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*****;
* Project          : ZRHM-REXA-07-JP
*
* Program name     : t1502042201_ZRHM-REXA-07_V1.sas
*
* Author          : L. Yan
*
* Date created     : 05/20/2015
*
* Purpose          : Table t1502042201.
*
* Revision History :
*
* Date      Author      Ref      Revision (Date in YYYYMMDD format)
*
*****;

%let prgname=T1502042201_ZRHM_REXA_07_JP_V1;
options mprint;

options sasautos=("W:\pmp07\macros" sasautos) notes;
%init(delivery=9);

%titlecsv(prgname=&prgname., version=5);

%put &title1;
%put &title2;
%put &APPENDIX;
%put &endpoint;
%put &outname.;

options missing="";

%macro cal_summary_pvalue(wher=, outnum=, var=, in=, pflg=, used=, paramcd=, avisit=);
title2 h=10pt j=1 "&used";

proc sort data=&in. out=anadt_&outnum.;
by usubjid;
where &wher. ;
run;

proc sort data=anadt_&outnum.;
by trtcd;
run;

proc means data = anadt_&outnum. noprint;
by trtcd;
var &var.;
output out=xlab_&outnum. n=n mean=mean median=med std=sd min=min max=max q1=q1 q3=q3 lclm=lclm uclm=uclm;
run;

data xlab_&outnum.;
set xlab_&outnum.;
n1 = trim(left(compress(put(n, 8.))));
if sd > . then mean1 = (trim(left(compress(put(mean, 8.1))))||' ( '||trim(left(compress(put(ceil(sd*100)/100, 8.2))))
)||')';
else mean1 = (trim(left(compress(put(mean, 8.1))))||' (NA)';
ci1=trim(left(compress(put(floor(lclm*100)/100, 8.2))))||' , '||trim(left(compress(put(ceil(uclm*100)/100, 8.2)))));
median1 = trim(left(compress(put(med, 8.1))));
q1q3 = trim(left(compress(put(q1, 8.2))))||' , '||trim(left(compress(put(q3, 8.2))));
min1 = trim(left(compress(put(min, 8.))))||' , '||trim(left(compress(put(max, 8.0))));
run;

/*
proc mixed data=anadt_&outnum.;

Class trtcd sex UCPDGR1;

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

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

ods output lsmeans=lsmeans_&outnum. (keep=trtcd lower upper estimate); *each arm;

ods output diffs=LSMeanDiffCL&outnum. (keep=trtcd lower upper probt estimate); * lsmean and C.I. for ratios;

ods output covparms=ROOTMSE&outnum.(rename=(estimate=mse)); *MSE;

run;
*/

title3 h=10pt j=1 "Paramcd: &paramcd, &avisit. Model: MIXED, Method: Log";

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proc mixed data=anadt &outnum.;
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_&outnum. (keep=trtp lower upper estimate); *each arm;
ods output diffs=LSMeanDiffCL&outnum. (keep=_trtp trtp lower upper probt estimate where=(TRTP="THSm2.2")); * lsmean and
C.I. for ratios;
ods output covparms=estimate&outnum.(rename=(estimate=rootmse)); *MSE;
run;
ods output close;

data pval&outnum.;
set LSMeanDiffCL&outnum.;
ProbtDiff=probt;
keep trtp ProbtDiff;
run;

data lsmeans_&outnum.;
set lsmeans_&outnum.;
lowercl=lower;
uppercl=upper;
lsmean=estimate;
keep trtp lowercl uppercl lsmean;
run;

data LSMeanDiffCL&outnum.;
set LSMeanDiffCL&outnum.;
lowercl=lower;
uppercl=upper;
difference=estimate;
keep trtp _trtp lowercl uppercl difference;
run;

data lsmeans_&outnum.;
set lsmeans_&outnum.;
if TRTP="THSm2.2" then trtcd=1;
else if TRTP="mCC" then trtcd=2;
else if TRTP="SA" then trtcd=3;

