

```

/*****

* AUTHOR : Nicola LAMA

* CREATED DATE: 12May2015

* DESCRIPTION: Post hoc on FEV1

* CHANGES

*      09Mar2016:   Added the following libray of programs at the end of this SAS program

                    - LIB-QC-init.sas

                    - LIB-QC-REXA.sas

*****/

%let rootlib=\\Pmichlausas03\pass\ZRH\Unblinded Data - Team 2\ZRHM-REXA-07-JP;

%let pgm=&rootlib.\PROGRAMS\TFLs QC;

%include "&pgm\LIB-QC-init.sas";

footnote "ZRHM-REXA-07-JP PH-001 FEV1.sas &sysdate &systemtime";

/* Load global macros for REXA07 QC. Data expected in SOURCE dataset*/

%include "&pgm\LIB-QC-REXA.sas";

%let precis=100; /* rounding precision */

%let CTRL_ARM=&label_THS;

```

```
/* ----- ADXP ----- */
```

```
/*
```

```
*/
```

```
proc sql; select TRT01P, count(*) as N from ADAM.ADSL where PPROT4FL="Y" group by 1; quit;
```

```
/*
```

```
Planned Treatment for Period 01          N
```

```
-----
```

```
SA                      37
```

```
THSm2.2                 70
```

```
mCC                     41
```

```
*/
```

```
proc sql; create table SOURCE as select A.* from ADAM.ADXP A
```

```
where PPROT4FL="Y" and PARAMCD="FEVPCT" and AVISITN=191 and ANL01FL="Y";
```

```
quit;
```

```
/*proc sql; select TRTP, count(*) as N from SOURCE group by 1; quit;*/
```

```
proc sql; select TRTP, count(*) as N from SOURCE where AVAL > . group by 1; quit;
```

```
/*
```

```
Planned Treatment          N
```

```
-----
```

```
SA                      37
```

```
THSm2.2                 70
```

```
mCC                     41
```

```
*/
```

```

TITLE 'Table XXX Analysis of FEV1 [%pred] - PP' ;

Title2 'THS vs SA/CC - ANALYSIS ';

filename myrtf "&dirReport.\ph001_ADXP_normGLM-&dtstamp..rtf";


ods graphics on; ods listing close; ods rtf file=myrtf nogtitle bodytitle;

/*
PROC GLM data=SOURCE order=data PLOTS=(DIAGNOSTICS RESIDUALS);

CLASS UCPDGR1 SEX TRTP;

MODEL AVAL=UCPDGR1 SEX BASE TRTP /alpha=0.05 CLPARM SOLUTION;

ESTIMATE 'THS vs mCC' TRTP 0 1 -1;

ESTIMATE 'THS vs SA' TRTP -1 1 0;

LSMEANS TRTP / pdiff =control(&label_THS) alpha=0.05 cl;

ods output ModelANOVA=modela;

ods output LSMeanCL=LSMeans;

ods output LSMeanDiffCL=LSMeansDiff;

ods output estimates=est;

ods output FitStatistics=fit;

by PARAMCD AVISITN AVISIT;

RUN;*/

%fitGLM3();

ods rtf close;filename myrtf clear;

```

```
Title2 'THS vs SA/CC - RESULTS (normal)';

filename myrtf "&dirReport.\ph001_ADXP_normResults-&dtstamp..rtf";

ods graphics on; ods listing close; ods rtf file=myrtf nogtitle bodytitle;

Title3 "";

%printGLM3(ph001_ADXP_normLSMEAN, ph001_ADXP_normRES, 100 );

ods rtf close; filename myrtf clear; ods listing; ods graphics off;
```

```
Title; Title2;

proc datasets; delete SOURCE; run;
```

```
/*----- LIB-QC-INIT.SAS */
```

```
/******
```

```
* AUTHOR : Nicola LAMA
```

```
* CREATED DATE: 06May2015
```

```
* DESCRIPTION: QC Library for Directory init
```

```
*
```

```
*****/
```

```
OPTIONS NOCENTER PS=70 LS=150 NOFMterr NODATE NONUMBER;
```

```
%let adam_dir=20150710;
```

```
%let sdtm_dir=20150703;
```

```
/*%let adam_dir=20150508;%let sdtm_dir=20150505;%let adam_dir=20150615;*/
```

```

/* General Macro var */

LIBNAME output "&rootlib.\OUTPUT\TABLES\&adam_dir";

LIBNAME ADAM "&rootlib.\DATA\ADAM\&adam_dir";

LIBNAME SDTM "&rootlib.\DATA\SDTM\&sdtm_dir";


%LET log=&rootlib.\LOG FILES\&adam_dir;

%LET dir1=&rootlib.\DATA\ADAM\&adam_dir;

%LET dirReport=&rootlib.\OUTPUT\COMPARE REPORTS\&adam_dir;

%LET ctrl=&rootlib.\OUTPUT\DATA\ADaM\&adam_dir;


/*%let dtstamp=%sysfunc(translate(%sysfunc(datetime()),datetime20.3),--,.:); */

%let dtstamp=%sysfunc(translate(%sysfunc(datetime()),datetime20.),--,.:));


/*----- LIB-QC-REXA.SAS */


/*****

* AUTHOR : Nicola LAMA

* CREATED DATE: 29Apr2015

* DESCRIPTION: QC Library for REXA study check

* CHANGES

*

*****/

%let label_CC = "mCC";

