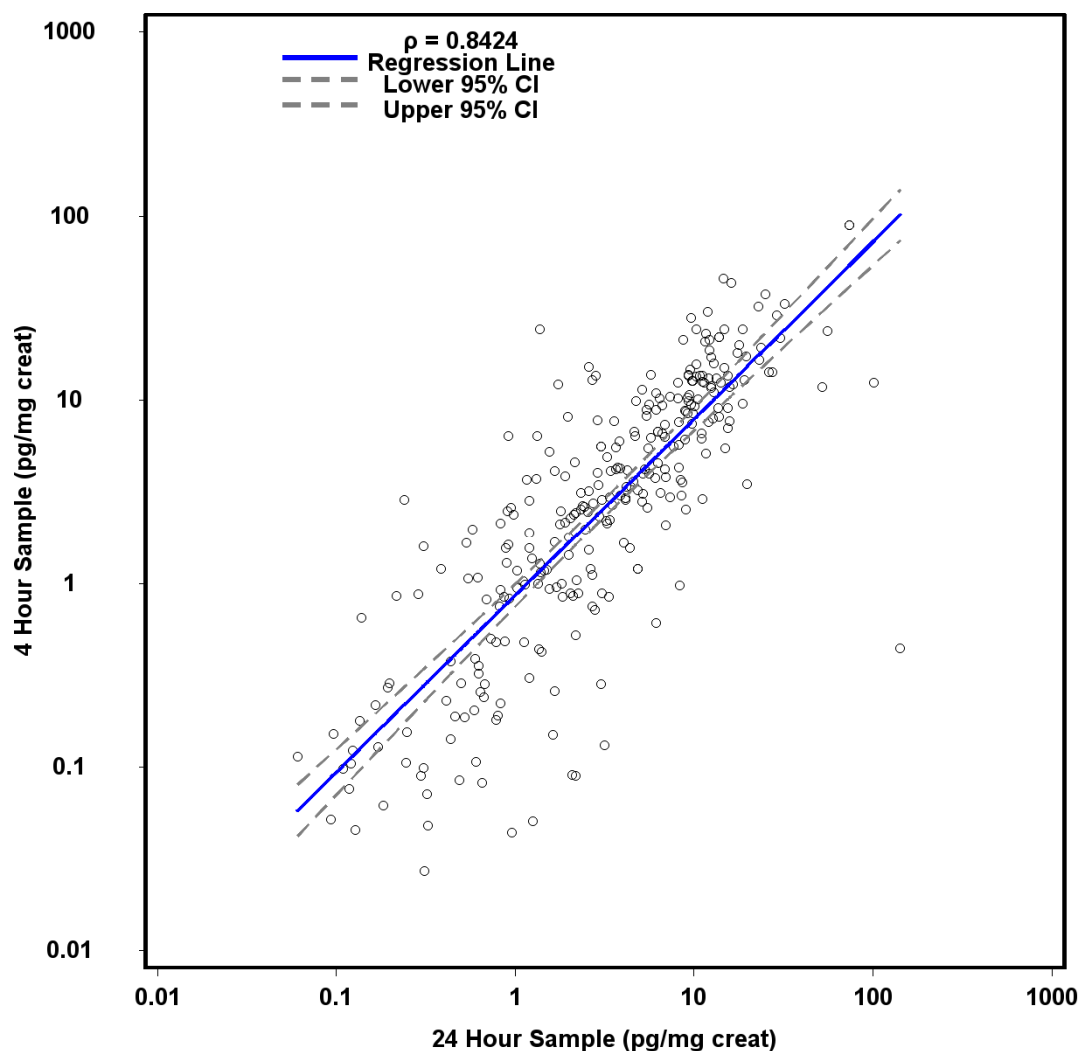
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_1ohp.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.17.1 Scatter Plot of Urinary Total NNN Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

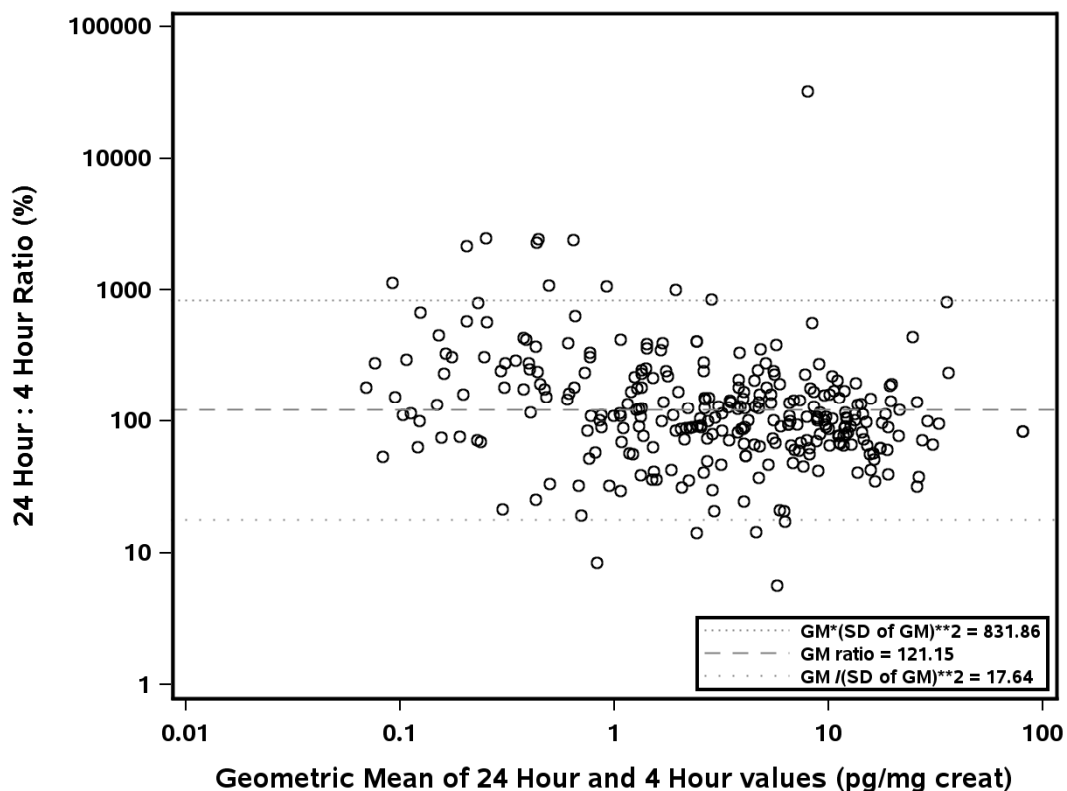
Note: Data from all 3 randomized groups are presented.  $p$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_nnn.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.17.2 Bland-Altman Plot for Concordance of Urinary Total NNN Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

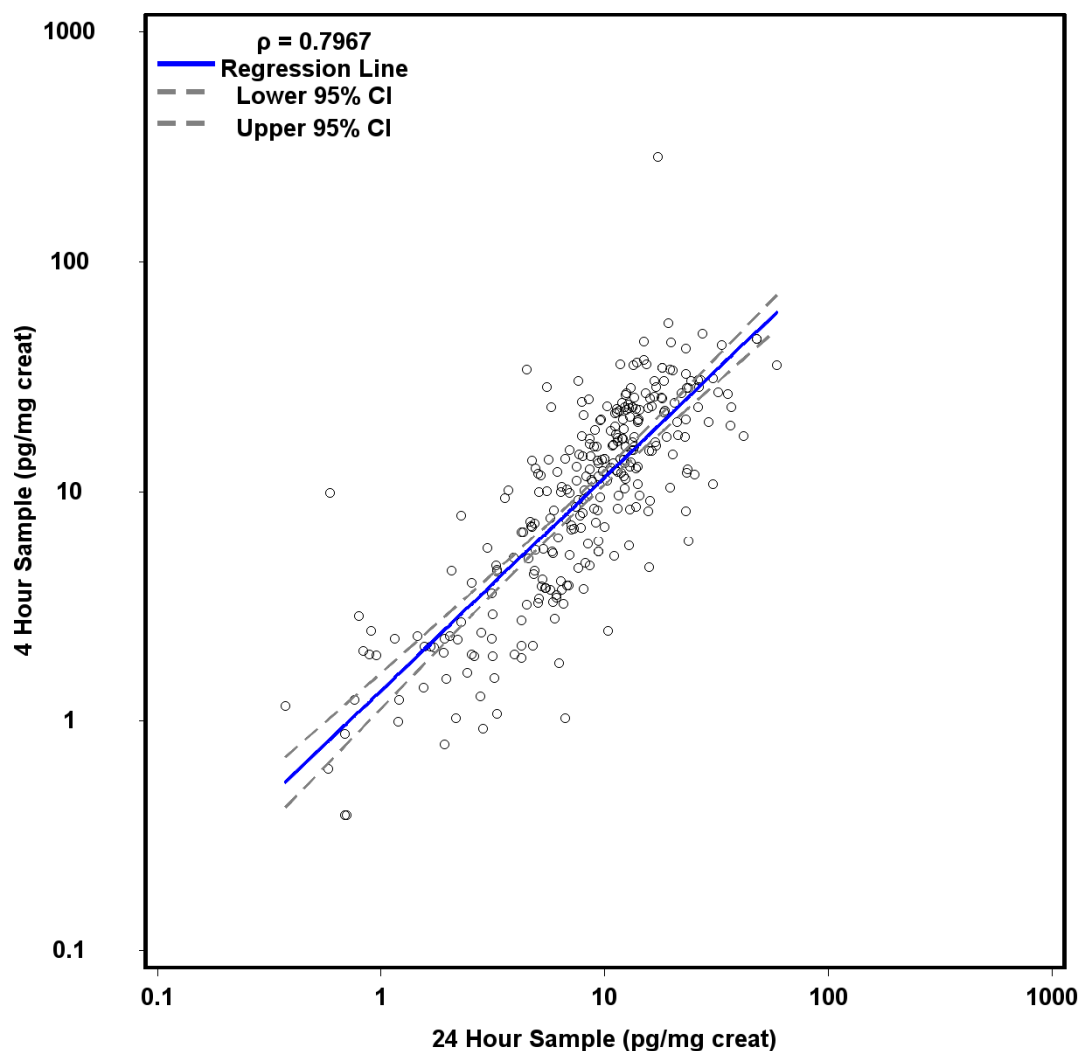
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_nnn.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.18.1 Scatter Plot of Urinary 4-ABP Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

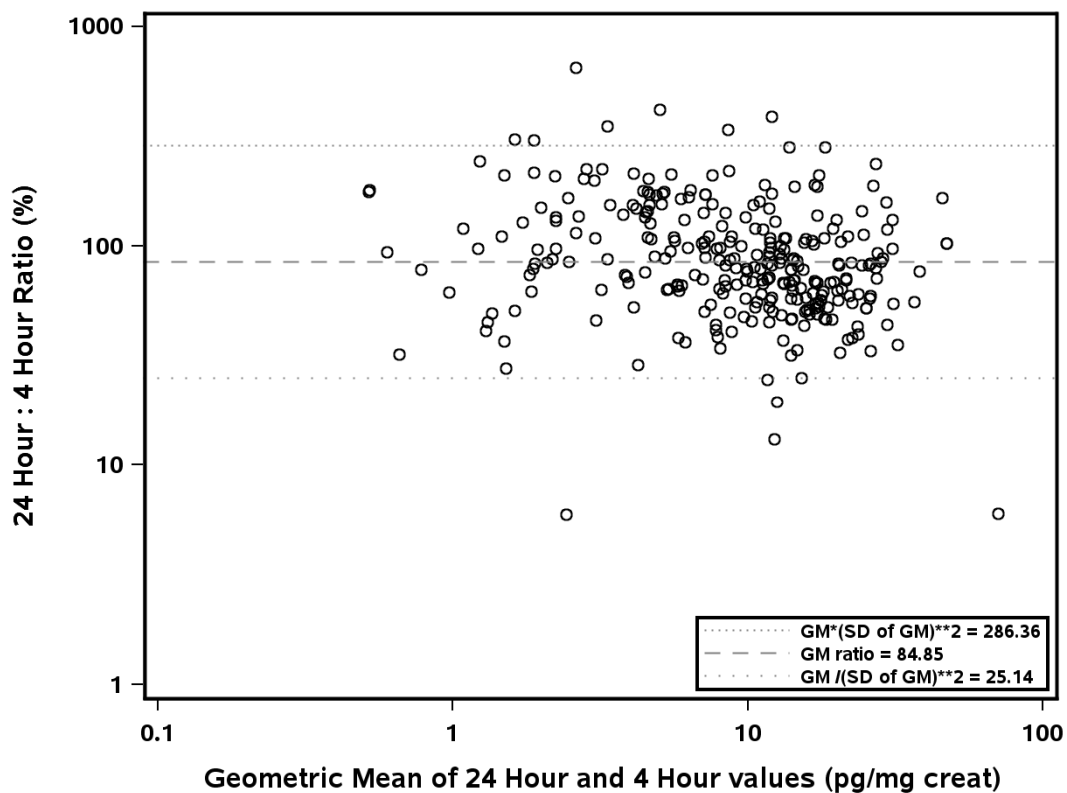
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_4abp.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.18.2 Bland-Altman Plot for Concordance of Urinary 4-ABP Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

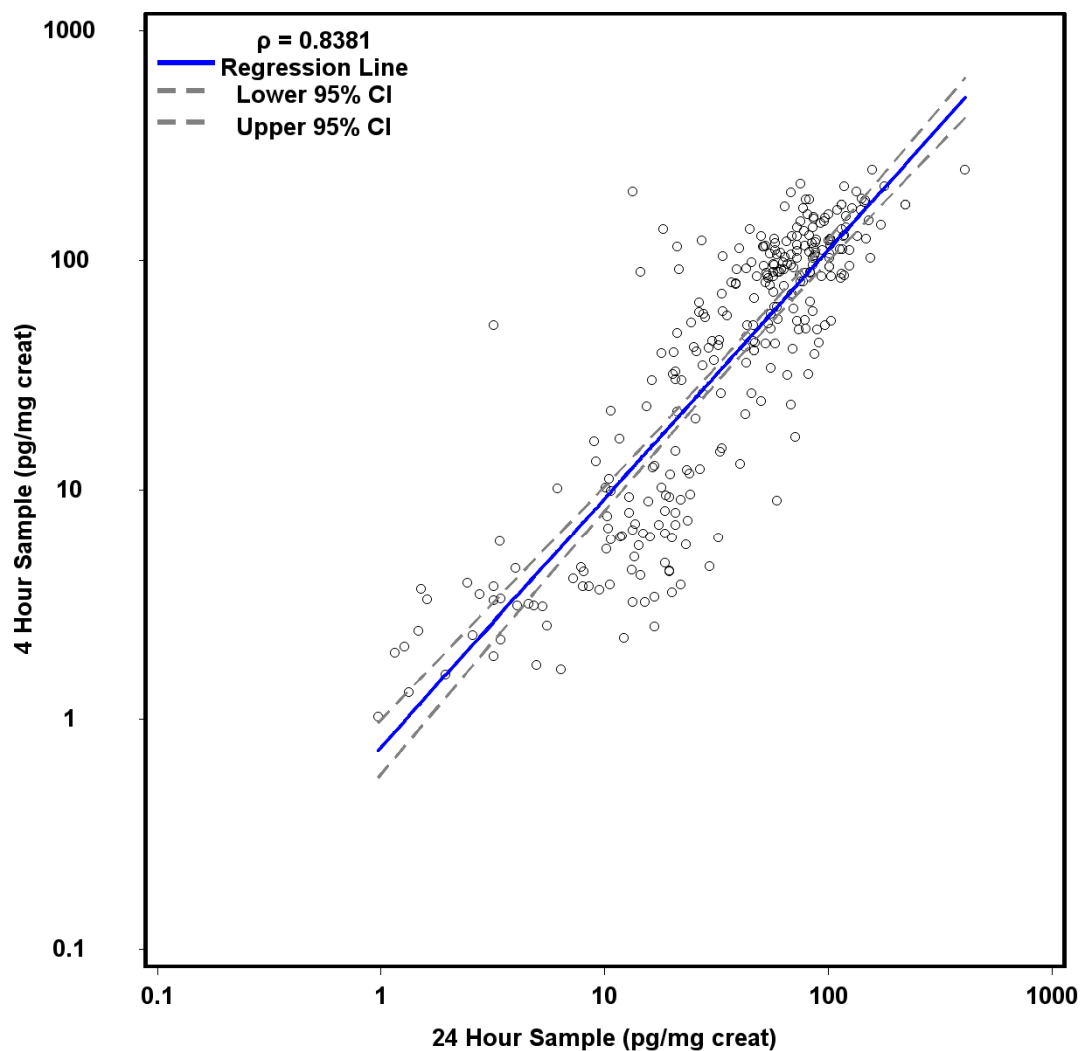
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_4abp.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.19.1 Scatter Plot of Urinary 1-NA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

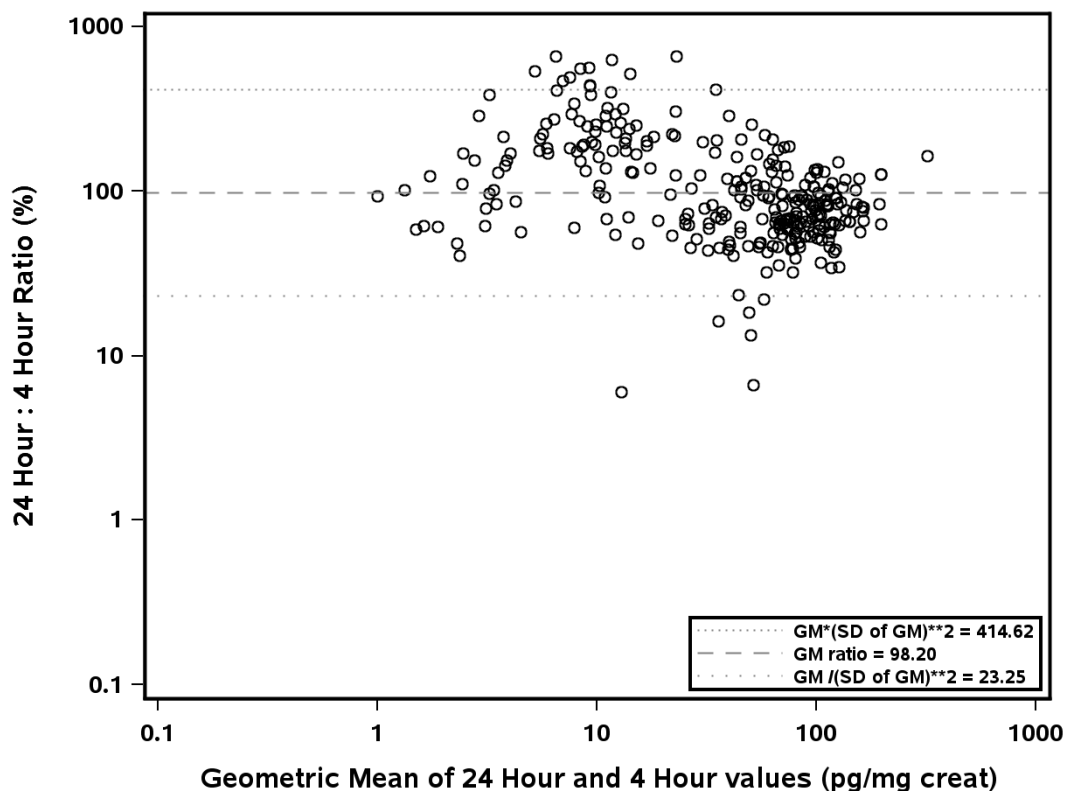
Note: Data from all 3 randomized groups are presented.  $p$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_1na.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.19.2 Bland-Altman Plot for Concordance of Urinary 1-NA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Data from all 3 randomized groups are presented.