Estimate1 = exp(lsmean); /* Ratio of geometric mean */
LowerCL = exp(lowercl); /* 95% CI lower bound */
UpperCL = exp(uppercl); /* 95% CI upper bound */
run;

data ROOTMSE&outnum.;
set estimate&outnum.;
*CVperc=100*sqrt(exp(rootmse**2)-1);
cvperc=100*sqrt(exp(rootmse)-1);
run;

proc sort data=lsmeans_&outnum. nodupkey;
by trtcd;
run;

data lsmeans_&outnum.;
length geomean geoci $100;
set lsmeans_&outnum.;
geomean=strip(put(ESTIMATE1, 8.2));
geoci=strip(put(floor(LowerCL*100)/100, 8.2)||", "||strip(put(ceil(UpperCL*100)/100, 8.2)));
keep trtcd geomean geoci;
run;

proc sort data=LSMeanDiffCL&outnum. nodup;
by TRTP _TRTP;
run;

data LSMeanDiffCL&outnum.;
set LSMeanDiffCL&outnum.;
myord=1;
run;

data ROOTMSE&outnum.;
set ROOTMSE&outnum.;
myord=1;
run;

data LSMeanDiffCL&outnum.;
merge LSMeanDiffCL&outnum. ROOTMSE&outnum.;
by myord;
run;

data LSMeanDiffCL&outnum.;
length geomean geoci $100;
set LSMeanDiffCL&outnum.;
if _TRTP eq "mCC" then trtcd=3;
if _TRTP eq "SA" then trtcd=5;

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        difference = 100*exp(difference); /* Ratio of geometric mean */
        lowercl = 100*exp(lowercl); /* 95% CI lower bound */
        uppercl = 100*exp(uppercl); /* 95% CI upper bound */

geomean=strip(put(difference, 8.2))||" ("||strip(put(ceil(CVperc*100)/100, 8.2)) ||")";
geoci=strip(put(floor(lowercl*100)/100, 8.2))||", "||strip(put(ceil(uppercl*100)/100, 8.2));
keep trtcd geomean geoci;
run;

data pval&outnum.;
set pval&outnum.;
if _n_=1;
trtcd=3;
keep trtcd ProbtDiff;
format ProbtDiff PVALUE6.3;
run;

proc sort data=LSMeanDiffCL&outnum.;
by trtcd;
run;

data LSMeanDiffCL&outnum.;
merge LSMeanDiffCL&outnum. pval&outnum.;
by trtcd;
run;

data mrep_&outnum.;
set lsmeans_&outnum. LSMeanDiffCL&outnum.;
run;

proc sort data=mrep_&outnum.;
by trtcd;
run;

proc sort data=xlab_&outnum.;
by trtcd;
run;

data xlab_&outnum.;
merge xlab_&outnum. (in=a) mrep_&outnum.;
by trtcd;
run;

data xlab_&outnum.;
set xlab_&outnum.;
if geoci ne "";
run;

proc transpose data = xlab_&outnum. out=xlab_1_&outnum.;
id trtcd;
var n1 geomean geoci;
run;

data rep_&outnum.;
length _name_ _1 _2 _3 ord1 $100;
set xlab_1_&outnum.;
ord1="&outnum.";
ordnum=input(ord1, best.);
if upcase(_name_)="N1" then do; _name_="n"; sord=0; end;
if upcase(_name_)="GEOMEAN" then do; _name_="Geometric LS Mean (CV%)"; sord=1; end;
if upcase(_name_)="GEOCI" then do; _name_="95% CI"; sord=2; end;

if upcase(_name_)="MEAN1" then do; _name_="Mean (SD)"; sord=3; end;
if upcase(_name_)="CI1" then do; _name_="95% CI"; sord=4; end;
if upcase(_name_)="MEDIAN1" then do; _name_="Median"; sord=5; end;
if upcase(_name_)="Q1Q3" then do; _name_="Q25, Q75"; sord=6; end;
if upcase(_name_)="MIN1" then do; _name_="Min, Max"; sord=7; end;
if upcase(_name_)="PROBTDIFF" then do; _name_="p-value (one-sided)"; sord=9; end;
run;

data rep;
set rep rep_&outnum.;
run;

%mend;

%macro cal_summary_pvalue1(where=, outnum=, var=, in=, pflg=);

proc sort data=&in. out=anadt_&outnum.;
by usbjid;
where &where. ;
run;

proc sort data=anadt_&outnum.;