```

```
%let label_SA = "SA";
```

```
%let label_THS = "THSm2.2";
```

```
/* ----- */
```

```
/* ----- */
```

```
/* ----- */
```

```
%MACRO fitGLM3_log();
```

```
proc sort data=SOURCE out=ANDAT; by PARAMCD AVISITN AVISIT TRTP USUBJID;
```

```
PROC GLM data=ANDAT order=data PLOTS=(DIAGNOSTICS RESIDUALS);
```

```
CLASS UCPDGR1 SEX TRTP;
```

```
MODEL LAVAL=UCPDGR1 SEX LBASE TRTP /alpha=0.05 CLPARM SOLUTION;
```

```
ESTIMATE 'THS vs mCC' TRTP 0 1 -1;
```

```
ESTIMATE 'THS vs SA' TRTP -1 1 0;
```

```
LSMEANS TRTP / pdiff =control(&label_THS) alpha=0.05 cl adjust=t;
```

```
/* check opposite - just to avoid two times the LSMEANS
```

```
LSMEANS TRTP / pdiff =control(&label_CC) alpha=0.05 cl adjust=t;
```

```
LSMEANS TRTP / pdiff =control(&label_SA) alpha=0.05 cl adjust=t;*/
```

```
ods output ModelANOVA=modela;
```

```
ods output LSMeanCL=LSMeans;
```

```
ods output LSMeanDiffCL=LSMeansDiff;
```

```

ods output estimates=est;

ods output FitStatistics=fit;

by PARAMCD AVISITN AVISIT;

RUN;

proc sql; drop table ANDAT; quit; run;

%MEND fitGLM3_log;


%MACRO printGLM3_log(outTableLSMean, outTableRatio);

/* Summary sample size*/

Title3 'Summary sample size';

proc sql; create table num as select PARAMCD, AVISITN, AVISIT, TRTP, count(*) as N from SOURCE group
by 1,2,3,4 order by 1,2; quit; Title3;

data num; set num;

if (TRTP eq &label_THS) then TRTPN=1;

if (TRTP eq &label_CC) then TRTPN=2;

if (TRTP eq &label_SA) then TRTPN=3;

run;

/* Anti-log transformation to obtain the ratio of Geometric Means (point estimate) and
its confidence interval (lower and upper bounds); */

data diffs; set est(keep=PARAMCD Parameter AVISITN AVISIT Estimate LowerCL UpperCL Probt);

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

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

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

Reduction = 100 - Estimate;

if (Parameter="THS vs mCC") then do;