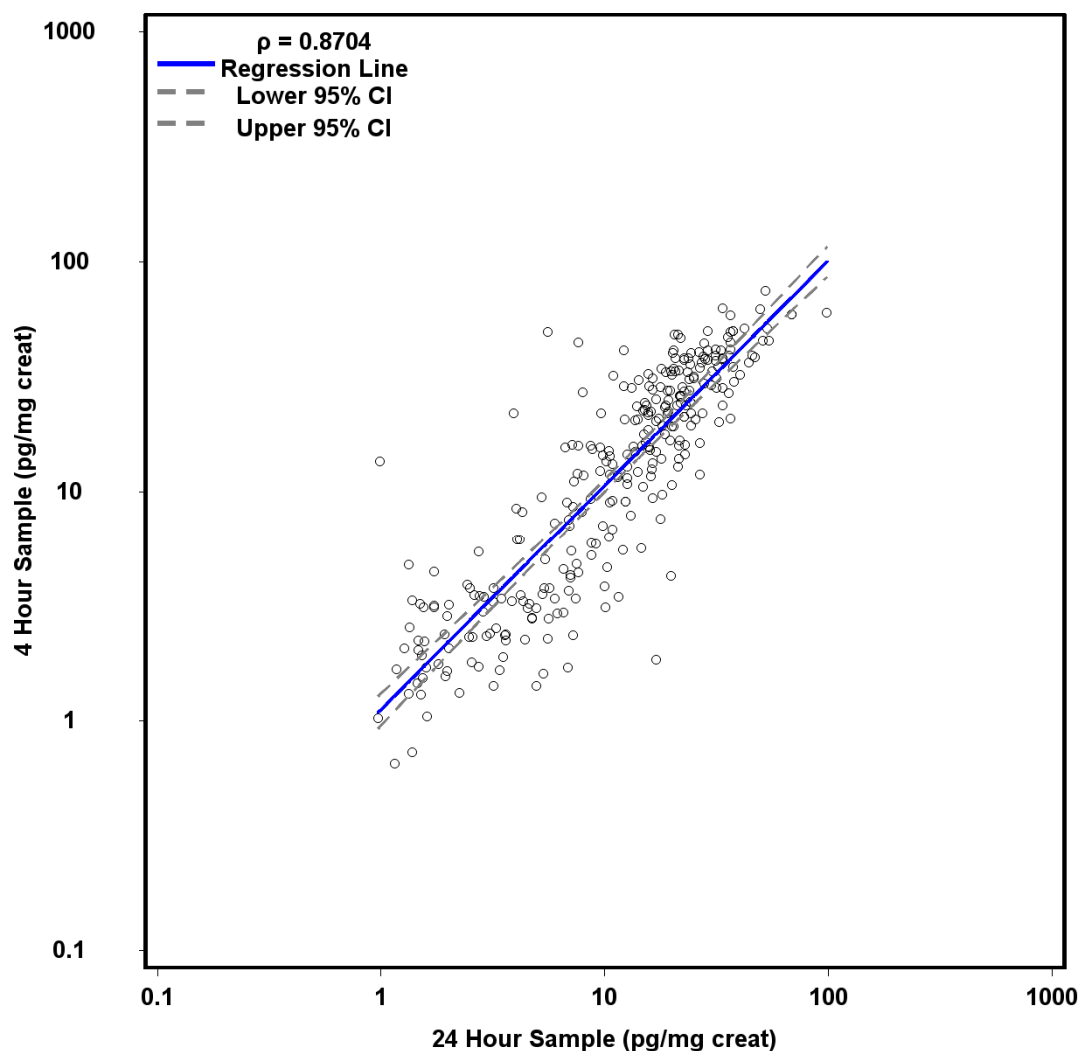
Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_1na.sas 01DEC15 Status: Final (Page 1 of 1)





**Figure 15.1.2.20.1 Scatter Plot of Urinary 2-NA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

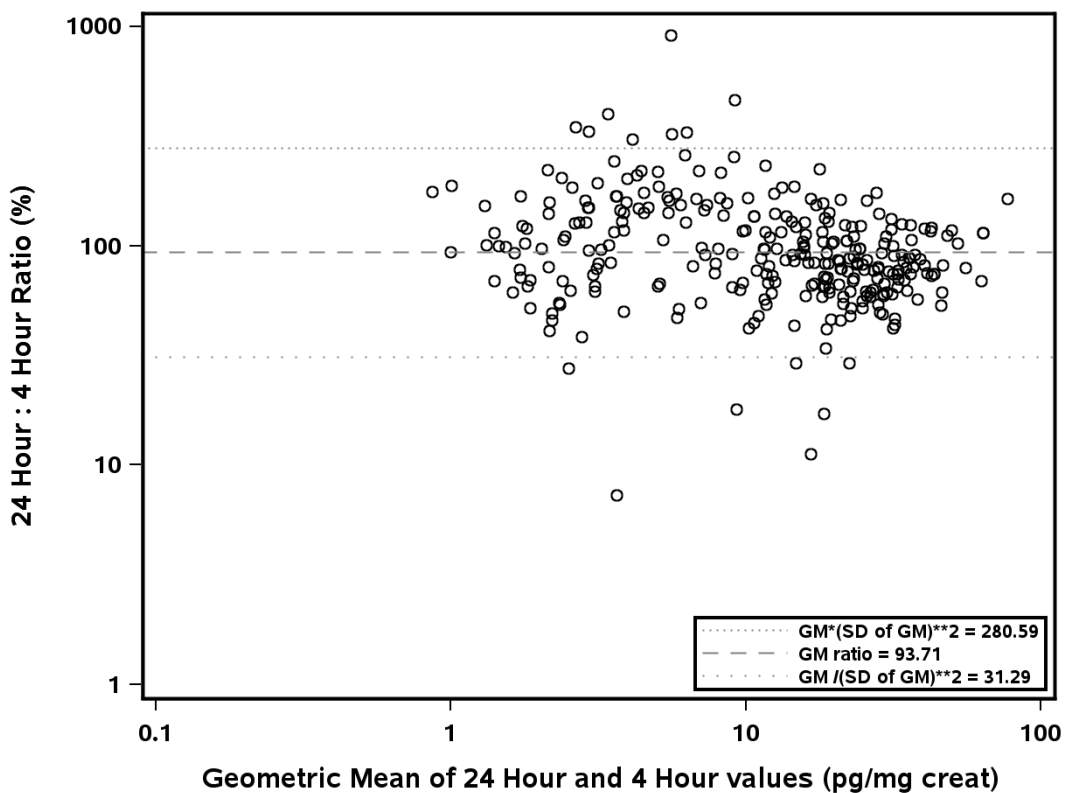
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_2na.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.20.2 Bland-Altman Plot for Concordance of Urinary 2-NA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

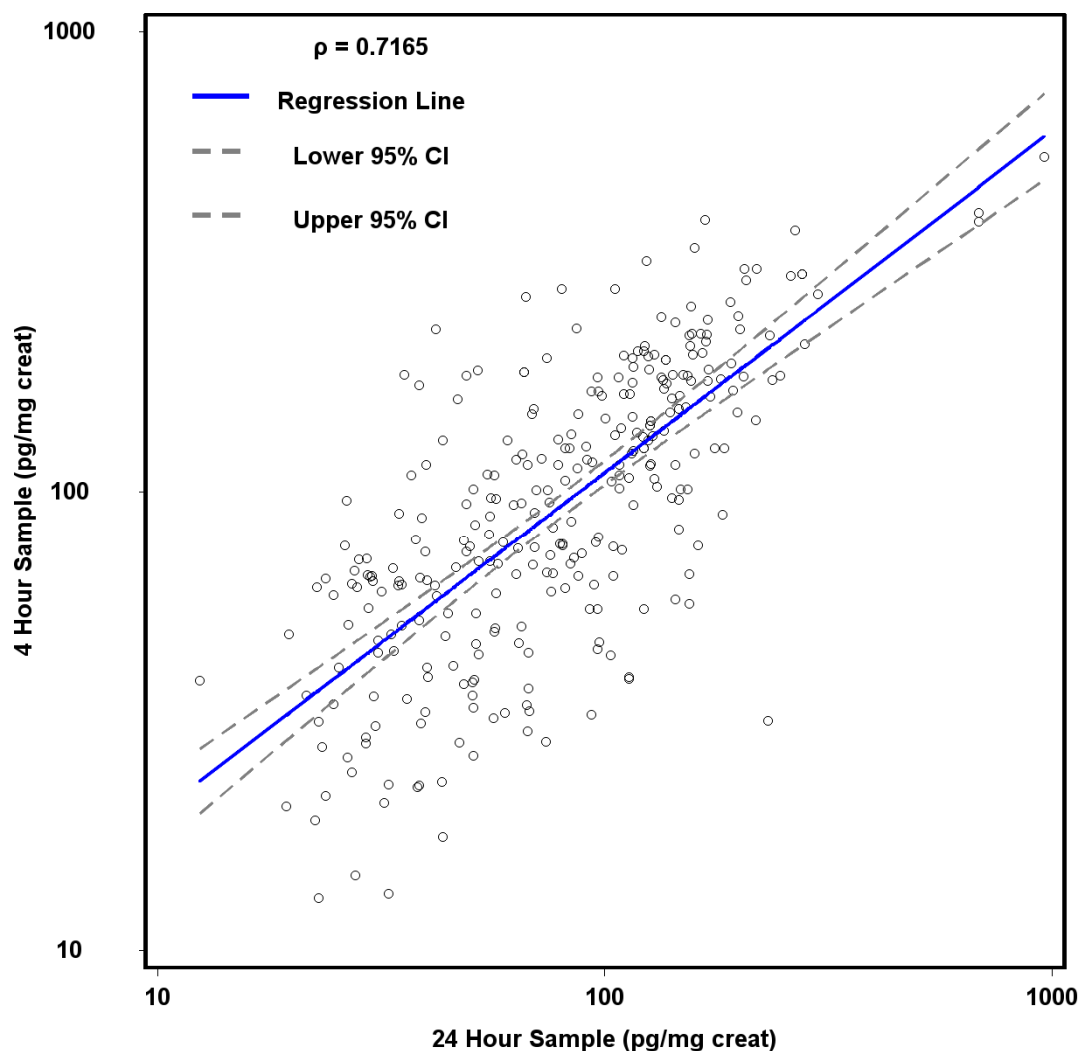
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_2na.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.21.1 Scatter Plot of Urinary O-TOL Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

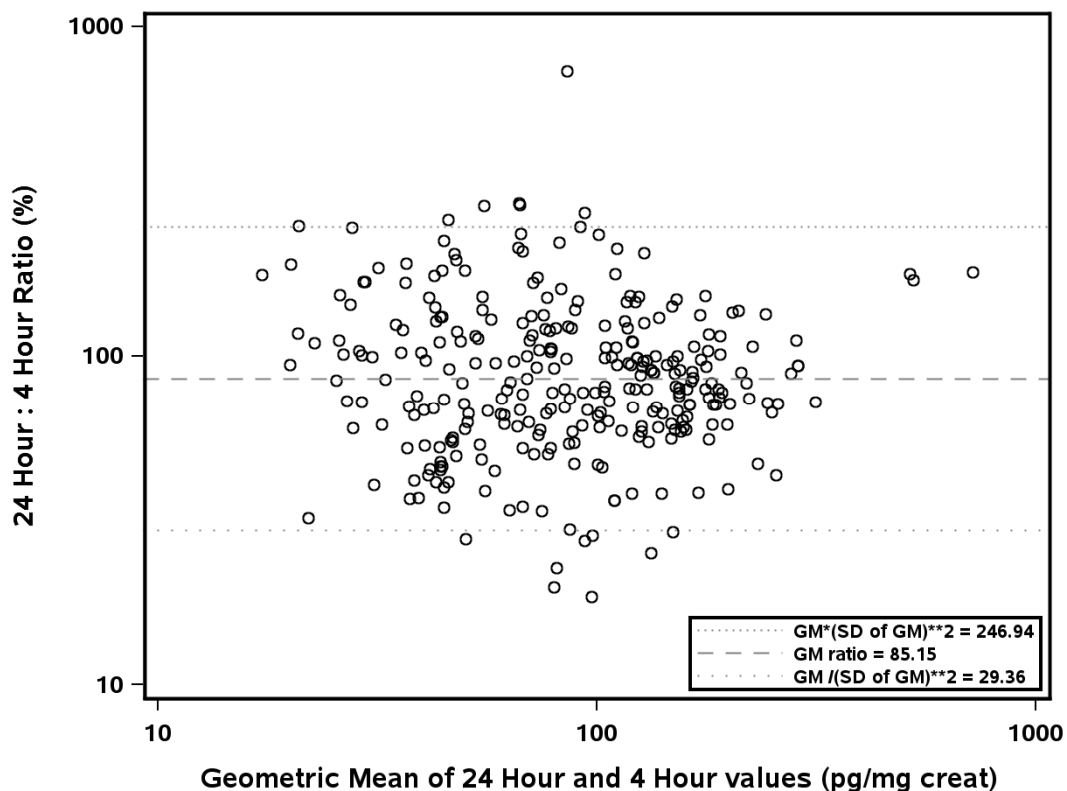
Note: Data from all 3 randomized groups are presented.  $p$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_otoi.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.21.2 Bland-Altman Plot for Concordance of Urinary O-TOL Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

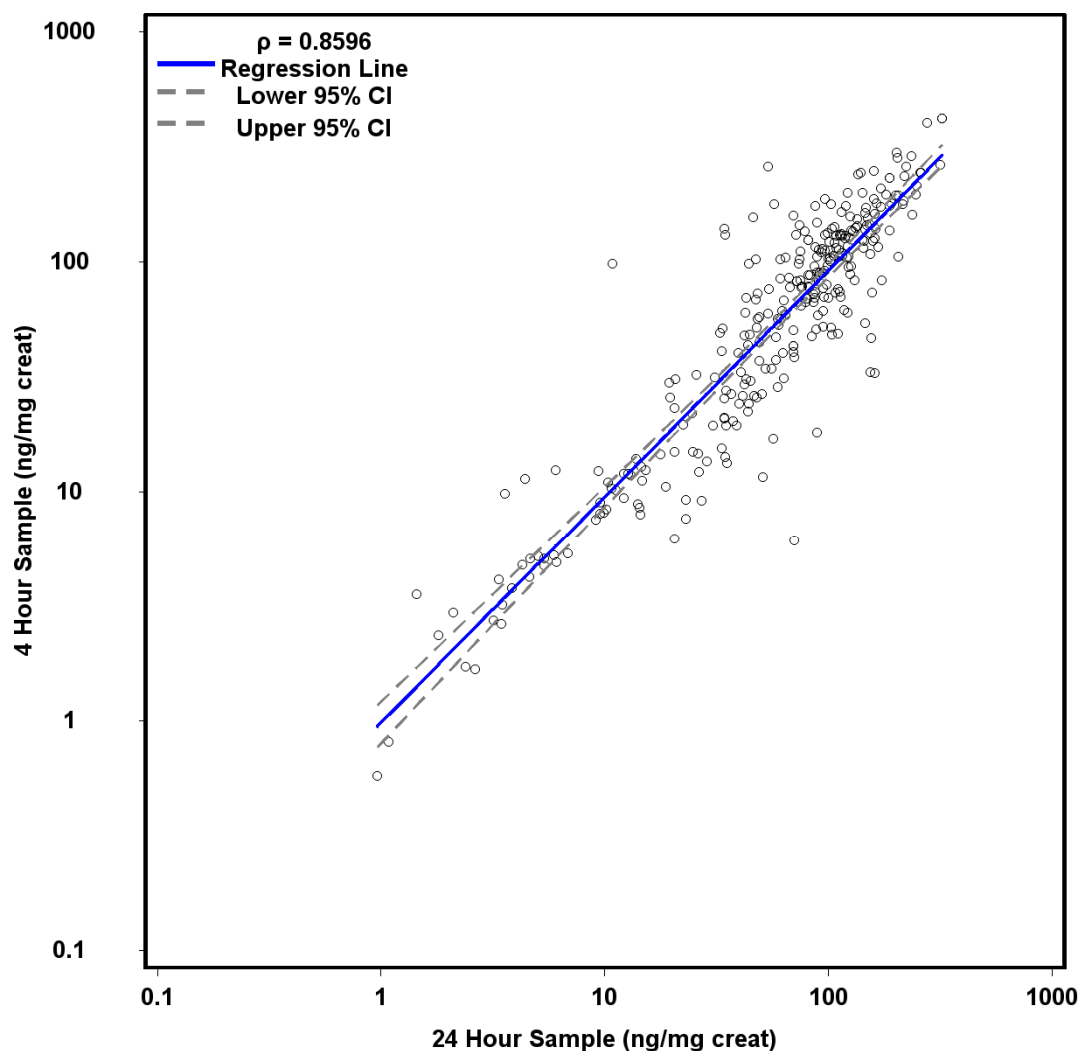
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_otol.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.22.1 Scatter Plot of Urinary CEMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

