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* Project : ZRHM-REXA-07-JP

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* Program name : t15020302_ZRHM-REXA-07_V1.sas

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* Author : M. SUN

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* Date created : 05/26/2015

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* Purpose : Table 15.2.3.2 Analysis of COHb, MHBMA, 3-HPMA, S-PMA,

* and Total NNAL on Day 5/90 Visit for THS 2.2 Menthol

* versus mCC and SA -PP Set

*

* Revision History :

*

* Date Author Ref Revision (Date in YYYYMMDD format)

*

*****,

%let prgname=T15020302_ZRHM_REXA_07_JP_V1;

options mprint;

ods escapechar='^';

options sasautos=("W:\pmp07\macros" sasautos) notes;

```
%init(delivery=9);
```

```
%titlecsv(prgname=&prgname.,version=3);
```

```
options missing="";
```

```
data adbx1;
```

```
set adam.adbx;
```

```
where anl02fl='Y';
```

```
if PARAMCD="CARBXHGB" and ATPT="DAY 5 - 20:00 - 21:30" and PPROT1FL="Y" then output;
```

```
if PARAMCD in ("UMHBMCRE", "U3HPMCRE", "USPMACRE","UNNALCRE") and upcase(AVISIT) eq "DAY 5" and PPROT1FL="Y" then output;
```

```
if PARAMCD in ("CARBXHGB", "UMHBMCRE", "U3HPMCRE", "USPMACRE","UNNALCRE") and upcase(AVISIT) eq "DAY 90" and PPROT4FL="Y" then output;
```

```
run;
```

```
data adbx2;
```

```
set adbx1;
```

```
logaval=log(AVAL);
```

```
logbase=log(BASE);
```

```
if paramcd='CARBXHGB' then ord=4;
```

```
if paramcd='UMHBMCRE' then ord=1;
```

```
if paramcd='U3HPMCRE' then ord=2;
```

```
if paramcd='USPMACRE' then ord=3;
```

```
if paramcd='UNNALCRE' then ord=5;
```

```
if upcase(AVISIT) eq "DAY 5" then dord=1;  
if upcase(AVISIT) eq "DAY 90" then dord=2;
```

```
run;
```

```
%macro doit;
```

```
%trtrtfg(pgmname=&loutname., pgmid=1, new=0, style=, bookmark=%lowercase(&outname.));
```

```
%do i=1 %to 5;
```

```
%do j=1 %to 2;
```

```
%if &j=2 %then %let getppfl=4; %else %let getppfl=1;;;
```

```
proc sort data=adbx2 out=adbx2&i&j nodupkey;
```

```
by ord dord;
```

```
where ord=&i and dord=&j;
```

```
run;
```

```
data adbx2&i&j;
```

```
set adbx2&i&j;
```

```
call symputx("param&i",param);
```

```
call symputx("day&i",avisit);
```

```
keep paramcd param avisit ord dord;
```

```
run;
```

title1 bold j=l "<title1 &title2";

title2 "The where clause used on the dataset adam.adbx: pprot&getppfl.fl='Y' and anl02fl='Y'";

title3 "param: &¶m&i, avisit: &&day&i" ;

proc glm data=adbx2;

where ord=&i and dord=&j;

class trtp sex UCPDGR1;

model logaval = logbase sex UCPDGR1 trtp;

lsmeans trtp / pdiff =control('mCC') alpha=0.05 cl adjust=t;

lsmeans trtp / pdiff =control('SA') alpha=0.05 cl adjust=t;

ods output LSMeans=pval&i&j (keep=ProbtDiff trtp where=(TRTP="THSm2.2")); *p-value;

ods output LSMeanCL=LSMeanCL&i&j (keep=trtp lowercl uppercl lsmean); *lsmean, C.I. for each arm;

ods output LSMeanDiffCL=LSMeanDiffCL&i&j (keep=trtp _trtp lowercl uppercl difference
where=(TRTP="THSm2.2")); *lsmean and C.I. for ratios;

ods output FitStatistics=ROOTMSE&i&j (keep=rootmse); *RootMSE;

run;quit;

proc freq data=adbx2 noprint;

where ord=&i and dord=&j and logaval>.;

tables trtp/out=countn&i&j;

run;

data countn&i&j.1(keep=ord dord row col1) countn&i&j.2(keep=ord dord row col2)
countn&i&j.3(keep=ord dord row col3);