```

```
if (Estimate < 100) then Probt1=Probt/2;

else Probt1=1-Probt/2;

end; else if (Parameter="THS vs SA") then Probt1=.;
```

```
Estimate = round(Estimate*&precis,1)/&precis;

Reduction = round(Reduction*&precis,1)/&precis;

LowerCL = floor(LowerCL*&precis)/&precis;

UpperCL = ceil(UpperCL*&precis)/&precis;

Probt = ceil(Probt*1000)/1000;

Probt1 = ceil(Probt1*1000)/1000;

run;
```

```
data fit; set fit;

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

CVperc=ceil((CVperc)*&precis)/&precis;

run;
```

```
data LSMeans; set LSMeans;

LSMean=round(exp(LSMean)*&precis, 1)/&precis;

LowerCL=floor(exp(LowerCL)*&precis)/&precis;

UpperCL=ceil(exp(UpperCL)*&precis)/&precis;

run;
```

```
proc sql; create table output.&outTableLSMean as

select A.PARAMCD, A.AVISITN, A.AVISIT, B.TRTPN, A.TRTP, B.N, A.LSMean format=BEST12., A.LowerCL
format=BEST12., A.UpperCL format=BEST12.

/*cat("(" ,LowerCL," ",UpperCL,")") AS CI95*/ from LSMeans A, num B where A.PARAMCD=B.PARAMCD

and A.AVISIT=B.AVISIT and A.TRTP=B.TRTP order by A.PARAMCD, A.AVISITN, B.TRTPN; quit;
```



```

proc sql; create table output.&outTableRatio as select
D.PARAMCD, D.AVISITN, D.AVISIT, D.Parameter,
D.Estimate AS RATIOp format=BEST12.,
D.LowerCL format=BEST12.,
D.UpperCL format=BEST12.,
D.Reduction format=BEST12.,
D.Probt AS P2side format=BEST12.,
D.Probt1 AS P1side format=BEST12.,
F.CVperc format=BEST12.
from diffs D, fit F where D.PARAMCD=F.PARAMCD and D.AVISITN=F.AVISITN; quit;

proc sql; drop table diffs; drop table fit; drop table LSMeans; drop table est; drop table modela;quit;

Title3 "LS MEANS by Exposure";

proc print data=output.&outTableLSMean/*(DROP=PARAM)*/ noobs; run; Title3;

/*%let var_drop = PARAM;

%if (&TEST_FL=0) %then %let var_drop = &var_drop Probt;*/

Title3 "Ratio (%)";

proc print data=output.&outTableRatio/*(DROP=&var_drop)*/ noobs; by PARAMCD; run; Title3;

%MEND printGLM3_log;

%MACRO fitGLM3();

```

```

proc sort data=SOURCE out=ANDAT; by PARAMCD AVISITN AVISIT TRTP USUBJID;

PROC GLM data=ANDAT order=data PLOTS=(DIAGNOSTICS RESIDUALS);

CLASS UCPDGR1 SEX TRTP;

MODEL AVAL=UCPDGR1 SEX BASE TRTP /alpha=0.05 CLPARM SOLUTION;

ESTIMATE 'THS vs mCC' TRTP 0 1 -1;

ESTIMATE 'THS vs SA' TRTP -1 1 0;

LSMEANS TRTP / pdiff =control(&label_THS) alpha=0.05 cl adjust=t;

/* check opposite - just to avoid two times the LSMEANS

LSMEANS TRTP / pdiff =control(&label_CC) alpha=0.05 cl adjust=t;

LSMEANS TRTP / pdiff =control(&label_SA) alpha=0.05 cl adjust=t;*/

ods output ModelANOVA=modela;

ods output LSMeanCL=LSMeans;

ods output LSMeanDiffCL=LSMeansDiff;

ods output estimates=est;

ods output FitStatistics=fit;

by PARAMCD AVISITN AVISIT;

RUN;

proc sql; drop table ANDAT; quit; run;

%MEND fitGLM3;

```

```

%MACRO printGLM3(outTableLSMean, outTableRES, precis);

```

```

/* Summary sample size*/

```

```

Title3 'Summary sample size';

```

```

proc sql; create table num as select PARAMCD, AVISITN, AVISIT, TRTP, count(*) as N

```

```

from SOURCE group by 1,2,3,4 order by 1,2; quit; Title3; run;

data num; set num;

if (TRTP eq &label_THS) then TRTPN=1;

if (TRTP eq &label_CC) then TRTPN=2;

if (TRTP eq &label_SA) then TRTPN=3;

run;

data diffs; set est(keep=PARAMCD Parameter AVISITN AVISIT Estimate LowerCL UpperCL Probt);

Estimate = round(Estimate*&precis,1)/&precis;

LowerCL = floor(LowerCL*&precis)/&precis;

UpperCL = ceil(UpperCL*&precis)/&precis;

Probt = ceil(Probt*1000)/1000;

run;

data fit; set fit;

RootMSE=ceil((RootMSE)*&precis)/&precis;

run;

data LSMeans; set LSMeans;

LSMean=round(LSMean*&precis, 1)/&precis;

LowerCL=floor(LowerCL*&precis)/&precis;

UpperCL=ceil(UpperCL*&precis)/&precis;

run;

proc sql; create table output.&outTableLSMean as

select A.PARAMCD, A.AVISITN, A.AVISIT, B.TRTPN, A.TRTP, B.N, A.LSMean format=BEST12., A.LowerCL
format=BEST12., A.UpperCL format=BEST12.

/*cat("(" ,LowerCL," ",UpperCL,")") AS CI95*/ from LSMeans A, num B where A.PARAMCD=B.PARAMCD