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by trtcd;
run;

proc means data = anadt_&outnum. noprint;
by trtcd;
var &var.;
output out=xlab_&outnum. n=n mean=mean median=med std=sd min=min max=max q1=q1 q3=q3 lclm=lclm uclm=uclm;
run;

data xlab_&outnum.;
set xlab_&outnum.;
n1 = trim(left(compress(put(n, 8.))));
if sd > . then mean1 = (trim(left(compress(put(mean, 8.1))))||' ('||trim(left(compress(put(ceil(sd*100)/100, 8.2))))
||')');
else mean1 = (trim(left(compress(put(mean, 8.1))))||' (NA)');
ci1=trim(left(compress(put(floor(lclm*100)/100, 8.2))))||', '||trim(left(compress(put(ceil(uclm*100)/100, 8.2)))));
median1 = trim(left(compress(put(med, 8.1)))));
q1q3 = trim(left(compress(put(q1, 8.2))))||', '||trim(left(compress(put(q3, 8.2)))));
min1 = trim(left(compress(put(min, 8.))))||', '||trim(left(compress(put(max, 8.0)))));
run;

ods output HodgesLehmann=HodgesLehmann_&outnum.;
Proc npar1way data=anadt_&outnum. h1 median; Class trtcd;
Var aval; Run;
ods output close;

data HodgesLehmann_&outnum.;
set HodgesLehmann_&outnum.;
trtcd=3;
median1=trim(left(compress(put(MIDPOINT, 8.1)))));
ci1=trim(left(compress(put(floor(LOWERCL*100)/100, 8.2))))||', '||trim(left(compress(put(ceil(UPPERCL*100)/100, 8.2)))));
;
run;

data xlab_&outnum.;
set xlab_&outnum. HodgesLehmann_&outnum.;
run;

proc transpose data = xlab_&outnum. out=xlab_1_&outnum.;
id trtcd;
var n1 median1 ci1;
run;

data rep_&outnum.;
length _name_ _1 _2 _3 ord1 $100;
set xlab_1_&outnum.;
ord1="&outnum";
ordnum=input(ord1, best.);
if upcase(_name_)="N1" then do; _name_="n"; sord=0; end;
if upcase(_name_)="GEOMEAN" then do; _name_="Geometric LS Mean (CV%)"; sord=1; end;
if upcase(_name_)="GEOCI" then do; _name_="95% CI"; sord=2; end;

if upcase(_name_)="MEAN1" then do; _name_="Mean (SD)"; sord=3; end;
if upcase(_name_)="CI1" then do; _name_="95% CI"; sord=5; end;
if upcase(_name_)="MEDIAN1" then do; _name_="Median"; sord=4; end;
if upcase(_name_)="Q1Q3" then do; _name_="Q25, Q75"; sord=6; end;
if upcase(_name_)="MIN1" then do; _name_="Min, Max"; sord=7; end;
run;

data rep;
set rep rep_&outnum.;
run;

%mend;

%macro mainloop(flg=, outn=, where=);

proc sort data=adam.adsl out=trt;
by usbjid;
where &flg.="Y";
run;

data trt;
set trt;
if TRT01A="THSm2.2" then trtcd=1;
else if TRT01A="mCC" then trtcd=2;
else if TRT01A="SA" then trtcd=3;
run;

data anldata1;
set adam.adpp;

used="The where clause used on the dataset adam.adpp: ANL01FL=Y and &flg. =Y";

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if AVISITn>=101 and trta in ("mCC" "THSm2.2") and aval>. and &flg="Y" and anl01fl="Y" and paramcd not in ("CTMAX" "NTMAX" "AX");
run;

data anldata1;
set anldata1;

if aval>0 then logaval=log(aval);
*if base>0 then logbase=log(base);
run;

proc sort data=anldata1 out=check(keep=paramn avisitn avisit used paramcd) nodupkey;
by paramn avisitn avisit;
run;

data trt_1;
set trt;
run;

data anldata1;
set anldata1;
if TRTP="THSm2.2" then trtcd=1;
else if TRTP="mCC" then trtcd=2;
else if TRTP="SA" then trtcd=3;
run;

data check;
set check;
ord=_n_;
run;