set countn&i&j;

```

length col1 col2 col3 $20; ord=&i; dord=&j;

if trtp='THSm2.2' then do;

  row=2; col1=put(count,3.); output countn&i&j.1;

end;

if trtp='mCC' then do;

  row=2; col2=put(count,3.); output countn&i&j.2;

end;

if trtp='SA' then do;

  row=2; col3=put(count,3.); output countn&i&j.3;

end;

run;

data LSMeanCL&i&j.1(keep=ord dord row col1) LSMeanCL&i&j.2(keep=ord dord row col2)
LSMeanCL&i&j.3(keep=ord dord row col3);

set LSMeanCL&i&j(obs=3);

lsmean = exp(lsmean); /* Ratio of geometric mean */
LowerCL = exp(LowerCL); /* 95% CI lower bound */
UpperCL = exp(UpperCL); /* 95% CI upper bound */

length col1 col2 col3 $20; ord=&i; dord=&j;

if trtp='THSm2.2' then do;

  row=3; col1=put(round(lsmean,0.01),7.2); output LSMeanCL&i&j.1;

  row=4; col1=put(round(floor(lowercl*100)/100,0.01),7.2)||',
'||strip(put(round(ceil(uppercl*100)/100,0.01),7.2)); output LSMeanCL&i&j.1;

end;

```

```

else if trtp='mCC' then do;

row=3; col2=put(round(lsmear,0.01),7.2); output LSMeanCL&i&j.2;

row=4; col2=put(round(floor(lowercl*100)/100,0.01),7.2)||',
'| |strip(put(round(ceil(uppercl*100)/100,0.01),7.2)); output LSMeanCL&i&j.2;

end;

else if trtp='SA' then do;

row=3; col3=put(round(lsmear,0.01),7.2); output LSMeanCL&i&j.3;

row=4; col3=put(round(floor(lowercl*100)/100,0.01),7.2)||',
'| |strip(put(round(ceil(uppercl*100)/100,0.01),7.2)); output LSMeanCL&i&j.3;

end;

run;

data LSMeanDiffCL&i&j.1(keep=ord dord row col4 difference) LSMeanDiffCL&i&j.2(keep=ord dord row
col5);

set LSMeanDiffCL&i&j;

difference = 100*exp(difference); /* Ratio of geometric mean */

LowerCL = 100*exp(LowerCL); /* 95% CI lower bound */

UpperCL = 100*exp(UpperCL); /* 95% CI upper bound */

length col4 col5 $20; ord=&i; dord=&j;

if _trtp='mCC' then do;

row=3; col4=put(round(difference,0.01),7.2); output LSMeanDiffCL&i&j.1;

row=4; col4=put(round(floor(lowercl*100)/100,0.01),7.2)||',
'| |strip(put(round(ceil(uppercl*100)/100,0.01),7.2)); output LSMeanDiffCL&i&j.1;

end;

if _trtp='SA' then do;

```

```

row=3; col5=put(round(difference,0.01),7.2); output LSMeanDiffCL&i&j.2;

row=4; col5=put(round(floor(lowercl*100)/100,0.01),7.2)||',
'| | strip(put(round(ceil(uppercl*100)/100,0.01),7.2)); output LSMeanDiffCL&i&j.2;

end;

run;

```

```

data ROOTMSE&i&j;

set ROOTMSE&i&j;

length col4cv $7; ord=&i; dord=&j;

CVperc=100*sqrt(exp(RootMSE**2)-1);

row=3; col4cv=put(round(ceil(CVperc*100)/100,0.01),7.2);

keep ord dord row col4cv;

run;

```

```

data pval&i&j;

set pval&i&j(obs=1);

set LSMeanDiffCL&i&j.1(where=(row=3) keep=row difference);

length col4 $20; ord=&i; dord=&j;

row=5;

if (difference < 100) then Probt1=ProbtDiff/2;

else Probt1=1-ProbtDiff/2;

col4=put(Probt1,pvalue6.3);

keep ord dord row col4;

run;

```

```

data struct&i&j;

```

```

set adbx2&i&j;

length hd $50 stat $40;

row=1; hd=param; output;

row=2; hd=propcase(avisit); stat='n'; output;

row=3; hd=''; stat='Geometric LS Mean (CV%)';output;

row=4; hd=''; stat='95% CI';output;

row=5; hd=''; stat='p-value (one-sided)';output;

keep ord dord row hd stat;

run;

data res&i&j;

    merge struct&i&j countn&i&j.1 countn&i&j.2 countn&i&j.3 LSMeanCL&i&j.1 LSMeanCL&i&j.2
    LSMeanCL&i&j.3 LSMeanDiffCL&i&j.1 LSMeanDiffCL&i&j.2 ROOTMSE&i&j pval&i&j;

    by ord dord row;

run;

data res&i&j;

    set res&i&j;

    if row=3 then col4=trim(col4)||'('||strip(col4cv)||')';

    if row=3 then col5=trim(col5)||'('||strip(col4cv)||')';

run;

%end;

%end;

ods rtf close;

