

*****,

* Project : ZRHM-REXA-07-JP

*

* Program name : t1502030102_ZRHM-REXA-07_V1.sas

*

* Author : M. SUN

*

* Date created : 05/26/2015

*

* Purpose : Table 15.2.3.1.2 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 using Mixed Model- PP Set

*

* Revision History :

*

* Date Author Ref Revision (Date in YYYYMMDD format)

*

*****,

%let prgname=T1502030102_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 ANL01FL="Y" and ANL02FL="Y" and DTYPE ne "LOCF";
```

```
if paramcd='CARBXHGB' and atpt='DAY 5 - 20:00 - 21:30' and pprot1fl='Y' then output;
```

```
if paramcd='UMHBMCRE' and upcase(avisit)='DAY 5' and pprot1fl='Y' then output;
```

```
if paramcd='U3HPMCRE' and upcase(avisit)='DAY 5' and pprot1fl='Y' then output;
```

```
if paramcd='USPMACRE' and upcase(avisit)='DAY 5' and pprot1fl='Y' then output;
```

```
if paramcd='UNNALCRE' and upcase(avisit)='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;
```

```
run;
```

```
%macro doit;
```

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

```
%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: pprot&getppfl.fl='Y' and anl02fl='Y' and  
anl01fl='Y' and dtype ne 'LOCF'";
```

```
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 mixed data=adbx2;

where ord=&i;

Class trtp sex UCPDGR1;

Model logaval = logbase sex UCPDGR1 trtp / outp=pred;

lsmeans trtp / pdiff =control('mCC') alpha=0.05 cl;

lsmeans trtp / pdiff =control('SA') alpha=0.05 cl;

ods output lsmeans=lsmeans&i (keep=trtp lower upper estimate); *each arm;

ods output diffs=diffs&i (keep=_trtp trtp lower upper probt estimate where=(TRTP="THSm2.2")); *
lsmean and C.I. for ratios;

ods output covparms=estimate&i(rename=(estimate=mse)); *MSE;

```

```
run;
```

```
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 lsmeans&i(obs=3);
```

```
lsmean = exp(estimate);
```

```
LowerCL = exp(Lower);
```

```
UpperCL = exp(Upper);
```

```
length col1 col2 $20; ord=&i;
```

```
if trtp='THSm2.2' then do;
```

```
row=3; col1=put(round(lsmear,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(lsmear,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 diffs&i;
```

```
difference = 100*exp(estimate);
```

```
LowerCL = 100*exp(Lower);
```

```
UpperCL = 100*exp(Upper);
```

```
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;
```

```
row=5;  
  
if (difference < 100) then Probt1=Probt/2;  
  
else Probt1=1-Probt/2;  
  
col3=put(Probt1,pvalue6.3); output;  
  
end;  
  
keep ord row col3;
```

```
run;
```

```
data ROOTMSE&i;  
  
set estimate&i;  
  
length col3cv $7; ord=&i;  
  
CVperc=100*sqrt(exp(mse)-1);  
  
row=3; col3cv=put(round(ceil(CVperc*100)/100,0.01),7.2);  
  
keep ord row col3cv;  
  
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;
```

```
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 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=%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 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 mixed model conducted with baseline value, "

"study arm, sex and mCC consumption reported at screening as fixed effect factors.";

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 " ";

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;
```