```

and A.AVISIT=B.AVISIT and A.TRTP=B.TRTP order by A.PARAMCD, A.AVISITN, B.TRTPN; quit;

```
proc sql; create table output.&outTableRES as select
```

```
D.PARAMCD, D.AVISITN, D.AVISIT, D.Parameter,
```

```
D.Estimate AS Difference format=BEST12.,
```

```
D.LowerCL format=BEST12.,
```

```
D.UpperCL format=BEST12.,
```

```
D.Probt AS P2side format=BEST12.,
```

```
F.RootMSE format=BEST12.
```

```
from diffs D, fit F where D.PARAMCD=F.PARAMCD and D.AVISITN=F.AVISITN; quit;
```

```
proc sql; drop table diffs; drop table fit; drop table LSMeans; drop table est; drop table modela;quit;
```

```
Title3 "LS MEANS by Exposure";
```

```
proc print data=output.&outTableLSMean/*(DROP=PARAM)*/ noobs; run; Title3;
```

```
/*%let var_drop = PARAM;
```

```
%if (&TEST_FL=0) %then %let var_drop = &var_drop Probt;*/
```

```
Title3 "Estimate (difference)";
```

```
proc print data=output.&outTableRES/*(DROP=&var_drop)*/ noobs; by PARAMCD; run; Title3;
```

```
%MEND printGLM3;
```

```
/* ----- */
```

```
/* ----- */
```

```

/* ----- */

%MACRO fitGLM_log(CTRL_ARM, estCoef);

PROC GLM data=SOURCE order=data PLOTS=(DIAGNOSTICS RESIDUALS);

  CLASS UCPDGR1 SEX TRTP;

  MODEL LAVAL=UCPDGR1 SEX LBASE TRTP /alpha=0.05 CLPARM SOLUTION;

  ESTIMATE 'THS vs Ctrl' TRTP &estCoef ; /*e.g. estCoef = -1 1*/

/* LSMEANS TRTP / pdiff =controlu(&CTRL_ARM) alpha=0.025 cl;*/

LSMEANS TRTP / pdiff =control(&CTRL_ARM) alpha=0.05 cl;

/*where TRTP in (&label_THS &CTRL_ARM); */

ods output ModelANOVA=modela;

ods output LSMeanCL=LSMeans;

ods output LSMeanDiffCL=LSMeansDiff;

ods output estimates=est;

ods output FitStatistics=fit;

by PARAMCD AVISITN AVISIT;

RUN;

%MEND fitGLM_log;

%MACRO printGLM_log(outTableLSMean, outTableRatio);

/* Summary sample size*/

Title3 'Summary sample size';

proc sql; select TRTP,PARAMCD, AVISITN, AVISIT, count(*) as N from SOURCE group by 1,2,3,4 order by
1,2; quit; Title3;

/* Anti-log transformation to obtain the ratio of Geometric Means (point estimate) and
its confidence interval (lower and upper bounds); */

```

```
data diffs; set est(keep=PARAMCD AVISITN AVISIT Estimate LowerCL UpperCL Probt);
```

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

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

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

```
Reduction = 100 - Estimate;
```

```
if (Estimate < 100) then Probt1=Probt/2;
```

```
else Probt1=1-Probt/2;
```

```
Estimate = round(Estimate*&precis,1)/&precis;
```

```
Reduction = round(Reduction*&precis,1)/&precis;
```

```
LowerCL = floor(LowerCL*&precis)/&precis;
```

```
UpperCL = ceil(UpperCL*&precis)/&precis;
```

```
Probt = ceil(Probt*&precis)/&precis;
```

```
Probt1 = ceil(Probt1*&precis)/&precis;
```

```
run;
```

```
data fit; set fit;
```

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

```
CVperc=100*ceil((CVperc)*&precis)/&precis;
```

```
run;
```

```
data LSMeans; set LSMeans;
```

```
LSMean=round(exp(LSMean)*&precis, 1)/&precis;
```

```
LowerCL=floor(exp(LowerCL)*&precis)/&precis;
```

```
UpperCL=ceil(exp(UpperCL)*&precis)/&precis;
```

```
run;
```

```
proc sql; create table output.&outTableLSMean as

select PARAMCD, AVISITN, AVISIT,TRTP, LSMean format=BEST12., LowerCL format=BEST12., UpperCL
format=BEST12.

/*cat("(",LowerCL,"",UpperCL,"") AS CI95*/ from LSMeans; quit;
```

```
proc sql; create table output.&outTableRatio as select

D.PARAMCD, D.AVISITN, D.AVISIT,

D.Estimate AS RATIOp format=BEST12.,

D.LowerCL format=BEST12.,

D.UpperCL format=BEST12.,

D.Reduction format=BEST12.,

D.Probt AS P2side format=BEST12.,

D.Probt1 AS P1side format=BEST12.,

F.CVperc format=BEST12.

from diffs D, fit F where D.PARAMCD=F.PARAMCD and D.AVISITN=F.AVISITN; quit;

proc sql; drop table diffs; drop table fit; drop table LSMeans; drop table est; drop table modela;quit;
```