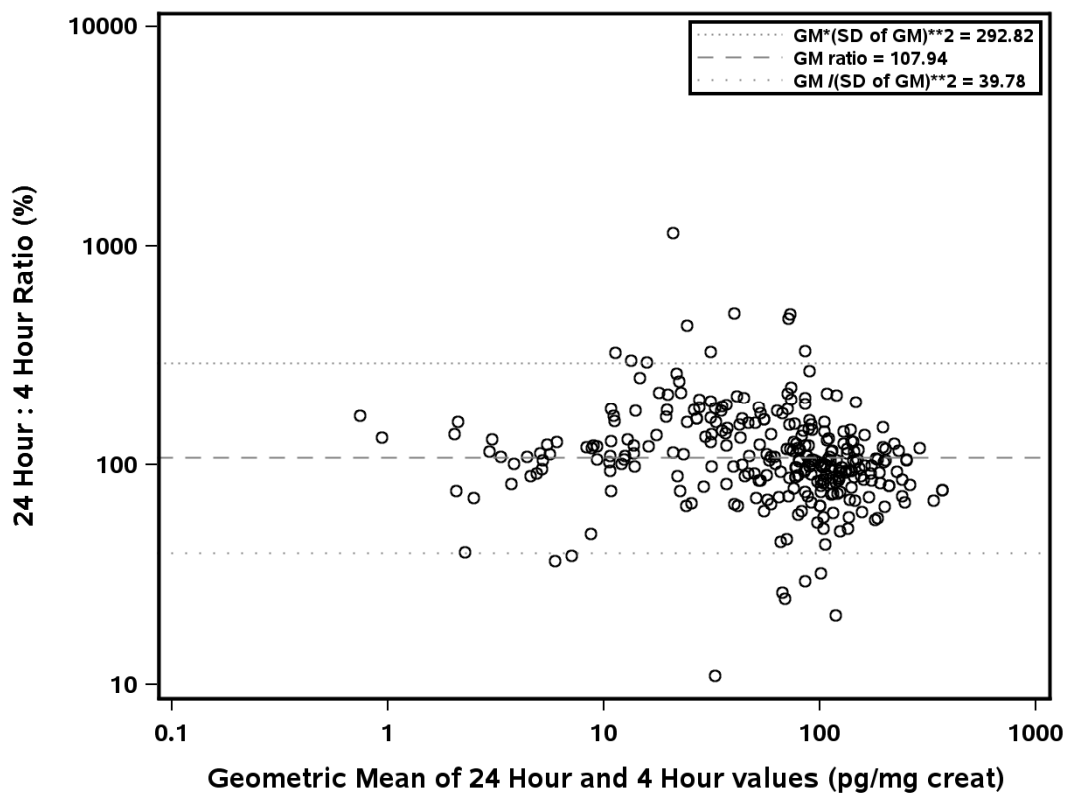
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_cema.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.22.2 Bland-Altman Plot for Concordance of Urinary CEMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

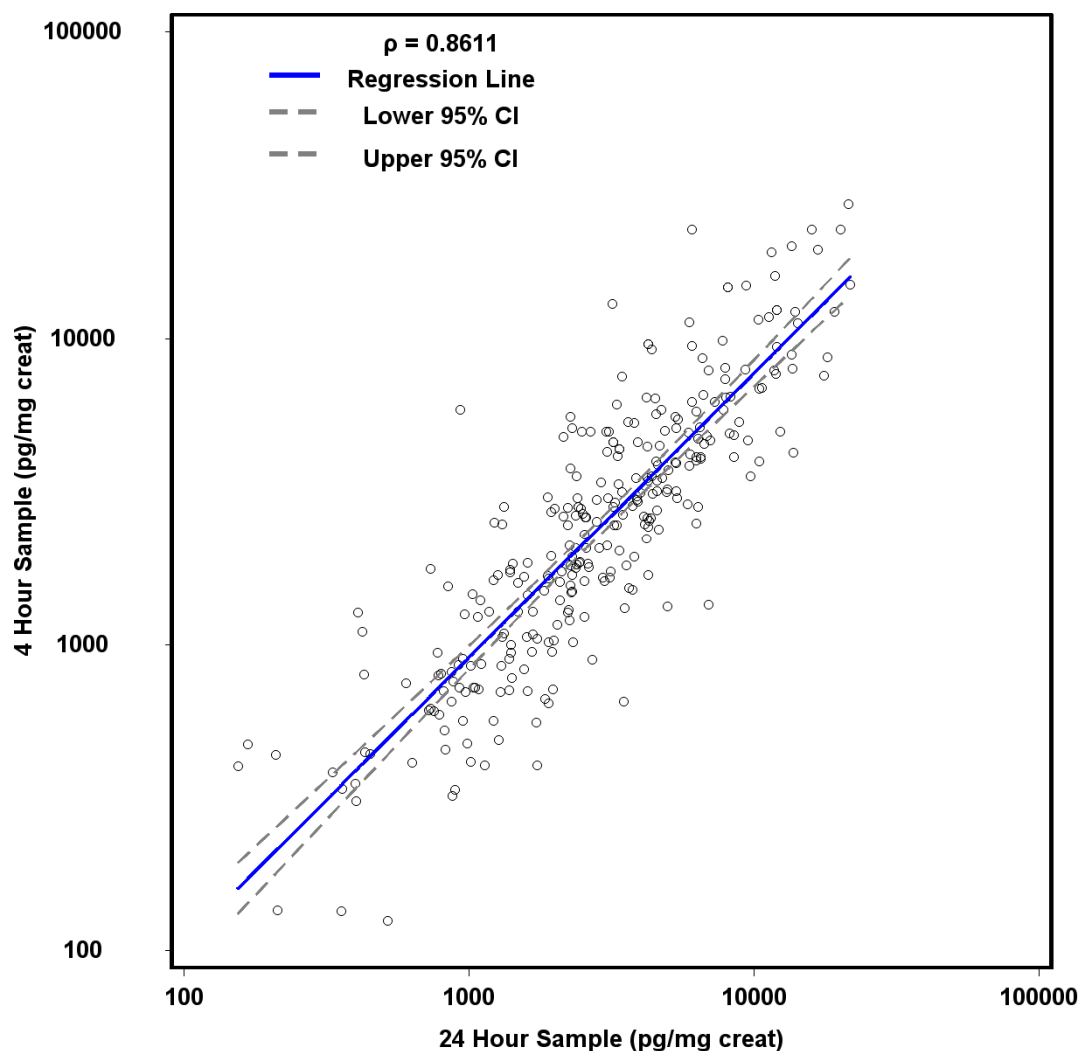
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_cema.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.23.1 Scatter Plot of Urinary HEMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

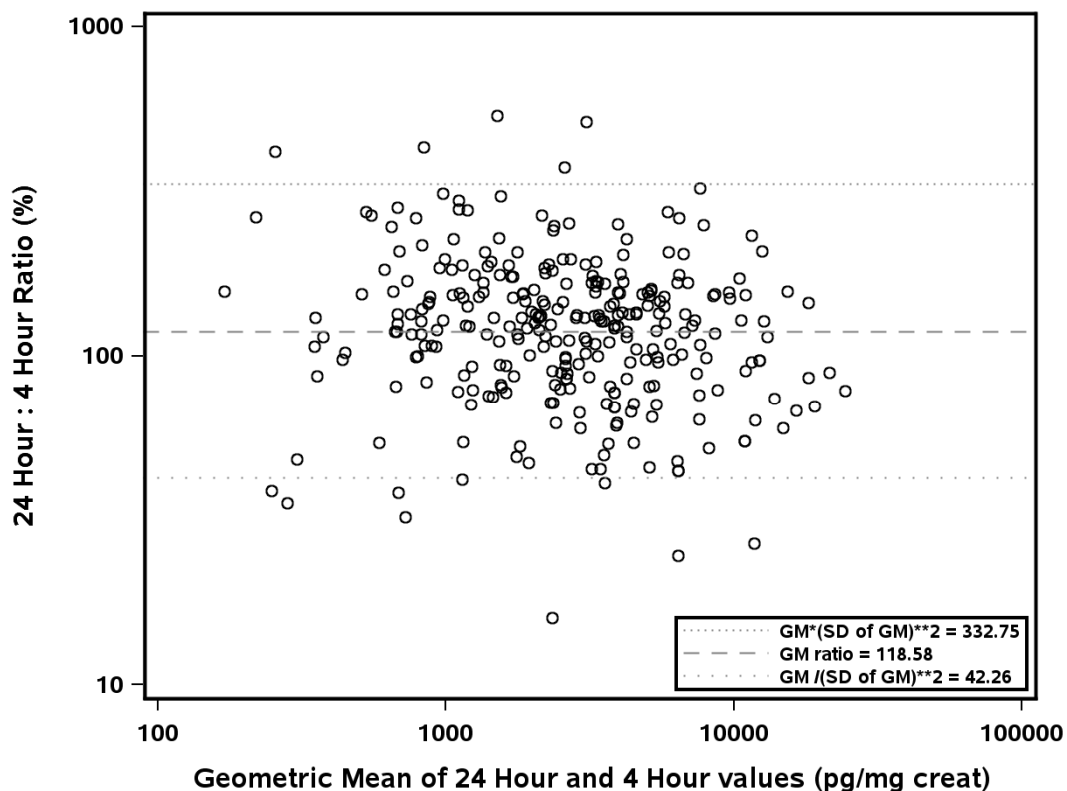
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_hema.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.23.2 Bland-Altman Plot for Concordance of Urinary HEMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Data from all 3 randomized groups are presented.

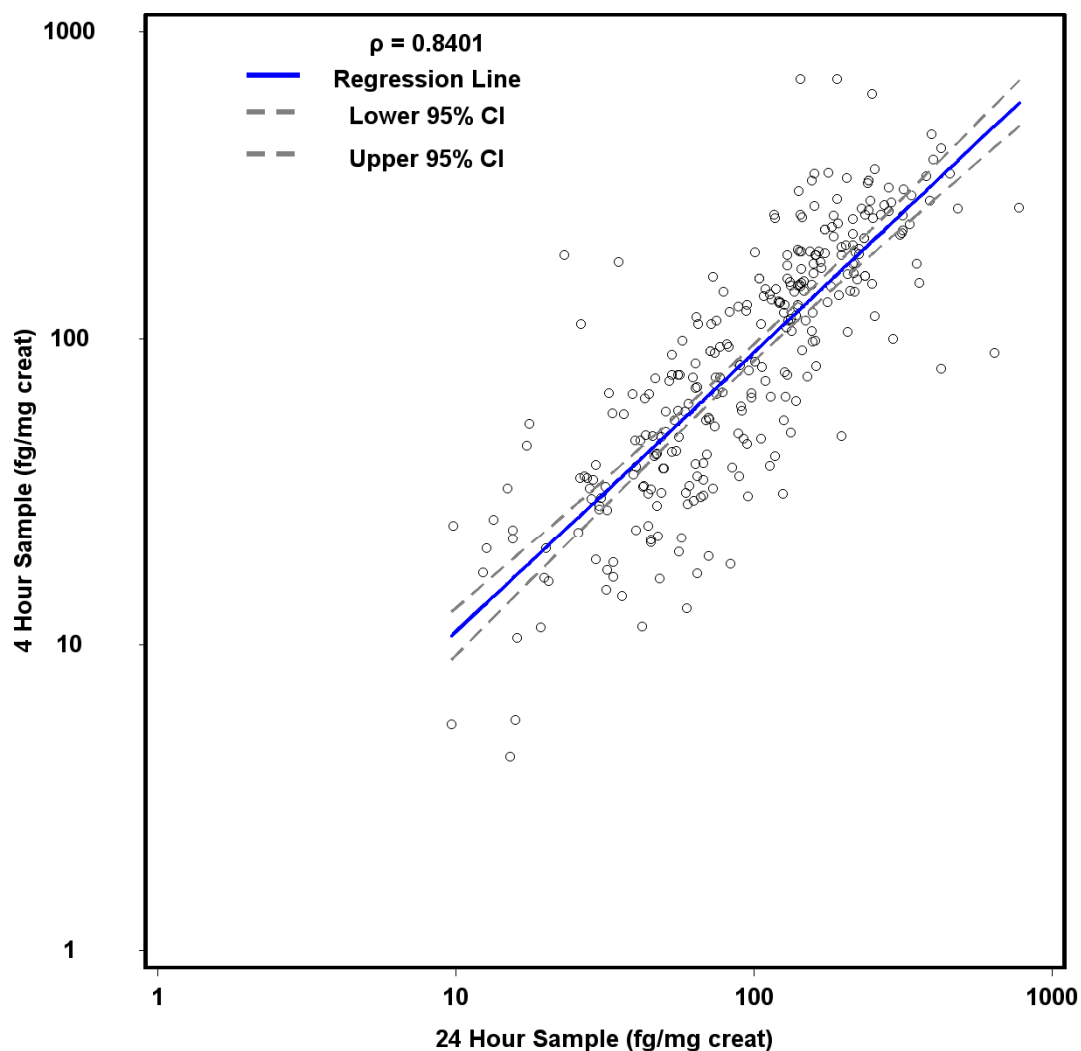
Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_hema.sas 01DEC15 Status: Final (Page 1 of 1)





**Figure 15.1.2.24.1 Scatter Plot of Urinary B[a]P Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

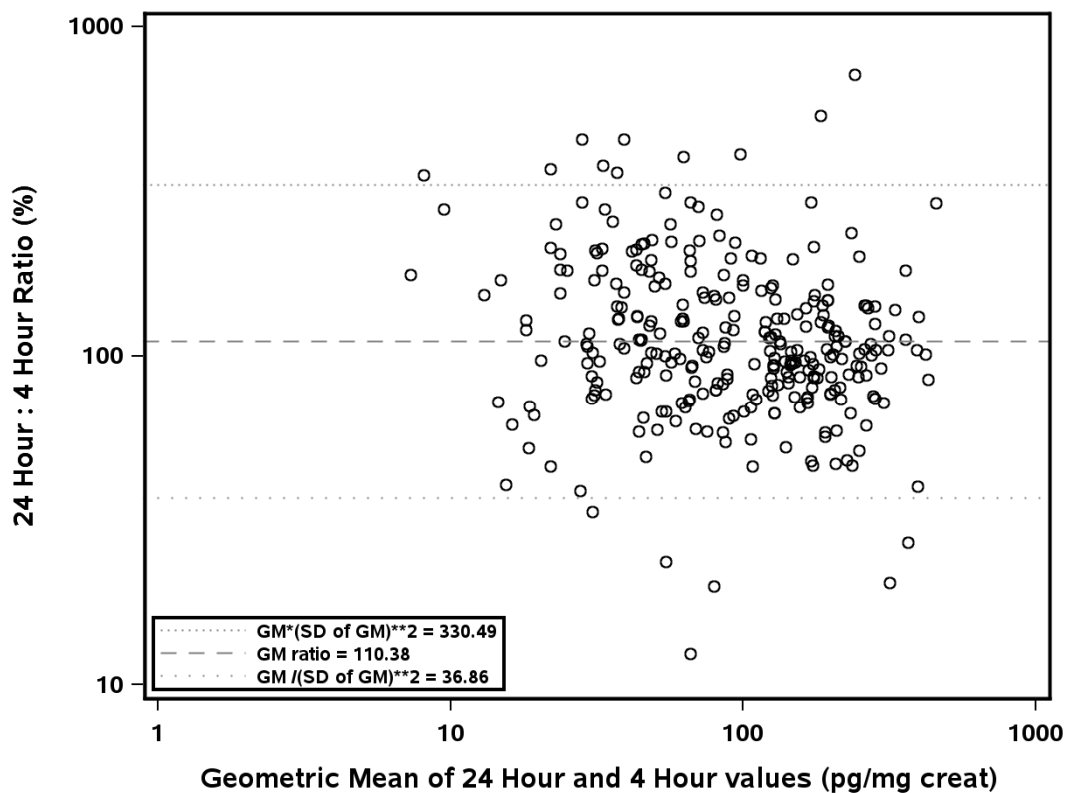
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_bap.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.24.2 Bland-Altman Plot for Concordance of Urinary B[a]P Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

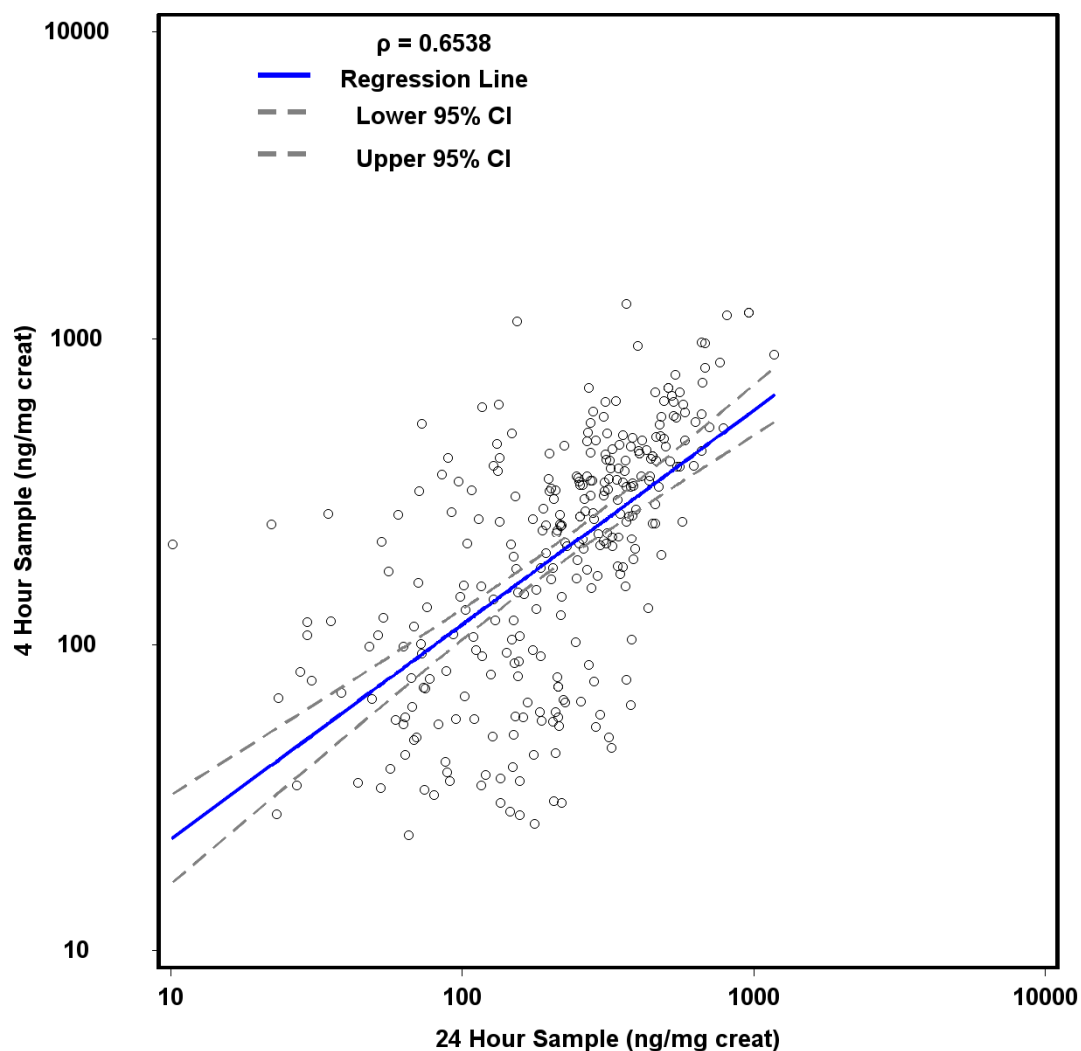
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_bap.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.25.1 Scatter Plot of Urinary HMPMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