%*cal_summary_pvalue(when=1, outnum=1, var=aval, in=anldata1, pflg=1);

data rep;
run;

data _null_;
set check;
call execute ('%cal_summary_pvalue(when=%str(avisitn=||avisitn|| and paramn=||paramn|| ), outnum=||ord||, var=logaval, in=anldata1, used=||used||, paramcd=||paramcd||, avisit=||avisit||);');
run;

data frep;
set rep;
ord=ORDNUM;
run;

data frep;
merge frep(in=a) check;
by ord;
if a;
if avisitn>.;
run;

data anldata1;
set adam.adpp;
if AVISITn>=101 and trta in ("mCC" "THSm2.2") and aval>. and &flg="Y" and anl01fl="Y" and paramcd in ("CTMAX" "NTMAX")
;
run;

data anldata1;
set anldata1;

if aval>0 then logaval=log(aval);
*if base>0 then logbase=log(base);
run;

proc sort data=anldata1 out=check(keep=paramn avisitn avisit) nodupkey;
by paramn avisitn avisit;
run;

data trt_1;
set trt;
run;

data anldata1;
set anldata1;
if TRTP="THSm2.2" then trtcd=1;
else if TRTP="mCC" then trtcd=2;
else if TRTP="SA" then trtcd=3;
run;

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data check;
set check;
ord=_n_+4;
run;

%*cal_summary_pvalue(where=1, outnum=1, var=aval, in=anldata1, pflg=1);

data rep;
run;

data _null_;
set check;
call execute ('%cal_summary_pvalue1(where=%str(avisitn='||avisitn||' and paramn='||paramn||' ), outnum='||ord||', va
r=aval, in=anldata1);');
run;

data frep1;
set rep;
ord=ORDNUM;
run;

data frep1;
merge frep1(in=a) check;
by ord;
if a;
if avisitn>.;
run;

proc sort data=trt_1 nodupkey;
by trtcd usubjid;
run;

proc freq data = trt_1 noprint;
tables trtcd/ out= denom;
run;

data _null_;
set denom end=eof;

retain total 0;

total = total+count;

if trtcd= 1 then do;
call symput('trt1', trim(left(put(count,8)))));
end;
if trtcd= 2 then do;
call symput('trt2', trim(left(put(count,8)))));
end;
if trtcd= 3 then do;
call symput('trt3', trim(left(put(count,8)))));
end;

run;

%put trt1=&trt1 trt2=&trt2 trt3=&trt3;

proc format;
value grp
49      ="Nicotine-Glucuronide (ng/mL)"
3       ="Cotinine (ng/mL)"
;
run;

data frep;
set frep;
if sord >.;
run;

proc sort data=frep;
by paramn;
run;

%macro cal_part_main();

data frep;
set frep;

%do i = 1 %to 100;
if (&i-1)*4<ordnum<=&i*4 then pagen=&i;
%end;

run;

```

```

%mend;

%cal_part_main();
data frep&outn.;
set frep frep1;
space=" ";

if paramn<=3 then groupid=1;
else groupid=2;

if pagen=. then pagen=2;
run;

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

title1 bold j=1 "&title1 &title2";

%mainloop(flag=PPROT1FL, outn=1, where=%str(avisitn<=105 and APUPER=1));
%*mainloop(flag=PPROT2FL, outn=2, where=%str(avisitn=130 and APUPER=2));
%*mainloop(flag=PPROT3FL, outn=3, where=%str(avisitn=160 and APUPER=3));
%*mainloop(flag=PPROT4FL, outn=4, where=%str(avisitn=190 and APUPER=4));

ods listing;
ods rtf close;
data odata.&prgname.;
set frep1 (in=a) /*frep2 (in=b) frep3 (in=c) frep4 (in=d)*/;
if a then group="PPROT1FL";
*if b then group="PPROT2FL";
*if c then group="PPROT3FL";
*if d then group="PPROT4FL";
run;
/*
proc sort data=adam.adpp out=fmt(keep=paramn param) nodupkey;
by paramn param;
run;

data fmt;
set fmt;
fmtname="grp";
start=paramn;
label=param;
run;

proc format cntlin=fmt;
run;
*/
proc format;
value grp
  1  ="Average Conc (ng/mL)"
  2  ="Max Conc (ng/mL)"
  3  ='Time of C^{sub MAX} (h)'
  4  ="Average Conc (ng/mL)"
  5  ="Max Conc (ng/mL)"
  6  ='Time of C^{sub MAX} (h)';
;
value grpf
1="Nicotine (ng/mL)"
2="Cotinine (ng/mL)";
run;

%*title(prgname1=&prgname.);

proc sort data=frep1;
by pagen;
run;