```



```
data final;

  set res11 res12 res21 res22 res31 res32 res41 res42 res51 res52;

  by ord dord row;

  if first.ord then pagen+1;

  drop difference;

run;
```

```
data final;

  set final;

  by ord dord;

  if first.dord and dord=2 then delete;

run;
```

```
data final;

  set final end=eof;

  by pagen;

  if eof then call symputx("totalpage",pagen);

run;
```

```
data odata.&prgname.;

set final;

run;
```

```
%trtrtfg(pgmname=&outname., pgmid=1, new=0, style=, bookmark=%lowcase(&outname.));
```

%do i=1 %to &totalpage;

title; footnote;

/*

title1 bold j=l "&title1 &title2";

title2 " ";

footnote1 bold h=12pt

"

footnote2 j=l h=9pt 'Note: Adjusted geometric least squares (LS) means and confidence intervals (CIs) from an ANCOVA model conducted on log-transformed '

'values with log-transformed baseline value, study arm, sex and mCC consumption reported at screening as fixed effect factors. Geometrical CV% of '

'the ratio is estimated from the residual mean squares.');

footnote3 j=l h=9pt "Note: mCC = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.";

footnote4 j=l h=9pt "Note: p-value for one-sided test for comparison between THSm2.2 and mCC. P-value at Day 90 is evaluated only if P-value at Day 5 "

"is significant, in all biomarkers except for Total NNAL.";

footnote5 j=l h=9pt "Note: For the primary objective, Total NNAL is evaluated at Day 90 while the other biomarkers are evaluated at Day 5. For the secondary objective, "

"Total NNAL is evaluated at Day 5 while the other biomarkers are evaluated at Day 90.";

footnote6 j=l h=9pt " ";

footnote7 h=9pt j=l "&APPENDIX.";

footnote8 h=9pt j=l "Study ID:ZRHM-REXA-07-JP Program: &prgname..sas Status:
&revversion./&fdate. Page: &i. of &totalpage";

*/

```
proc report data=final headskip headline nowd split='~' style=[outputwidth=100%] style(header  
column)=[protectspecialchars=off];
```

```
where pagen=&i;
```

```
column pagen ord dord hd stat col1 col2 col3 col4 col5;
```

```
define pagen /order order=internal noprint;
```

```
define ord /order order=internal noprint;
```

```
define dord /order order=internal noprint;
```

```
define hd /display "Variable" style(column)=[cellwidth=12% just=l] style(header)=[just=l];
```

```
define stat /display "Statistic" style(column)=[cellwidth=15% just=l] style(header)=[just=l];
```

```
define col1 /display "THSm2.2" style(column)=[cellwidth=9% just=c];
```

```
define col2 /display "mCC" style(column)=[cellwidth=9% just=c];
```

```
define col3 /display "SA" style(column)=[cellwidth=9% just=c];
```

```
define col4 /display "THSm2.2 : mCC~Ratio (%)" style(column)=[cellwidth=10% just=c];
```

```
define col5 /display "THSm2.2 : SA~Ratio (%)" style(column)=[cellwidth=10% just=c];
```

```
COMPUTE before pagen;
```

```
LINE @1 " ";
```

```
ENDCOMP;
```

```
COMPUTE after dord;
```

```
LINE @1 "";
```

```
ENDCOMP;
```

```
compute before _page_ /style=[fontweight=bold fontsize=3.75];
```

line @1 "&title1 &title2";

line @1 "^R/RTF\brdrb\brdrs\brdrw30\brsp20\b ' '";

endcomp;

compute after _page_/style=[fontsize=1.75];

line @1 'Note: Adjusted geometric least squares (LS) means and confidence intervals (CIs) from an ANCOVA model conducted on log-transformed '

'values with log-transformed baseline value, study arm, sex and mCC consumption reported at screening as fixed effect factors. Geometrical CV% of '

'the ratio is estimated from the residual mean squares.';

line @1 "Note: mCC = Conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.";

line @1 "Note: p-value for one-sided test for comparison between THSm2.2 and mCC. P-value at Day 90 is evaluated only if P-value at Day 5 "

"is significant, in all biomarkers except for Total NNAL.";

line @1 "Note: For the primary objective, Total NNAL is evaluated at Day 90 while the other biomarkers are evaluated at Day 5. For the secondary objective, "

"Total NNAL is evaluated at Day 5 while the other biomarkers are evaluated at Day 90.";

line @1 " ";

line @1 "&APPENDIX.";

line @1 "Study ID:ZRHM-REXA-07-JP Program: &fprgname..sas Status: &repversion./&fdate.
Page: &i. of &totalpage";

endcomp;

run;

```
%end;
```

```
ods listing;
```

```
ods rtf close;
```

```
%mend;
```

```
%doit;
```