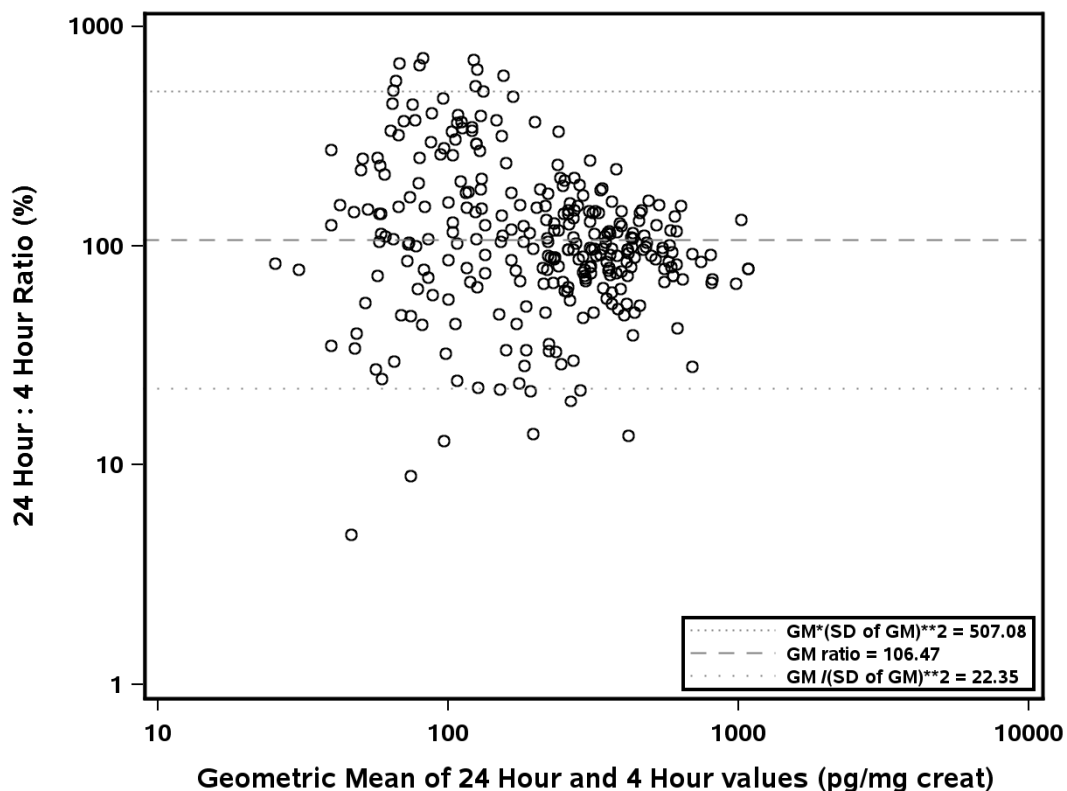
Note: Data from all 3 randomized groups are presented.  $p$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_hmpma.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.25.2 Bland-Altman Plot for Concordance of Urinary HMPMA Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

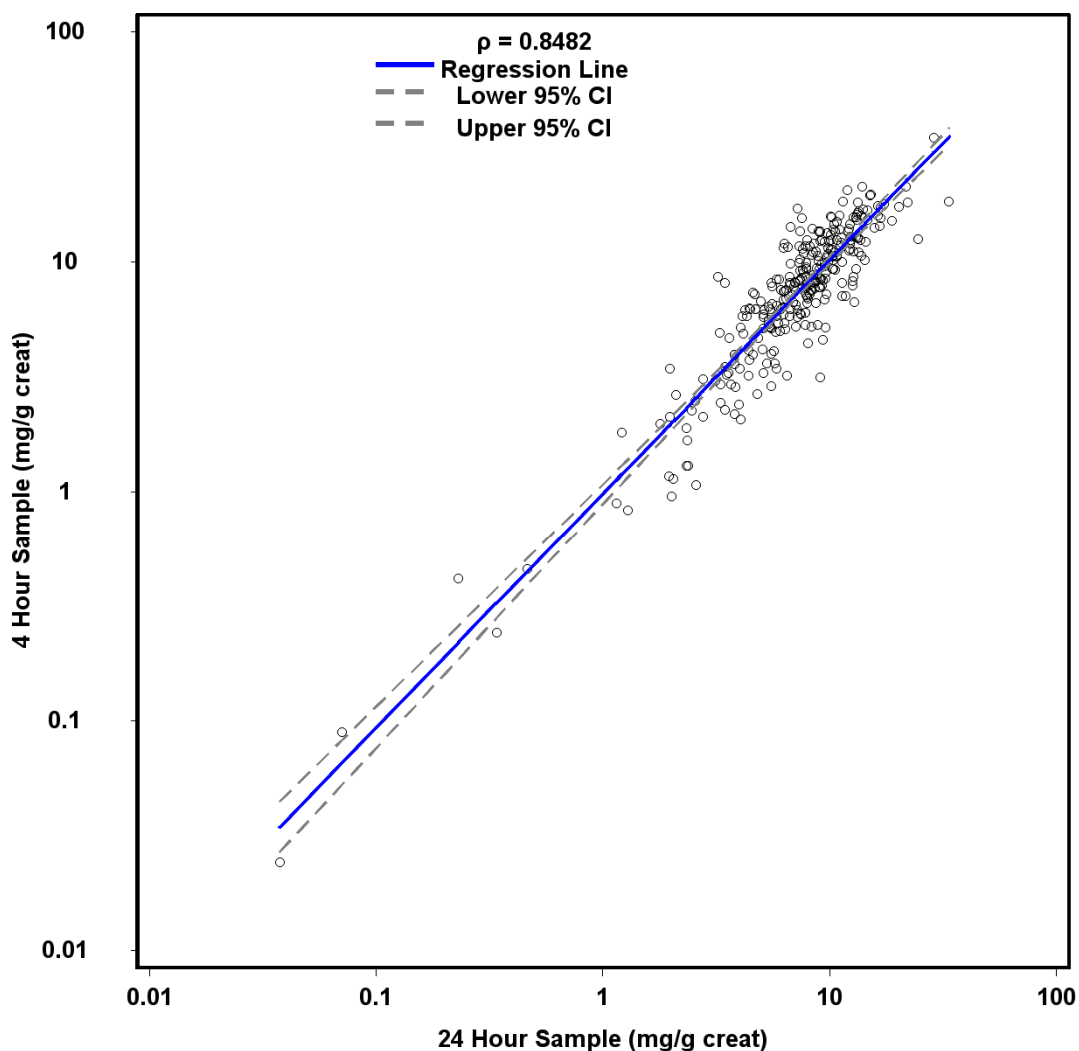
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_hmpma.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.26.1 Scatter Plot of Urinary NEQ Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

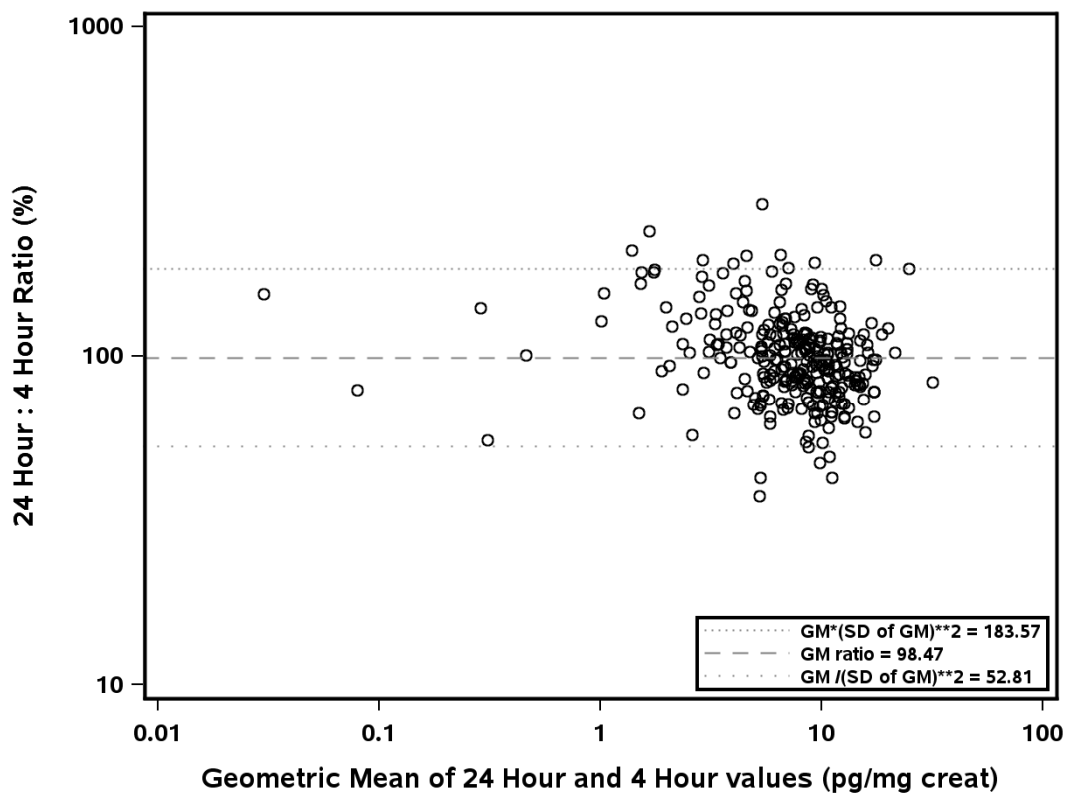
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_neq.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.26.2 Bland-Altman Plot for Concordance of Urinary NEQ Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

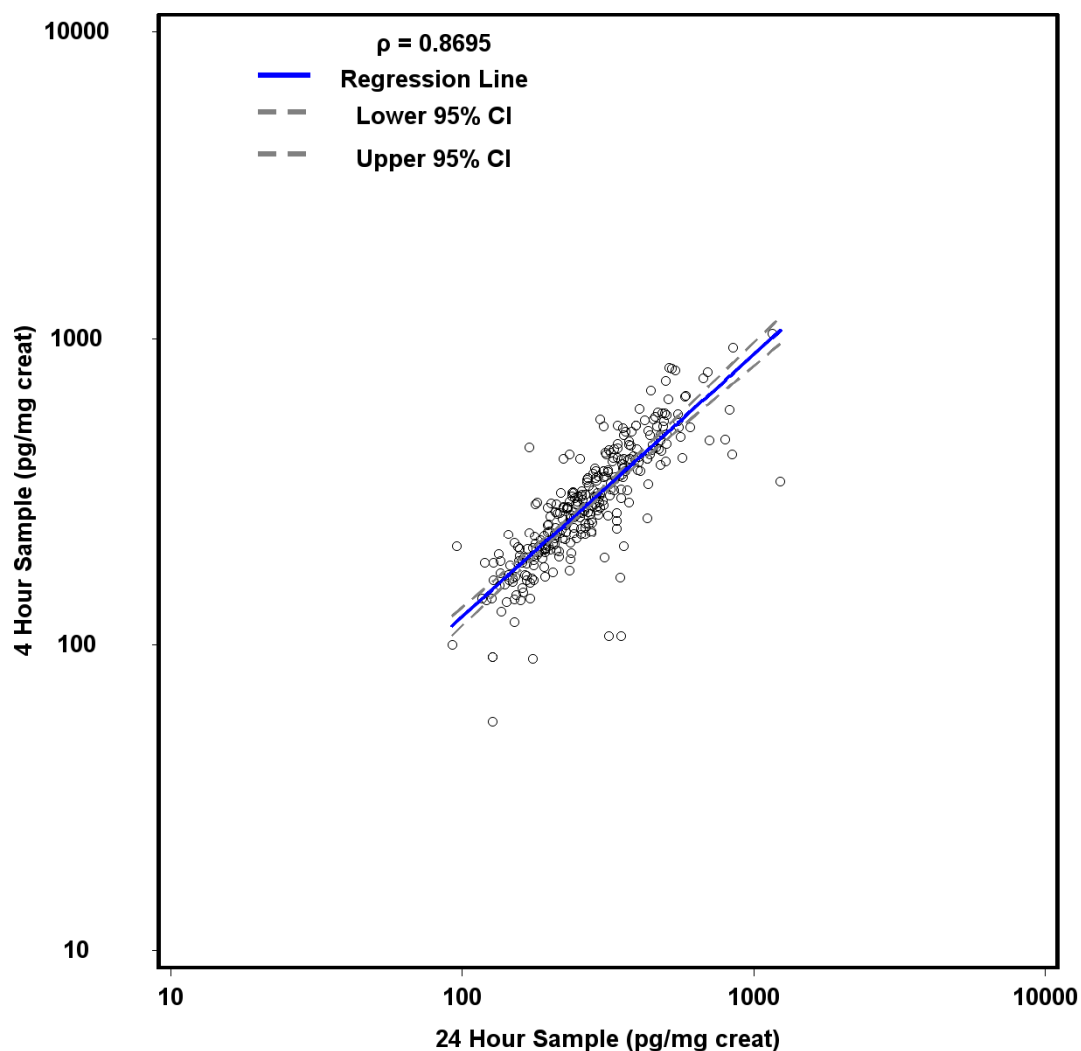
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_neq.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.27.1 Scatter Plot of Urinary 8-epi-PGF2a Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

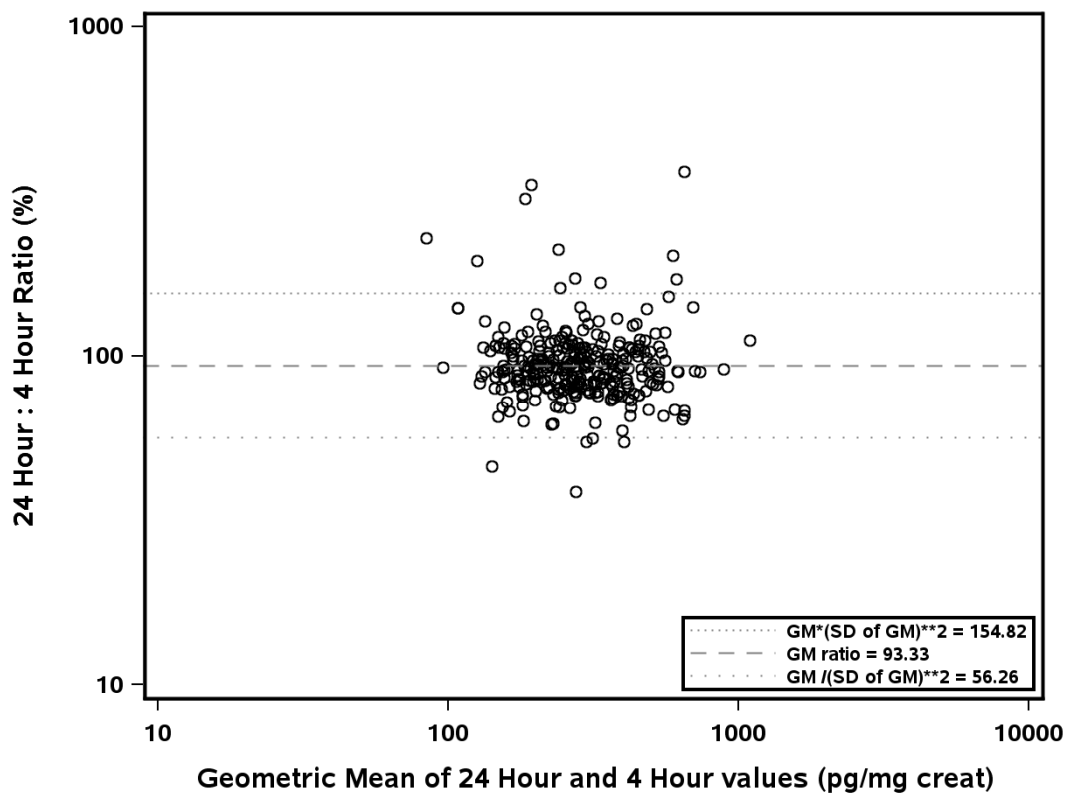
Note: Data from all 3 randomized groups are presented.  $p$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_8epi.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.27.2 Bland-Altman Plot for Concordance of Urinary 8-epi-PGF2a Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Note: Data from all 3 randomized groups are presented.

