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* Project : ZRHM-REXA-07-JP

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* Program name : t1502030103_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 15.2.3.1.3 Sensitivity Analysis of COHb, MHBMA,

* 3-HPMA, S-PMA, and Total NNAL on Day 5/90 Visit for THS 2.2

* Menthol versus mCC for the Primary Objective - Compliant Population

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* Revision History :

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* Date Author Ref Revision (Date in YYYYMMDD format)

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*****,

%let prgname=T1502030103_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 COMPP1FL='Y' then output;

  if paramcd='UMHBMCRE' and upcase(avisit)='DAY 5' and COMPP1FL='Y' then output;

  if paramcd='U3HPMCRE' and upcase(avisit)='DAY 5' and COMPP1FL='Y' then output;

  if paramcd='USPMACRE' and upcase(avisit)='DAY 5' and COMPP1FL='Y' then output;

  if paramcd='UNNALCRE' and upcase(avisit)='DAY 90' and COMPP4FL='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;

```

```
run;
```

```
%macro doit;
```

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

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

```
%if &i=5 %then %let getppfl=4; %else %let getppfl=1;;;
```

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

```
by ord;
```

```
where ord=&i;
```

```
run;
```

```
data adbx2&i;
```

```
set adbx2&i;
```

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

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

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

```
run;
```

```
title1 bold j=l "&lttitle1 &title2";
```

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

```
title3 "param: &&param&i, avisit: &&day&i" ;
```

```

proc glm data=adbx2;

where ord=&i;

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 (keep=ProbtDiff trtp where=(TRTP="THSm2.2")); *p-value;

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

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

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

run;quit;

```

```

proc freq data=adbx2 noprint;

where ord=&i and logaval>;

tables trtp/out=countn&i;

run;

```

```

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

set countn&i;

length col1 col2 $20; ord=&i;

if trtp='THSm2.2' then do;

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

end;

```

```

if trtp='mCC' then do;

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

  end;

run;


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

set LSMeanCL&i(obs=3);

lsmean = exp(lsmear); /* Ratio of geometric mean */

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

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

length col1 col2 $20; ord=&i;


if trtp='THSm2.2' then do;

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

  end;

else if trtp='mCC' then do;

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

  end;


run;


data LSMeanDiffCL&i;

```

```

set LSMeanDiffCL&i;

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 col3 $20; ord=&i;

```

```

if _trtp='mCC' then do;

row=3; col3=put(round(difference,0.01),7.2); output;

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;

end;

```

```

keep ord row col3 difference;

```

```

run;

```

```

data ROOTMSE&i;

set ROOTMSE&i;

length col3cv $7; ord=&i;

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

row=3; col3cv=put(round(ceil(CVperc*100)/100,0.01),7.2);

keep ord row col3cv;

run;

```

```

data pval&i;

```

```

set pval&i(obs=1);

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

length col3 $20; ord=&i;

row=5;

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

else Probt1=1-ProbtDiff/2;

col3=put(Probt1,pvalue6.3);

keep ord row col3;

run;

```

```

data struct&i;

set adbx2&i;

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 row hd stat;

run;

```

```

data res&i;

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

by ord row;

run;

```

```
data res&i;  
  
  set res&i;  
  
  if row=3 then col3=trim(col3)||' ('||strip(col3cv)||')';  
  
run;
```

```
%end;
```

```
ods rtf close;
```

```
data final;  
  
  set res1-res5;  
  
  by ord row;  
  
  pagen=ceil(ord/2);  
  
  drop difference col3cv;  
  
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=%lowercase(&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 products.";

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:  
&repversion./&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 hd stat col1 col2 col3;
```

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

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

```
define hd /display "Variable" style(column)=[cellwidth=18% just=l] style(header)=[just=l];
```

```
define stat /display "Statistic" style(column)=[cellwidth=18% just=l] style(header)=[just=l];
```

```
define col1 /display "THSm2.2" style(column)=[cellwidth=14% just=c];
```

```
define col2 /display "mCC" style(column)=[cellwidth=14% just=c];
```

```
define col3 /display "THSm2.2 : mCC~Ratio (%)" style(column)=[cellwidth=14% just=c];
```

```
COMPUTE before pagen;
```

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

```
ENDCOMP;
```

```
COMPUTE after ord;
```

```
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 = Menthol conventional cigarettes; THSm2.2 = Tobacco Heating System 2.2 Menthol.";

line @1 "Note: p-value is for the 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;
```