%global totalpage;

data _null_;
set frep1 end=eof;

if eof then do;
call symput('totalpage', trim(left(put(pagen,8)))));
end;

run;

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

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```

proc report data=frep1 headskip headline spacing=4 nowd split='~' style=[outputwidth=100%] style(header column)=[protec
tspecialchars=off];
where pagen=1;
  column pagen groupid paramn sord _name_ _1 space _2 space _3;
  define pagen /order order=internal noprint;
  define groupid /order order=internal noprint;
  define paramn /order "Variable" format=grp. flow style(column)=[cellwidth=10% just=l font_weight=bold];
  define sord /order order=internal noprint;
  define _name_ /display "Statistic" flow style(column)=[cellwidth=10% just=l];
  define _1 /display "THSm2.2" flow style(column)=[cellwidth=10% just=c];
  define space /display " " flow style(column)=[cellwidth=0.5% just=c];
  define _2 /display "mCC" flow style(column)=[cellwidth=10% just=c];
  define space /display " " flow style(column)=[cellwidth=0.5% just=c];
  define _3 /display "THSm2.2 : mCC Ratio (%)" flow style(column)=[cellwidth=10% just=c];

COMPUTE before groupid /style=[fontweight=bold];
LINE @1 groupid grp.;
ENDCOMP;

COMPUTE after paramn ;
LINE @1 "";
ENDCOMP;

compute before pagen;
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: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Ment
hol.";
line @1 "Note: Adjusted geometric least squares (LS) means and confidence intervals (CIs) from an mixed model conducted
on log-transformed Day 5 values with study";
line @1 "arm, sex and mCC consumption reported at screening as fixed effect factors. Geometrical CV% of the ratio is est
imated from the residual mean squares.";
line @1 "(1): For tpeak the medians for each product and the median difference and 95% confidence interval between THS 2
.2 Menthol and mCC is reported.";
line @1 "The 95% CI is based on the Hodges-Lehmann estimate.";

line @1 " ";
line @1 "&APPENDIX.";
line @1 "Study ID:ZRHM-REXA-07-JP Program: &fprgrname..sas Status: &repversion./&date. Page: 1 o
f &totalpage";
endcomp;

break after pagen/page;

run;

proc report data=frep1 headskip headline spacing=4 nowd split='~' style=[outputwidth=100%] style(header column)=[protec
tspecialchars=off];
where pagen=2;
  column pagen groupid paramn sord _name_ _1 space _2 space _3;
  define pagen /order order=internal noprint;
  define groupid /order order=internal noprint;
  define paramn /order "Variable" format=grp. flow style(column)=[cellwidth=10% just=l font_weight=bold];
  define sord /order order=internal noprint;

  define _name_ /display "Statistic" flow style(column)=[cellwidth=10% just=l];
  define _1 /display "THSm2.2" flow style(column)=[cellwidth=10% just=c];
  define space /display " " flow style(column)=[cellwidth=0.5% just=c];

  define _2 /display "mCC" flow style(column)=[cellwidth=10% just=c];
  define space /display " " flow style(column)=[cellwidth=0.5% just=c];

  define _3 /display "THSm2.2 - mCC Difference (h)" flow style(column)=[cellwidth=10% just=c];

COMPUTE before groupid /style=[fontweight=bold];
LINE @1 groupid grp.;
ENDCOMP;

COMPUTE after paramn ;
LINE @1 "";
ENDCOMP;

compute before pagen;

```



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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: mCC = Menthol conventional cigarettes; SA = Smoking abstinence; THSm2.2 = Tobacco Heating System 2.2 Menthol.";
line @1 "Note: Adjusted geometric least squares (LS) means and confidence intervals (CIs) from an mixed model conducted on log-transformed Day 5 values with study";
line @1 "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 "(1): For tpeak the medians for each product and the median difference and 95% confidence interval between THS 2.2 Menthol and mCC is reported.";
line @1 "The 95% CI is based on the Hodges-Lehmann estimate.";

line @1 " ";
line @1 "&APPENDIX.";
line @1 "Study ID:ZRHM-REXA-07-JP          Program: &fprgname..sas          Status: &repversion./&fdate.          Page: 2 of &totalpage";
endcomp;

break after pagen/page;

run;

ods listing;
ods rtf close;

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