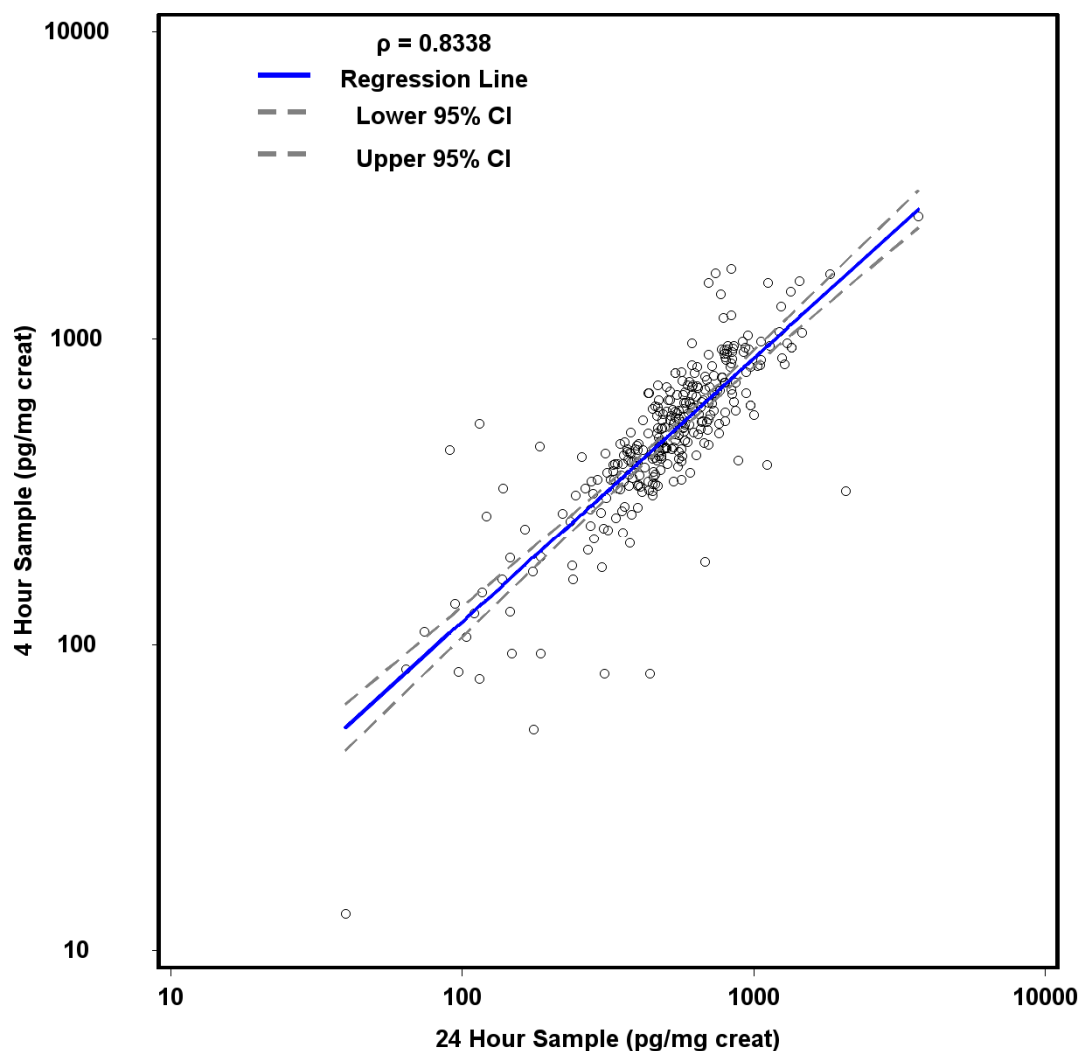
Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_8epi.sas 01DEC15 Status: Final (Page 1 of 1)





**Figure 15.1.2.28.1 Scatter Plot of Urinary 11-DTX-B2 Concentration Adjusted for Creatinine from 24 Hour Urine Collection versus 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

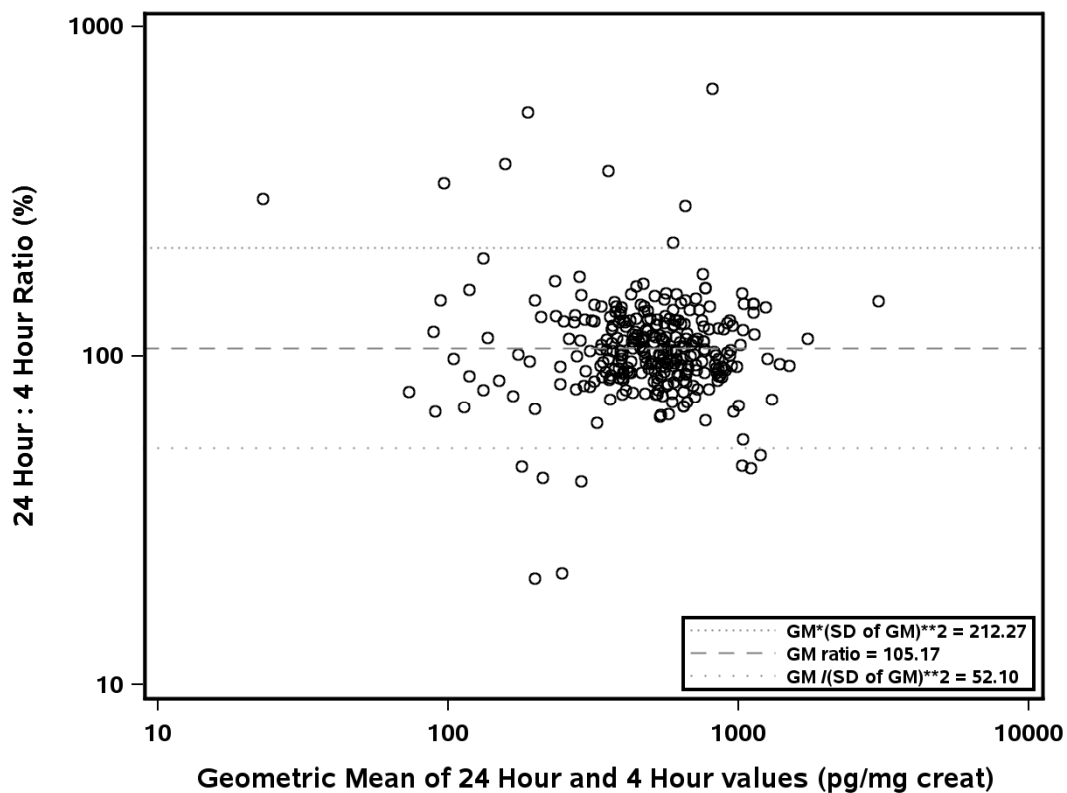
Note: Data from all 3 randomized groups are presented.  $\rho$  = Spearman rank correlation coefficient.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_sc\_11dtx.sas 30NOV15 Status: Final (Page 1 of 1)



**Figure 15.1.2.28.2 Bland-Altman Plot for Concordance of Urinary 11-DTX-B2 Concentration Adjusted for Creatinine from 24 Hour Urine Collection and 4 Hour Urine Fraction at Baseline and Day 90 Visit - FAS**



Note: GM = Geometric Mean. SD = Standard Deviation.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

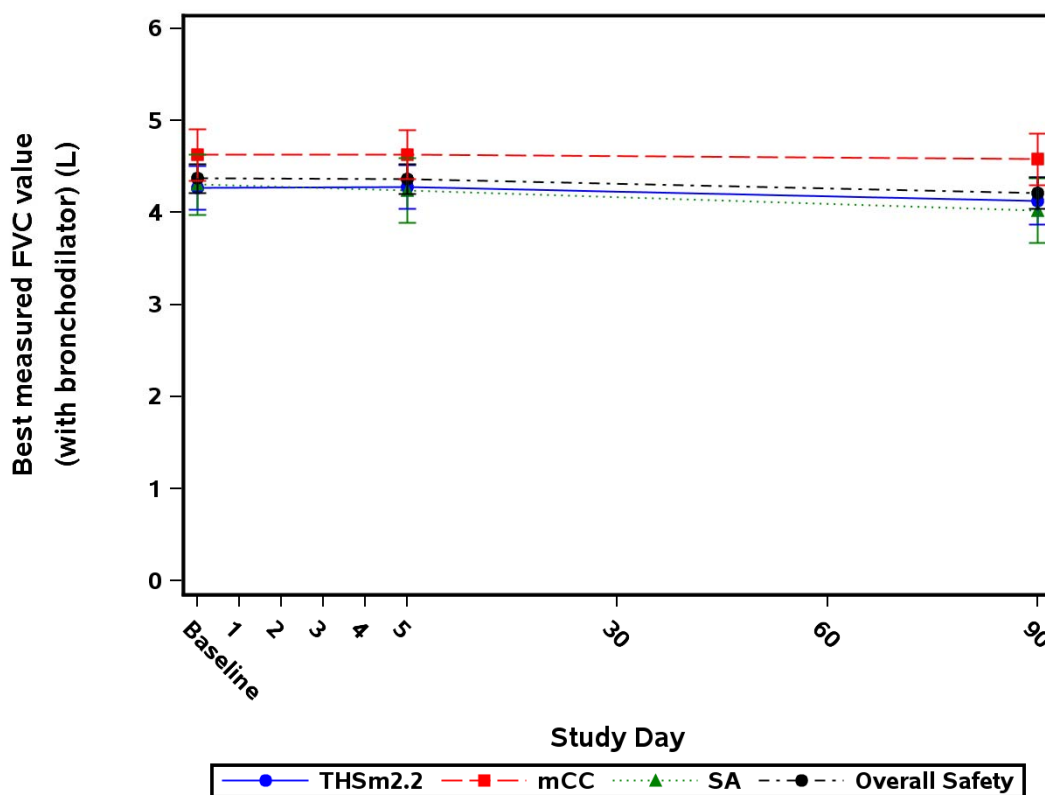
Note: Data from all 3 randomized groups are presented.

Appendix 15.3.3.1, 15.3.3.5.

Study ID: ZRHM-REXA-08-US Program: f\_ba\_11dtx.sas 01DEC15 Status: Final (Page 1 of 1)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



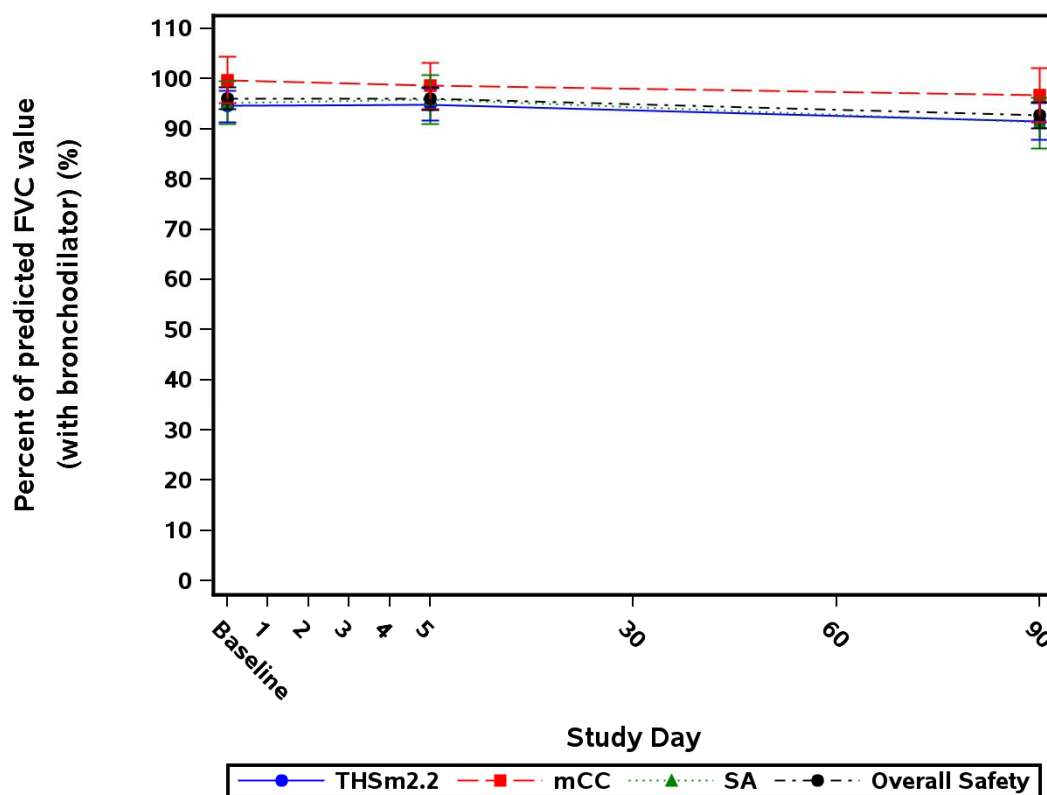
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 1 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



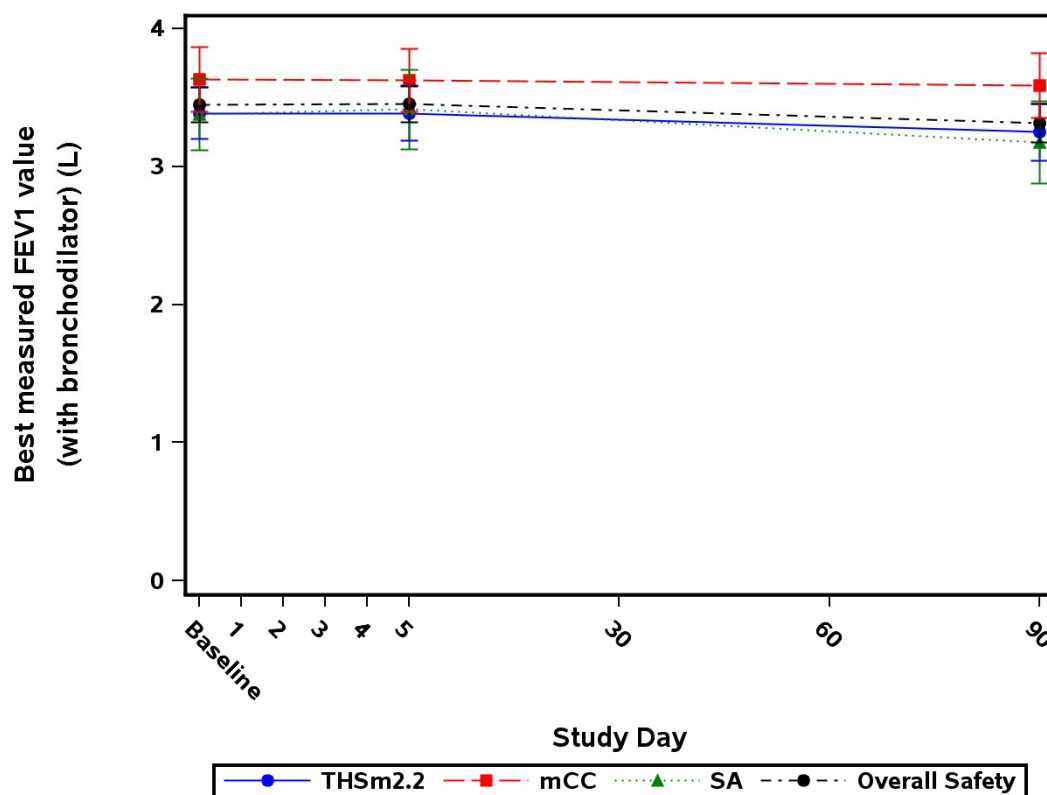
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 2 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



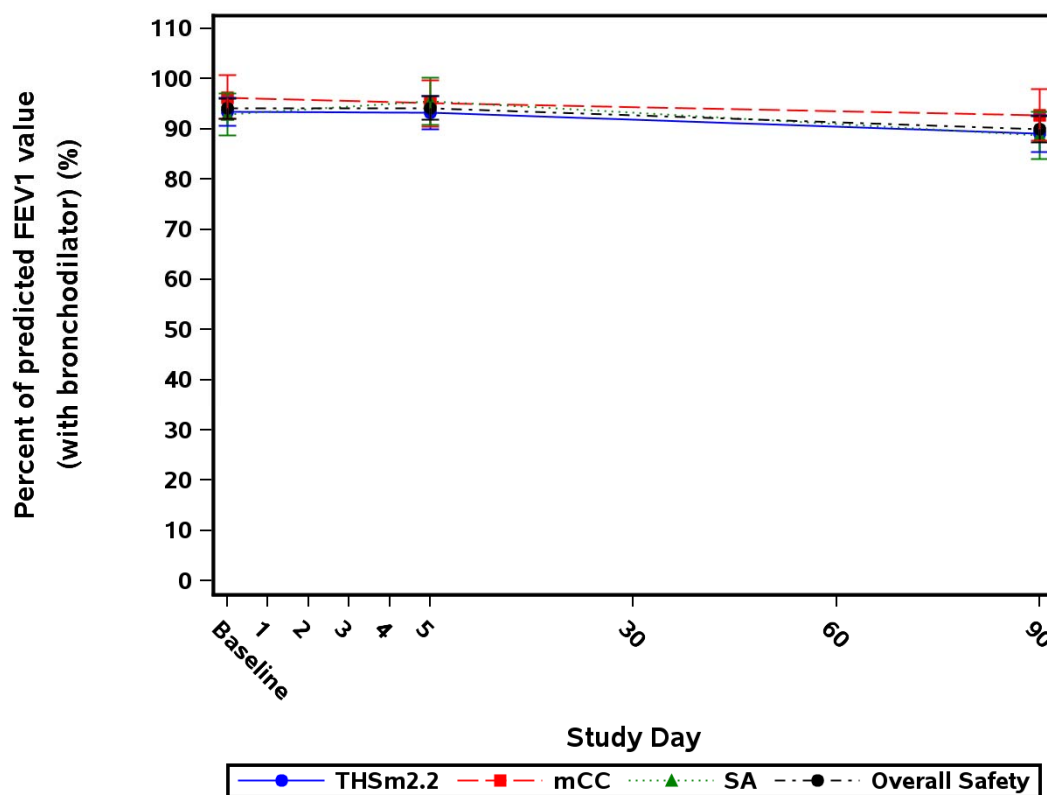
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 3 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



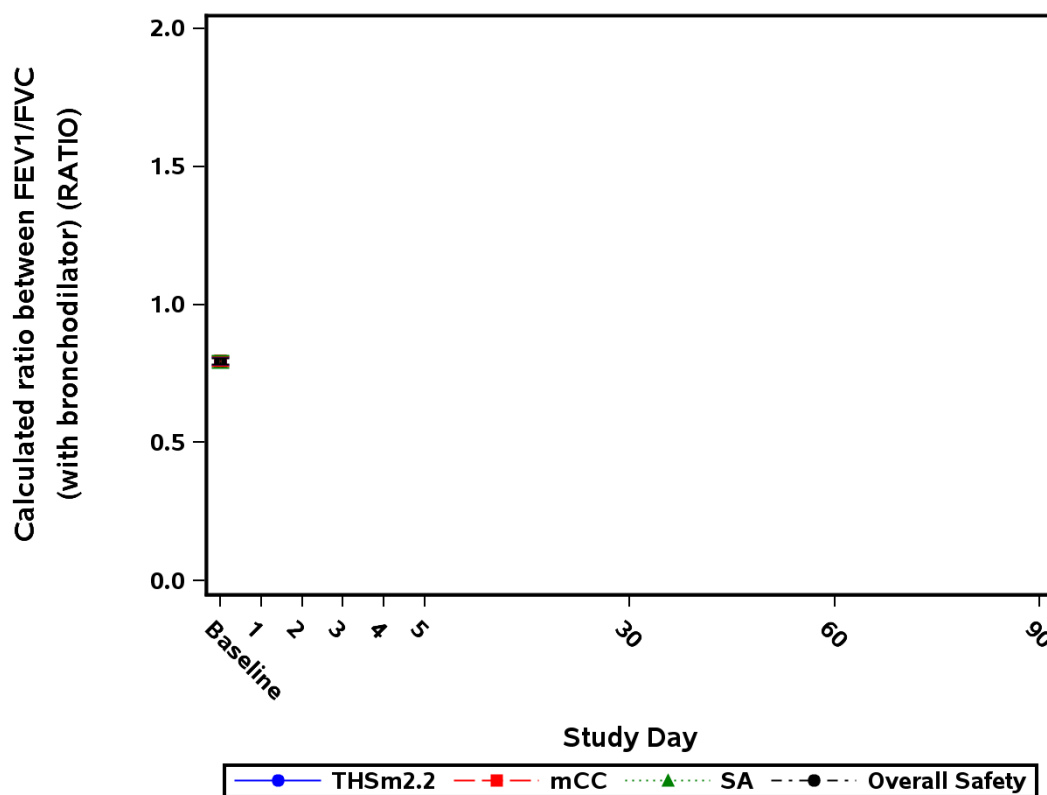
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 4 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