Title3 "LS MEANS by Exposure";

```
proc print data=output.&outTableLSMean/*(DROP=PARAM)*/ noobs; run; Title3;
```

```
/*%let var_drop = PARAM;
```

```
%if (&TEST_FL=0) %then %let var_drop = &var_drop Probt;*/
```

Title3 "Ratio (%)";

```
proc print data=output.&outTableRatio/*(DROP=&var_drop)*/ noobs; by PARAMCD; run; Title3;
```

```
%MEND printGLM_log;
```

```
/* ----- */
```

```
/* ----- */
```

```
/* ----- */
```

```
%MACRO fitGLM(CTRL_ARM, estCoef);
```

```
PROC GLM data=SOURCE order=data PLOTS=(DIAGNOSTICS RESIDUALS);
```

```
CLASS UCPDGR1 SEX TRTP;
```

```
MODEL AVAL=UCPDGR1 SEX BASE TRTP /alpha=0.05 CLPARM SOLUTION;
```

```
ESTIMATE 'THS vs Ctrl' TRTP &estCoef ; /*e.g. estCoef = -1 1*/
```

```
/* LSMEANS TRTP / pdiff =controlu(&CTRL_ARM) alpha=0.025 cl;*/
```

```
LSMEANS TRTP / pdiff =control(&CTRL_ARM) alpha=0.05 cl;
```

```
/*where TRTP in (&label_THS &CTRL_ARM); */
```

```
ods output ModelANOVA=modela;
```

```
ods output LSMeanCL=LSMeans;
```

```
ods output LSMeanDiffCL=LSMeansDiff;
```

```
ods output estimates=est;
```

```
ods output FitStatistics=fit;
```

```
by PARAMCD AVISITN AVISIT;
```

```
RUN;
```

```
%MEND fitGLM;
```

```
%MACRO printGLM(outTableLSMean, outTableDiff);
```



```
/* Summary sample size*/
```

```
Title3 'Summary sample size';
```

```
proc sql; select TRTP,PARAMCD, AVISITN, AVISIT, count(*) as N from SOURCE group by 1,2,3,4 order by 1,2; quit; Title3;
```

```
data diffs; set est(keep=PARAMCD AVISITN AVISIT Estimate LowerCL UpperCL Probt);
```

```
Estimate = round(Estimate*&precis,1)/&precis;
```

```
Reduction = round(Reduction*&precis,1)/&precis;
```

```
LowerCL = floor(LowerCL*&precis)/&precis;
```

```
UpperCL = ceil(UpperCL*&precis)/&precis;
```

```
Probt = ceil(Probt*&precis)/&precis;
```

```
run;
```

```
data fit; set fit;
```

```
RootMSE=ceil((RootMSE*&precis)/&precis;
```

```
run;
```

```
data LSMeans; set LSMeans;
```

```
LSMean=round(LSMean*&precis, 1)/&precis;
```

```
LowerCL=floor(LowerCL*&precis)/&precis;
```

```
UpperCL=ceil(UpperCL*&precis)/&precis;
```

```
run;
```

```
proc sql; create table output.&outTableLSMean as
```

```
select PARAMCD, AVISITN, AVISIT,TRTP, LSMean format=BEST12., LowerCL format=BEST12., UpperCL format=BEST12.
```

```
/*cat("(",LowerCL,"",UpperCL,"") AS CI95*/ from LSMeans; quit;
```

```

proc sql; create table output.&outTableDiff as select

D.PARAMCD, D.AVISITN, D.AVISIT,

D.Estimate AS Difference format=BEST12.,

D.LowerCL format=BEST12.,

D.UpperCL format=BEST12.,

D.Reduction format=BEST12.,

D.Probt AS P2side format=BEST12.,

F.RootMSE format=BEST12.

from diffs D, fit F where D.PARAMCD=F.PARAMCD and D.AVISITN=F.AVISITN; quit;

proc sql; drop table diffs; drop table fit; drop table LSMeans; drop table est; drop table modela;quit;

Title3 "LS MEANS by Exposure";

proc print data=output.&outTableLSMean/*(DROP=PARAM)*/ noobs; run; Title3;

/*%let var_drop = PARAM;

%if (&TEST_FL=0) %then %let var_drop = &var_drop Probt;*/

Title3 "THS Effect (difference)";

proc print data=output.&outTableDiff/*(DROP=&var_drop)*/ noobs; by PARAMCD; run; Title3;

%MEND printGLM;

```