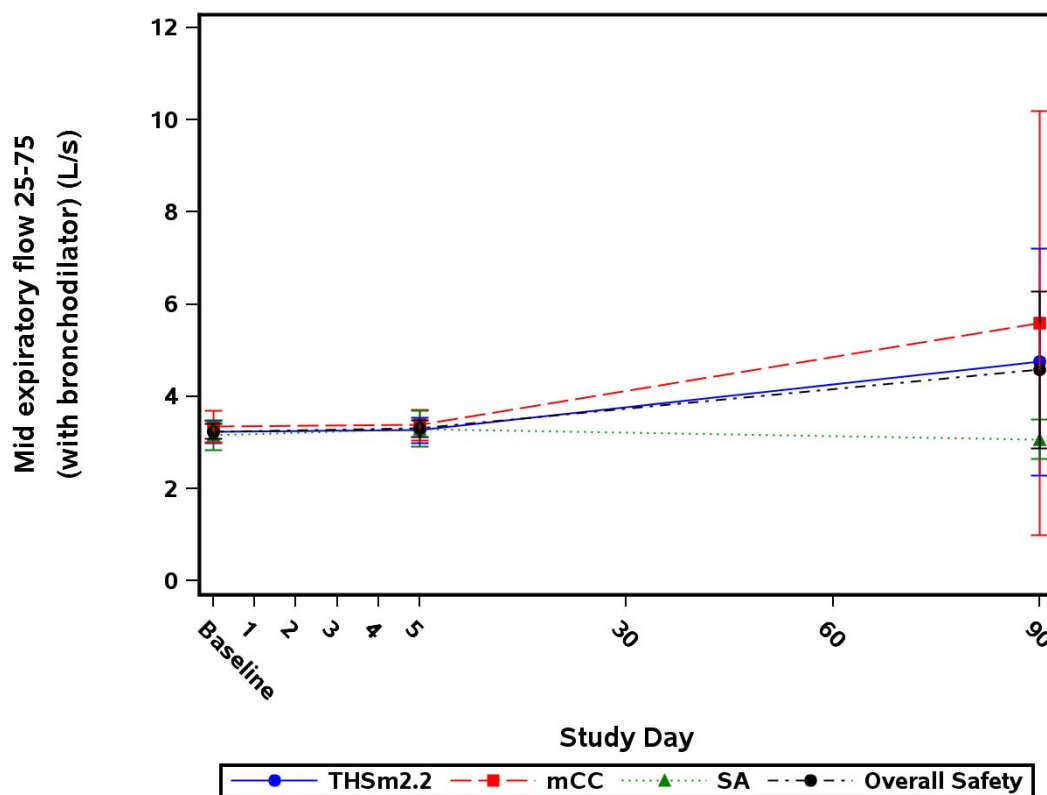
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 5 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

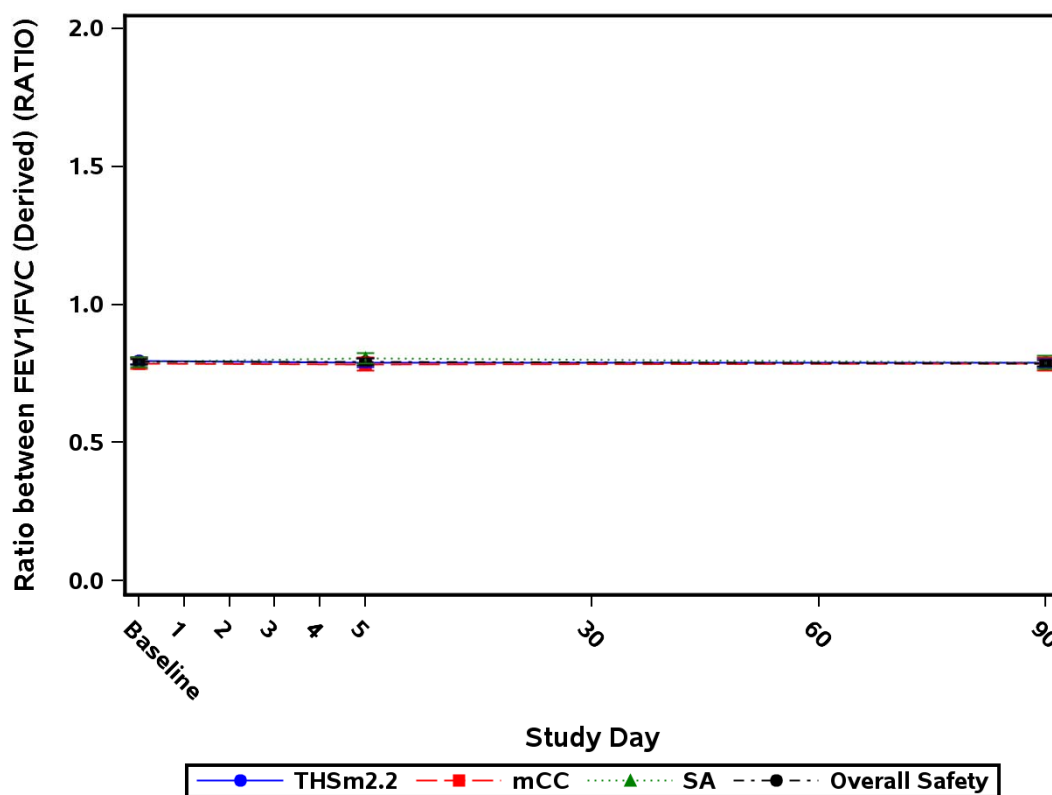
Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 6 of 13)





**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



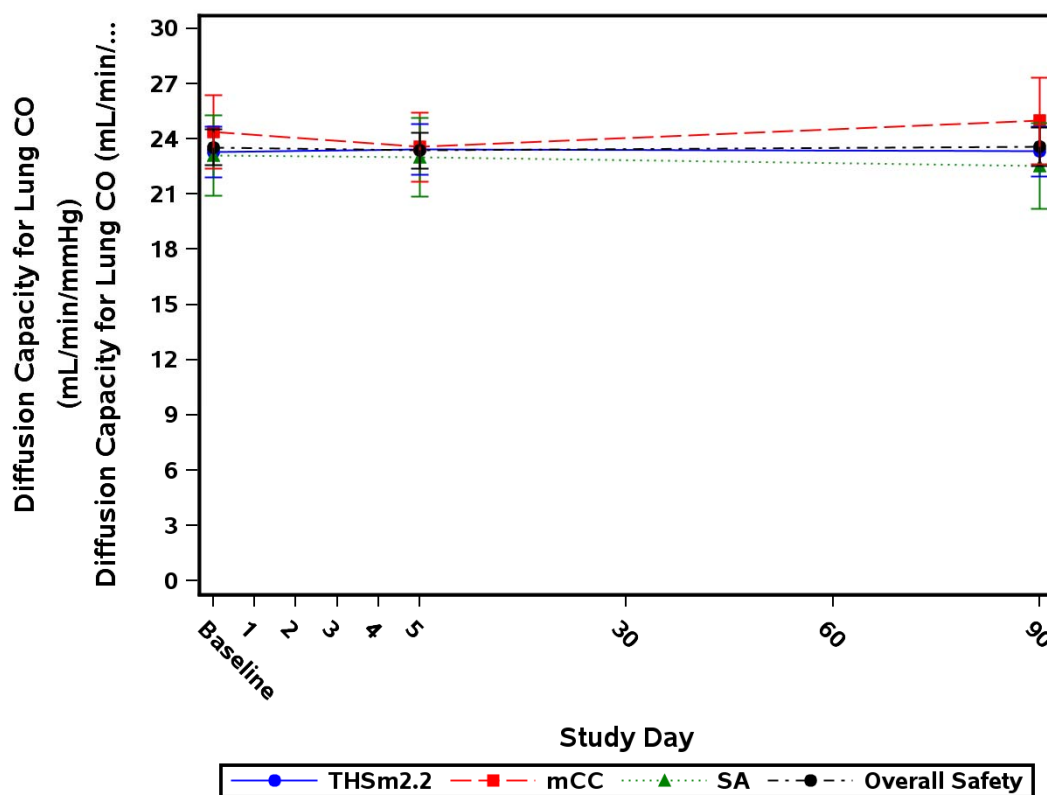
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 7 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



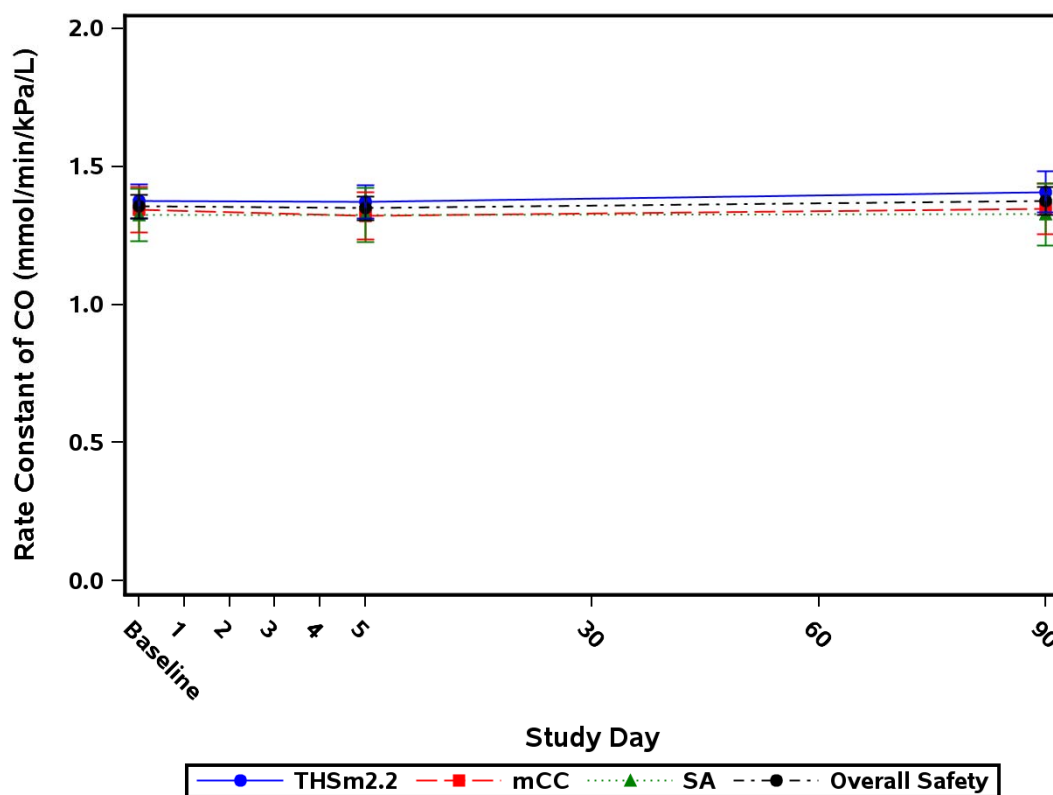
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 8 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



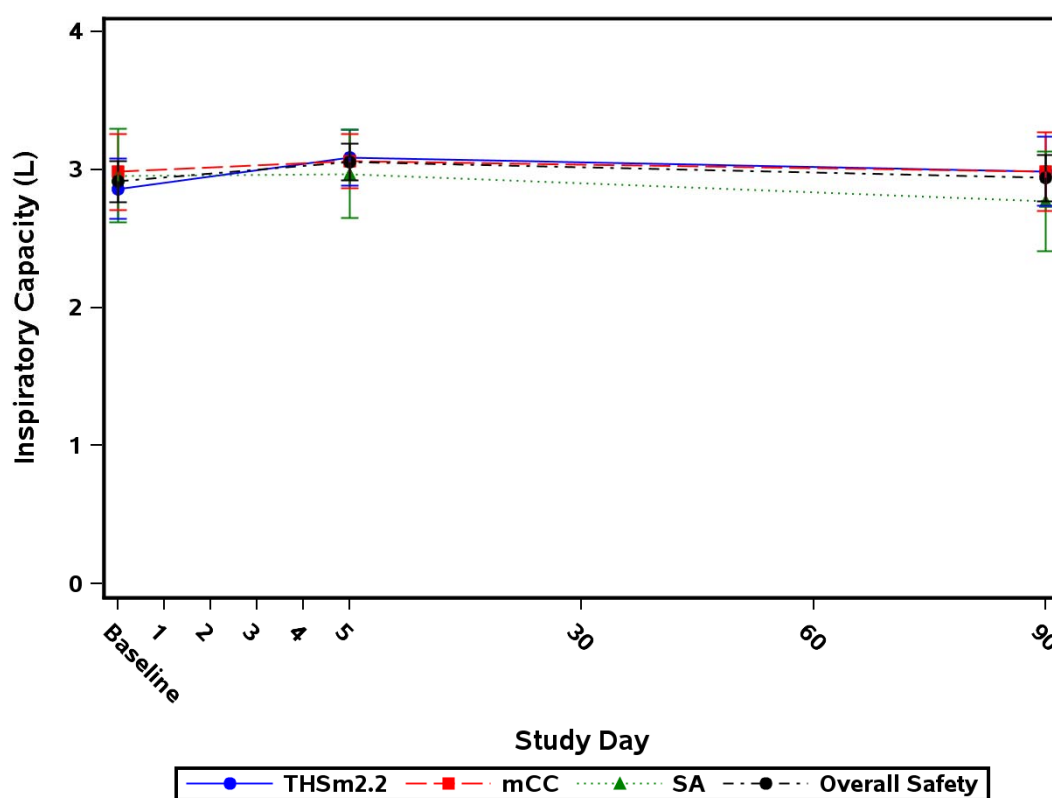
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 9 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



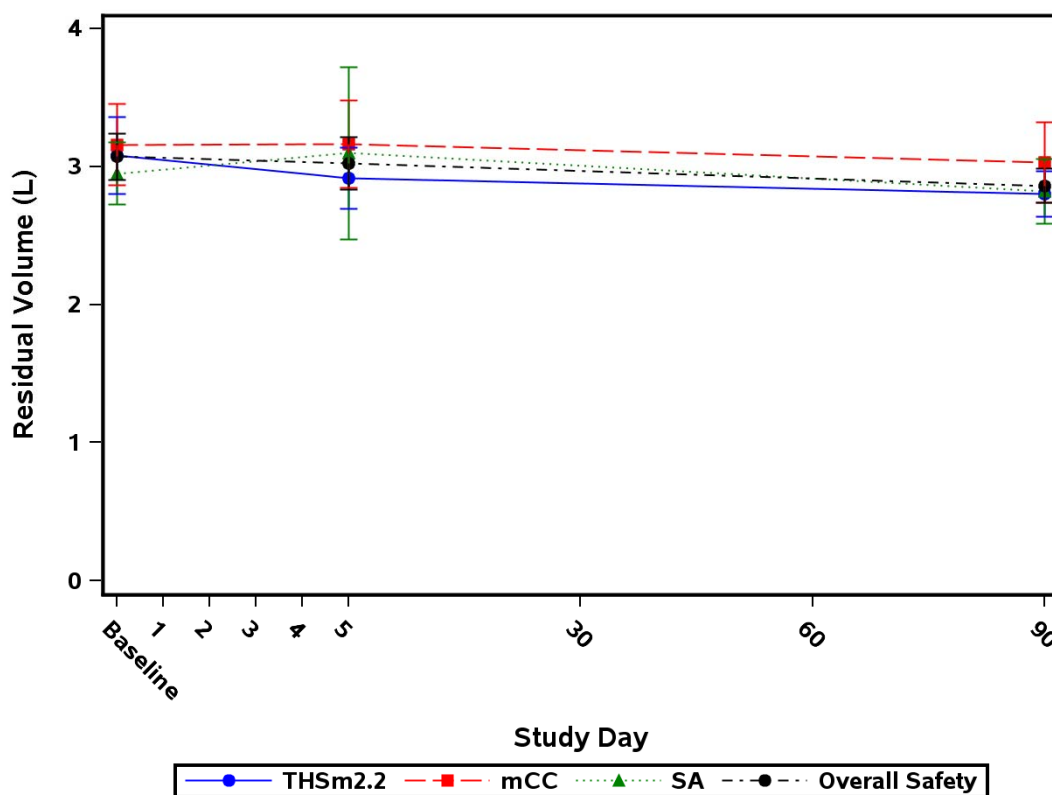
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 10 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



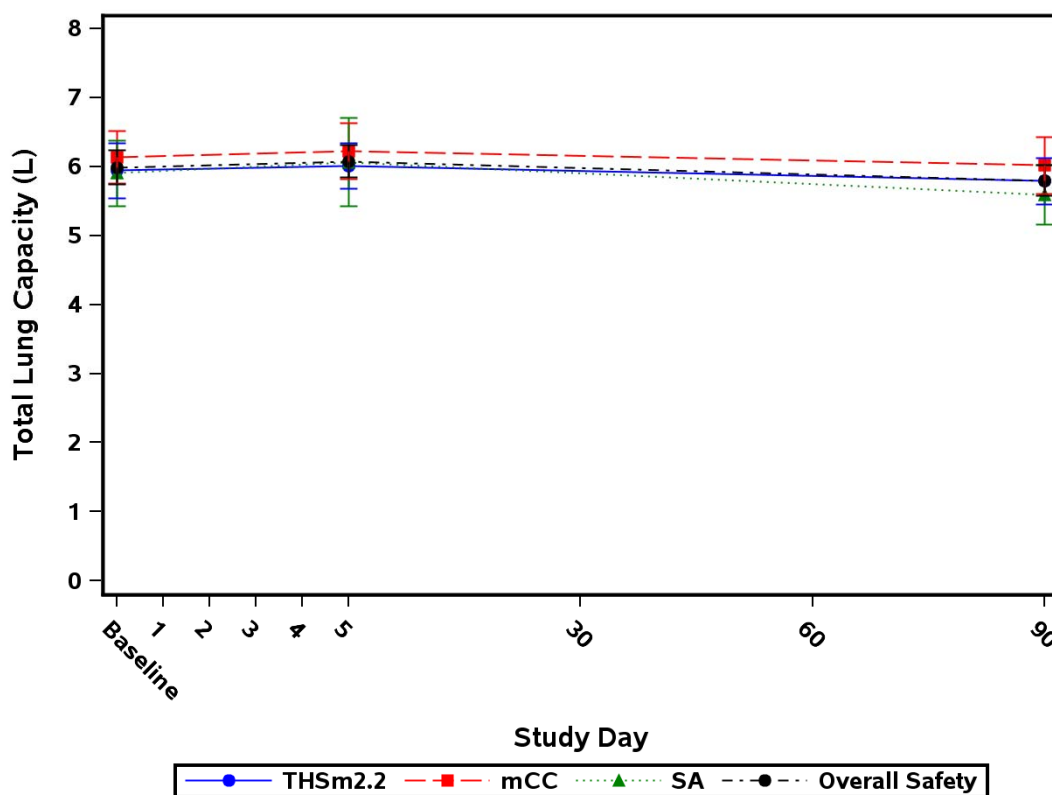
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 11 of 13)



**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



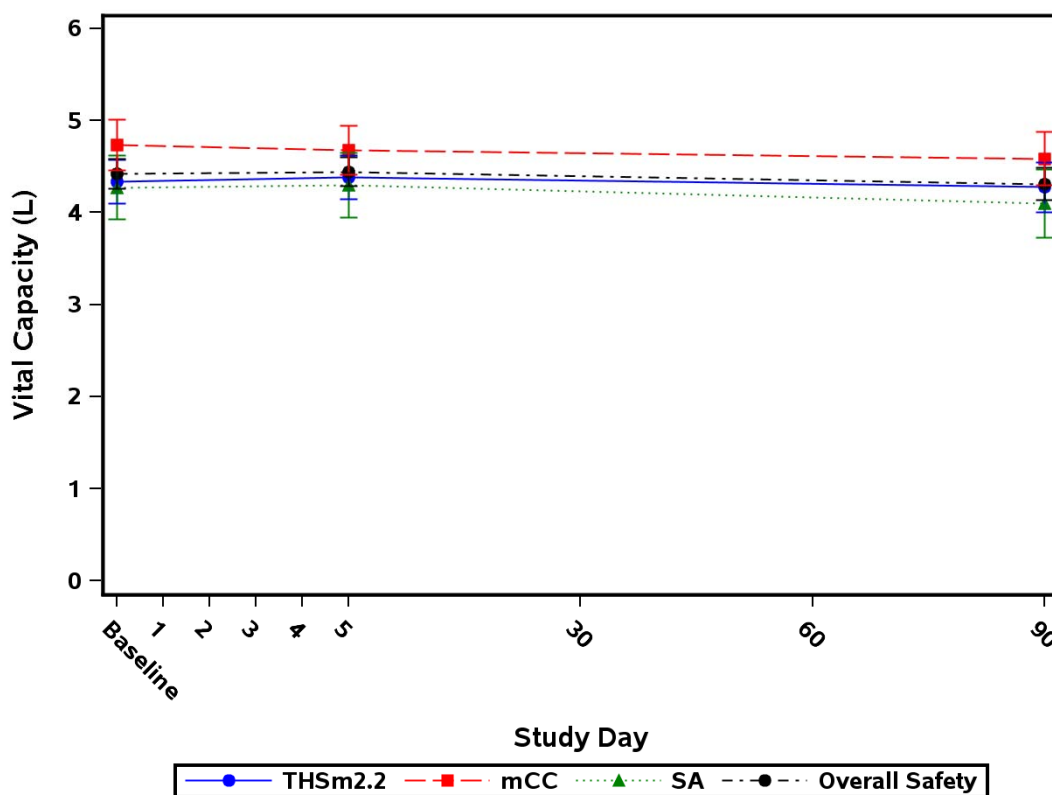
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 12 of 13)



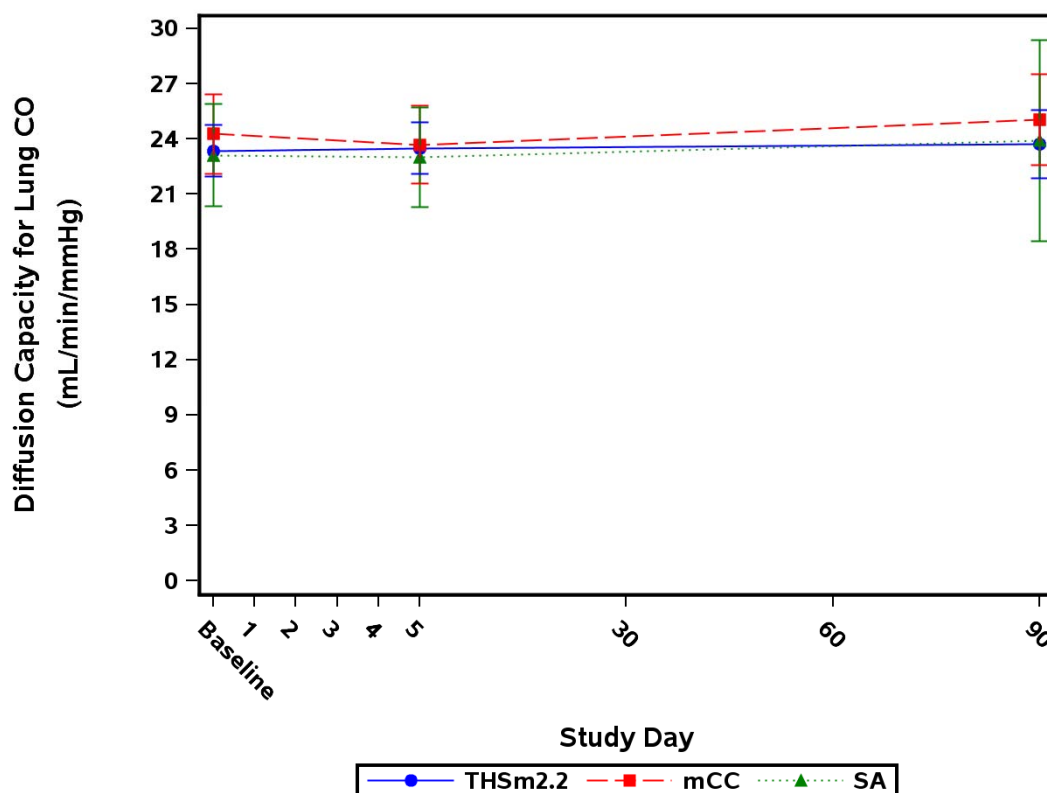
**Figure 15.1.2.30 Full Lung Function Results Arithmetic Mean and 95% CI - Safety Population**



Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Appendix 15.2.6.22

Study ID: ZRHM-REXA-08-US Program: f\_lungf\_saf.sas 16MAR16 Status: Final (Page 13 of 13)

**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

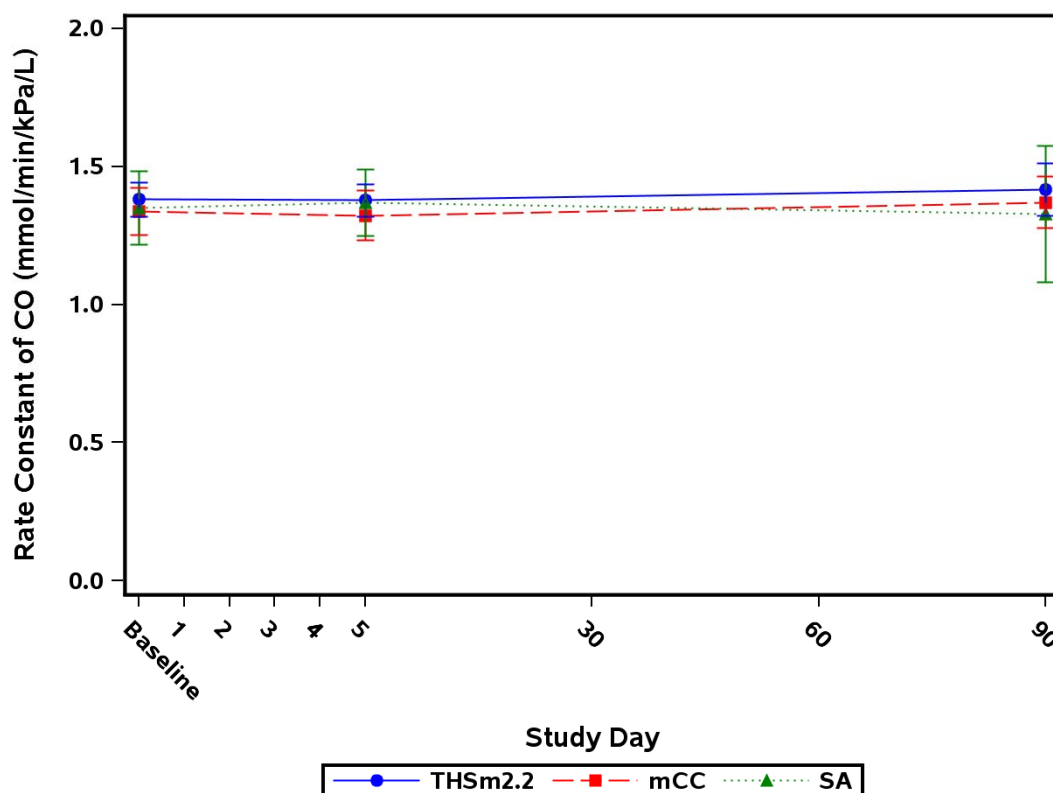
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.70

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

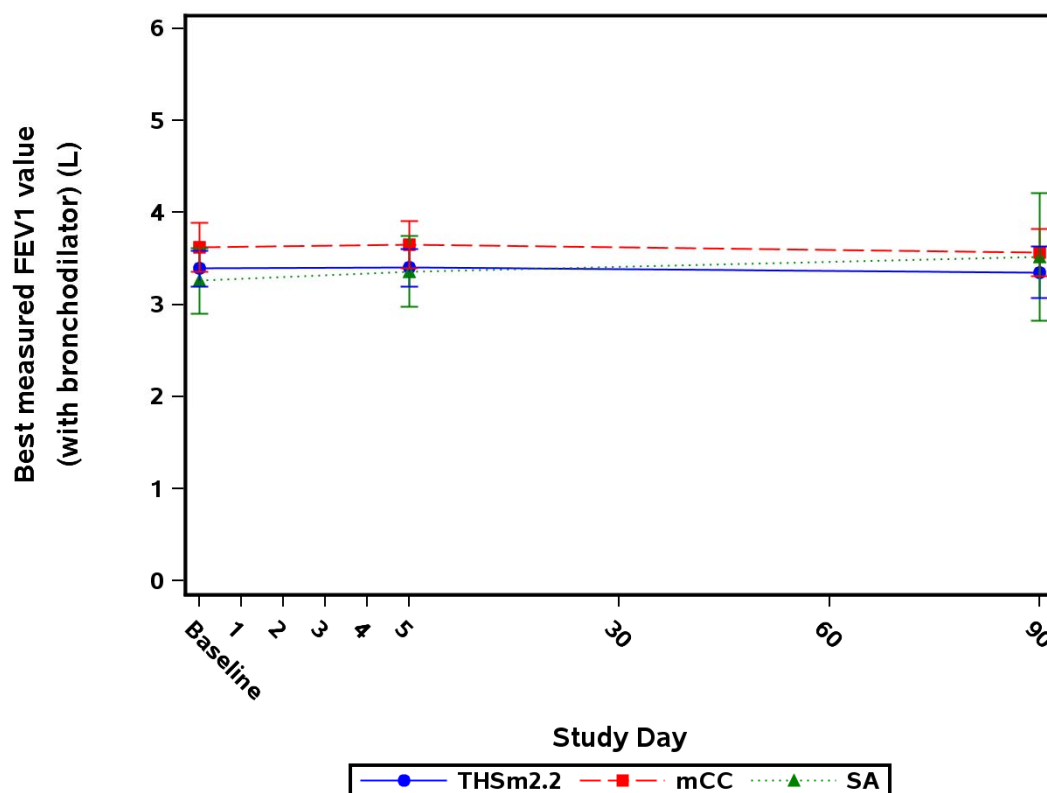
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

Appendix 15.2.4.70

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

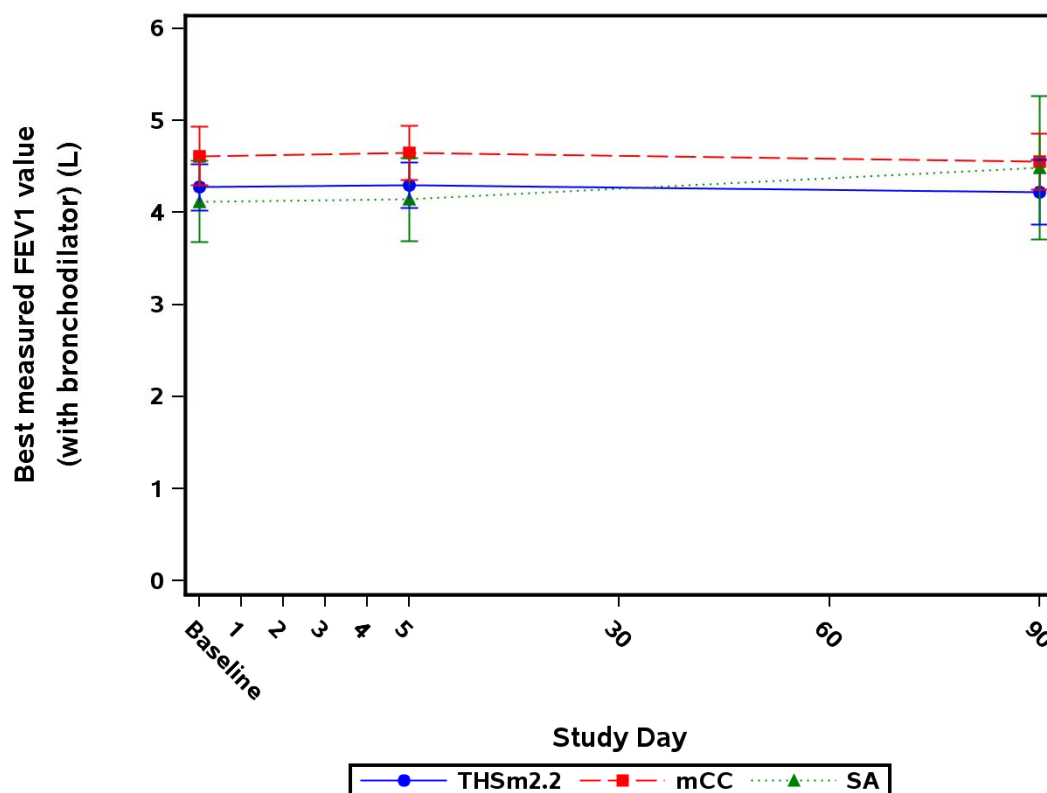
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

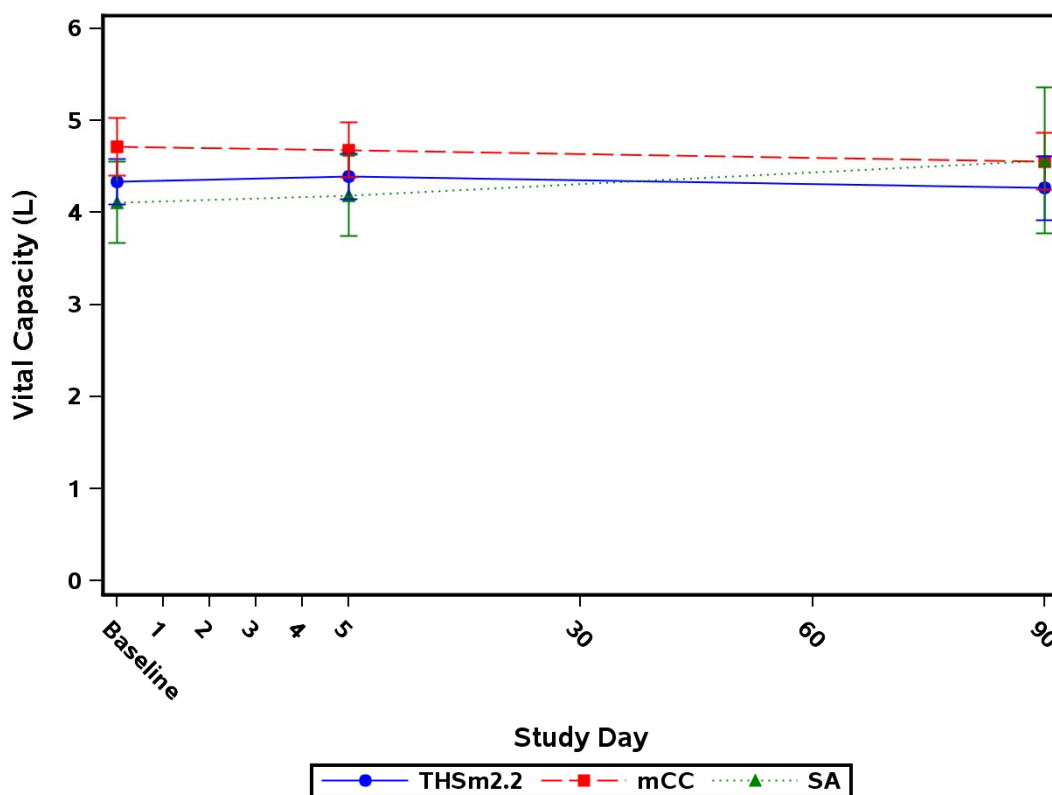
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

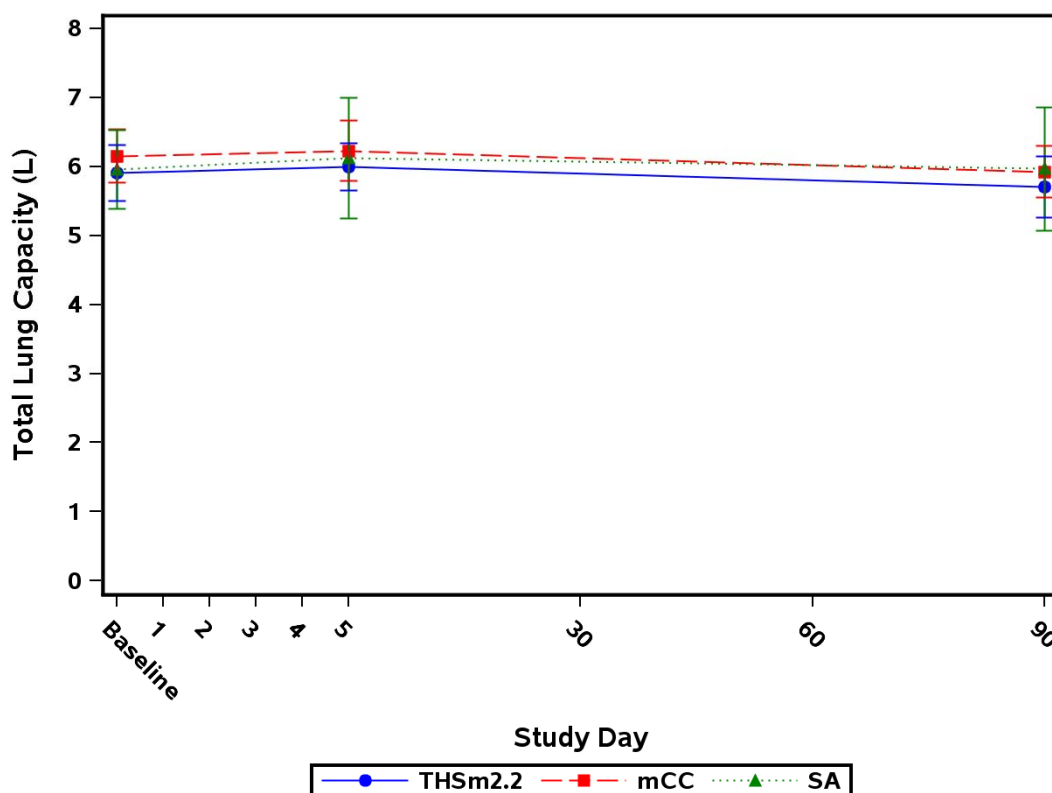
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

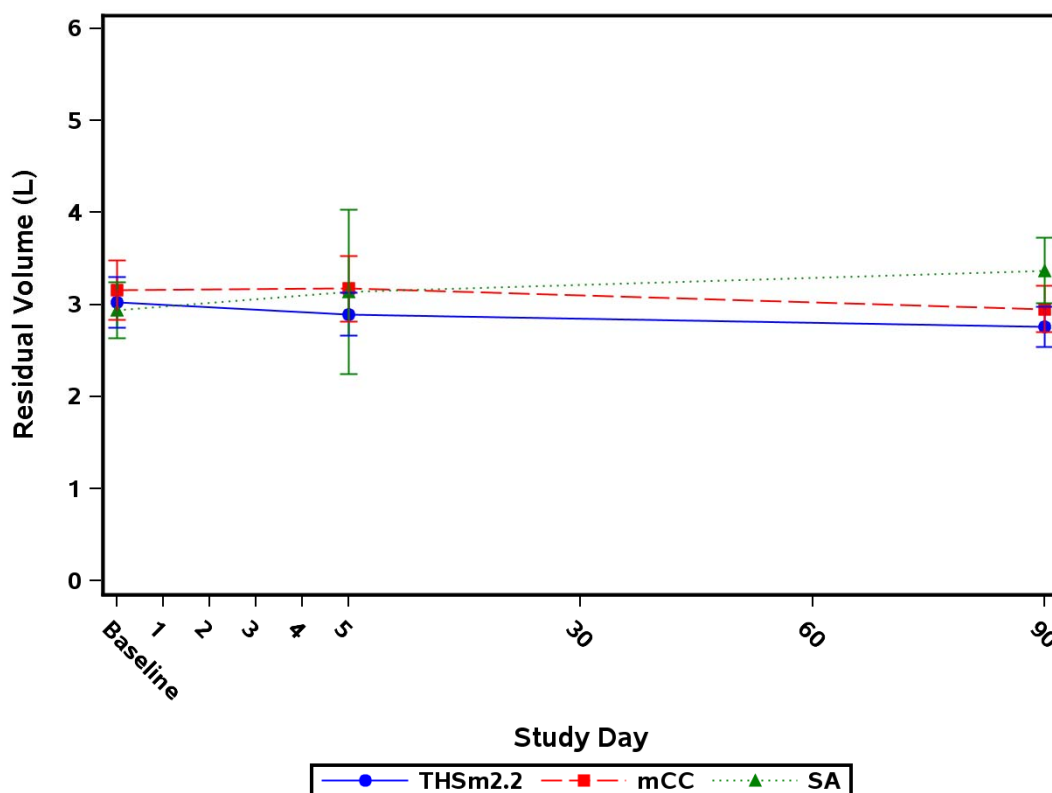
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

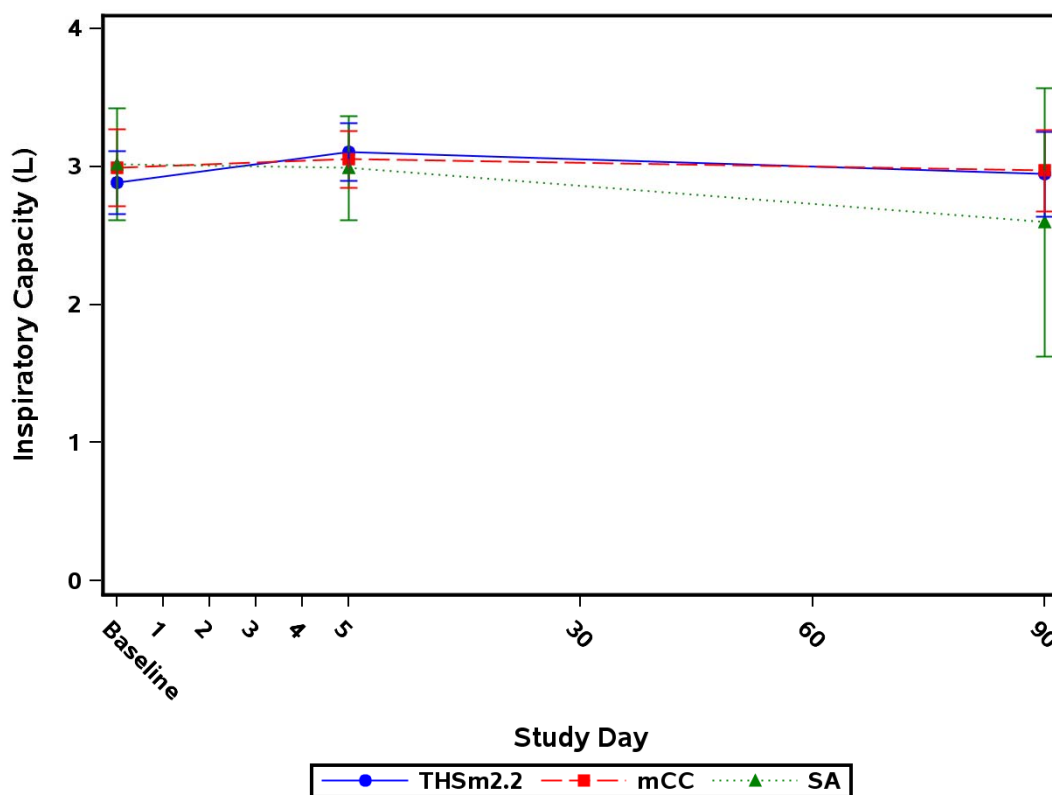
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

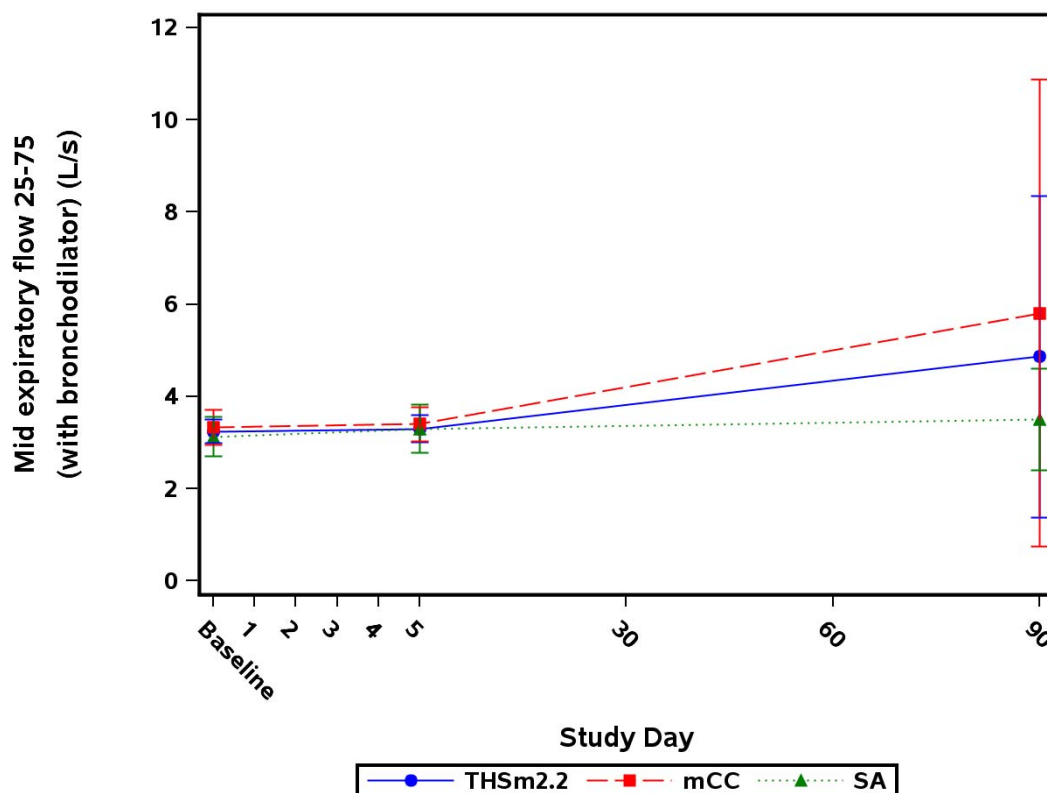
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

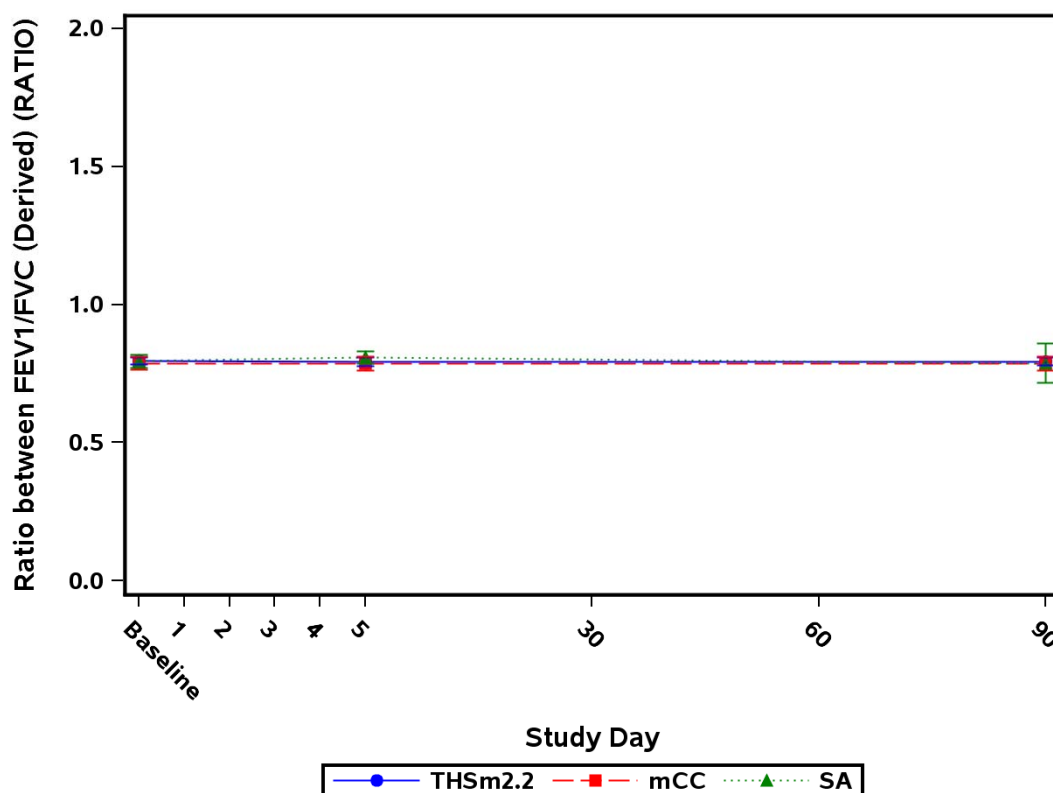
Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

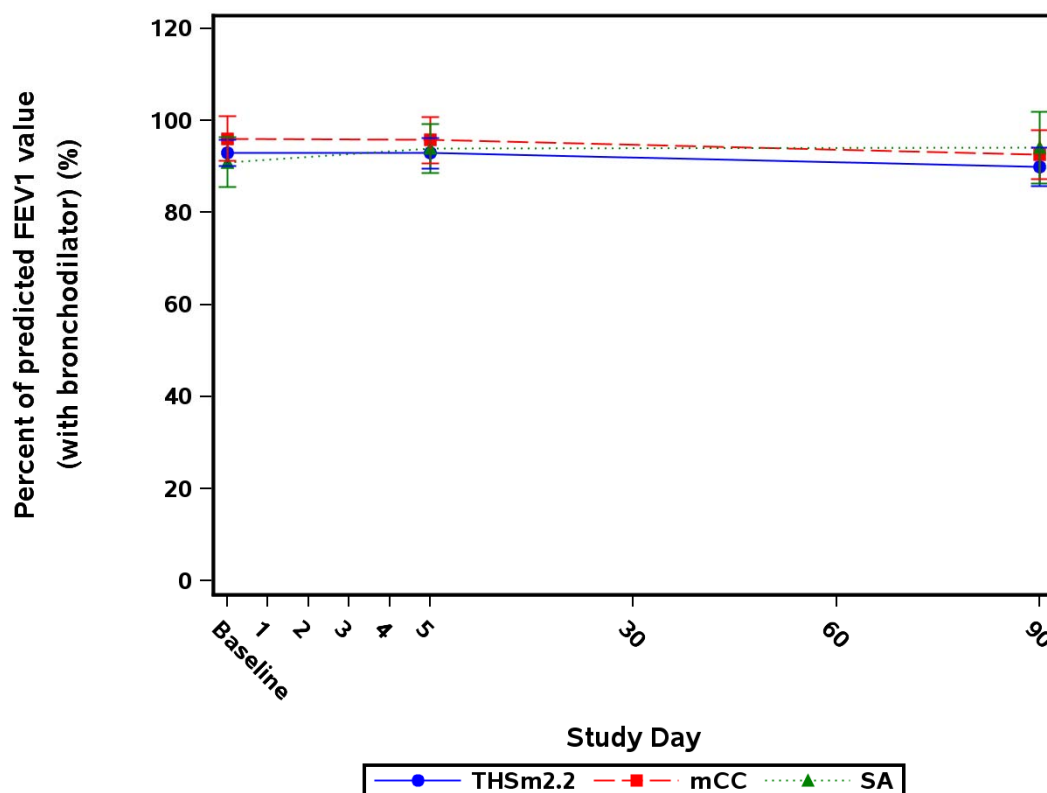
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

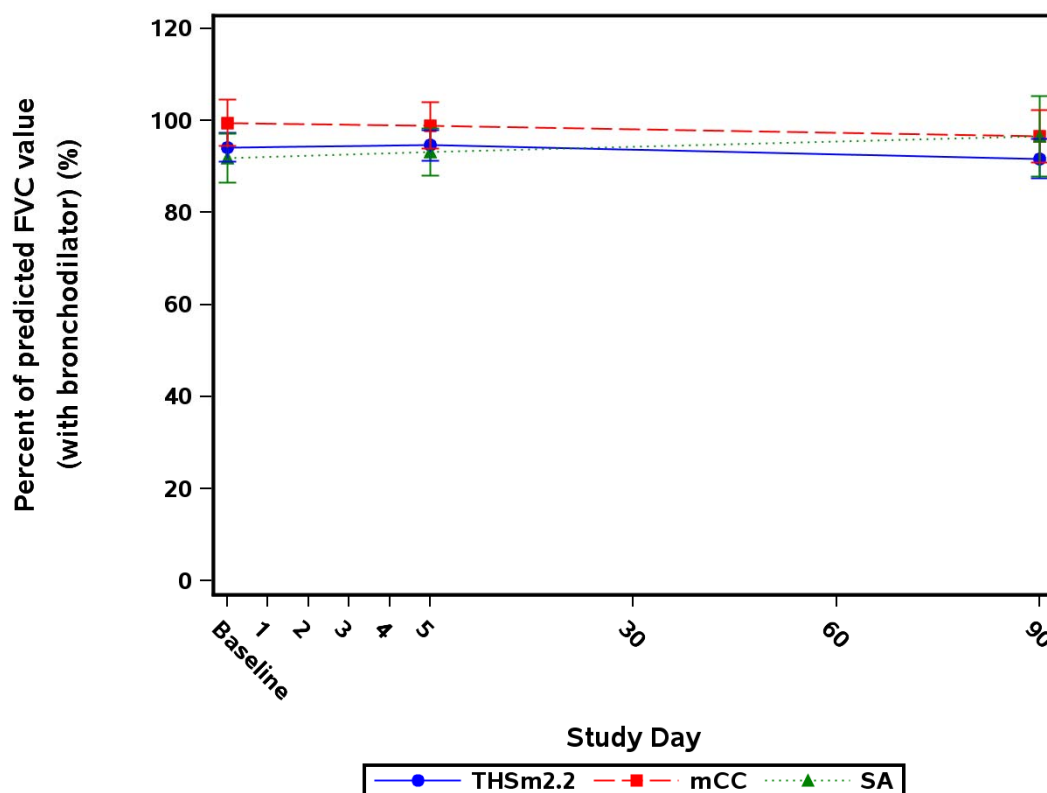
Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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**Figure 15.1.2.31 Full Lung Function Results Arithmetic Mean and 95% CI - PP Set**

Note: Baseline is summarized using the baseline data from the PP Set for Period 1.

Note: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.

Note: Baseline is the last assessment prior to first product use in mCC/THS 2.2 arms on Day 1 or last assessment prior to 10:00 AM in SA arm on Day 1.

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### **15.1.3 Other Assessments**

Not applicable.