Analysis of Drug X phase III

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Cochran- Mantel-Haenszel (CMH) test

The PASI at visit 6 was compared between treatments

adjusted for baseline body weight group (<=100kg and >100kg) and dichotomous baseline PASI score by median

Ho: no overall treatment difference

Cochran- Mantel-Haenszel (CMH) test: The PASI 75 at visit 6 compared between test drug arms

The FREQ Procedure

Summary Statistics for ARMCD by AVAL
Controlling for weightgrp and basemedian

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)				
Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	803.0318	<.0001
2	Row Mean Scores Differ	3	1190.0421	<.0001
3	General Association	96	1516.6704	<.0001

Total Sample Size = 1831

Reject Ho at 0.05 level

Significant overall treatment difference

Primary analysis: Binary logistic regression

Response: PASI 75

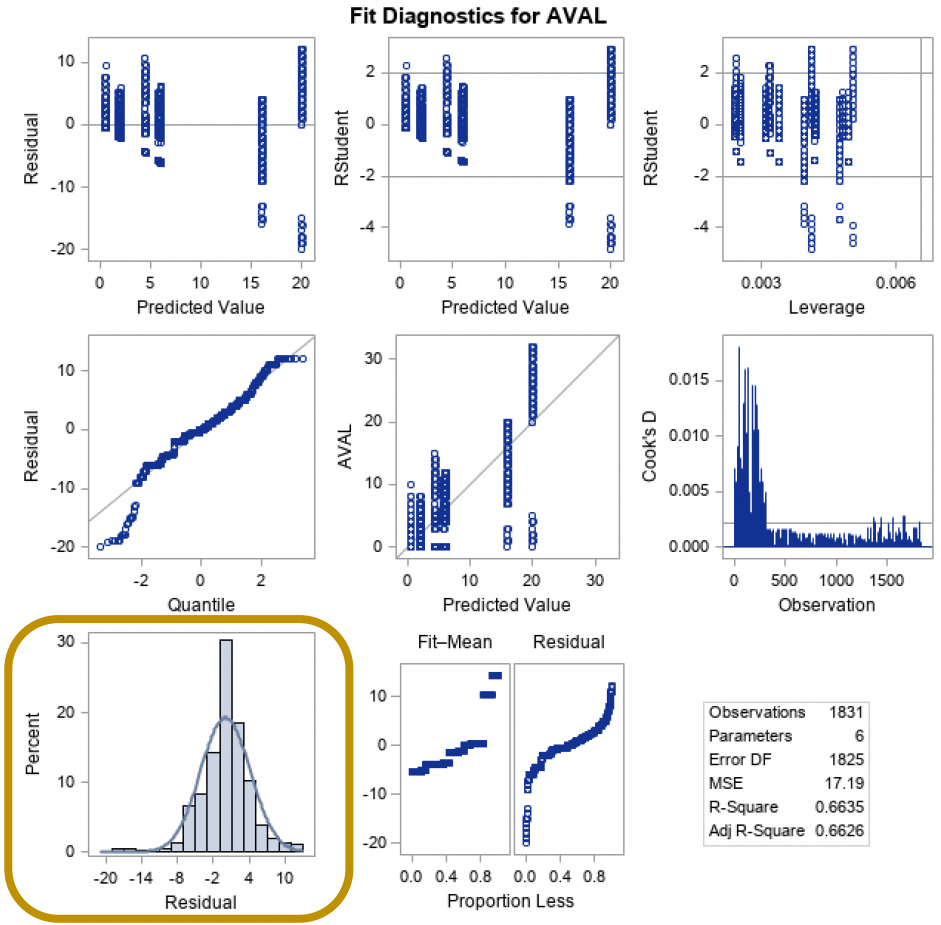
(whether patient had a 75% or greater reduction from baseline in the PASI score)

Covariates:

treatment,
baseline body weight group
dichotomous baseline PASI score by median

No obvious violation of assumptions

Check assumptions



Primary analysis: Binary logistic regression

Response: PASI 75

(whether patient had a 75% or greater reduction from baseline in the PASI score)

Covariates:

treatment,
baseline body weight group
dichotomous baseline PASI score by median

Randomized experiments

No obvious correlation

Check correlations

primary analysis: PASI 75 at visit 6 by logistic regression

The REG Procedure

Number of Observations Read	1831
Number of Observations Used	1831

Correlation

Variable	arm2	arm3	arm4	weightgrp	basemedian	AVAL
arm2	1.0000	-0.3129	-0.3137	0.0164	0.0083	-0.1214
arm3	-0.3129	1.0000	-0.5008	-0.0095	-0.0352	-0.1891
arm4	-0.3137	-0.5008	1.0000	0.0132	0.0484	-0.3205
weightgrp	0.0164	-0.0095	0.0132	1.0000	-0.0304	-0.0180
basemedian	0.0083	-0.0352	0.0484	-0.0304	1.0000	0.2541
AVAL	-0.1214	-0.1891	-0.3205	-0.0180	0.2541	1.0000

Primary analysis: Binary logistic regression

Response: PASI 75

(whether patient had a 75% or greater reduction from baseline in the PASI score)

Covariates:

treatment,
baseline body weight group
dichotomous baseline PASI score by median

Overall model is significant

All covariate except weight group are significant

ANOVA table and hypothesis testing of covariates

primary analysis: PASI 75 at visit 6 by logistic regression

The REG Procedure
Model: MODEL1
Dependent Variable: AVAL

Number of Observations Read	1831
Number of Observations Used	1831

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	61857	12371	719.70	<.0001
Error	1825	31371	17.18955		
Corrected Total	1830	93228			

Root MSE	4.14603	R-Square	0.6635
Dependent Mean	5.77662	Adj R-Sq	0.6626
Coeff Var	71.77251		

Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	16.00635	0.26097	61.34	<.0001
arm2	1	-14.16895	0.33623	-42.14	<.0001
arm3	1	-13.98327	0.28952	-48.30	<.0001
arm4	1	-15.53691	0.28966	-53.64	<.0001
weightgrp	1	0.11030	0.20391	0.54	0.5886
basemedian	1	3.96435	0.19431	20.40	<.0001

Supplemental analysis: linear mixed effect model

Response:

continuous endpoint PASI

(% reduction from baseline in PASI score))

Covariates:

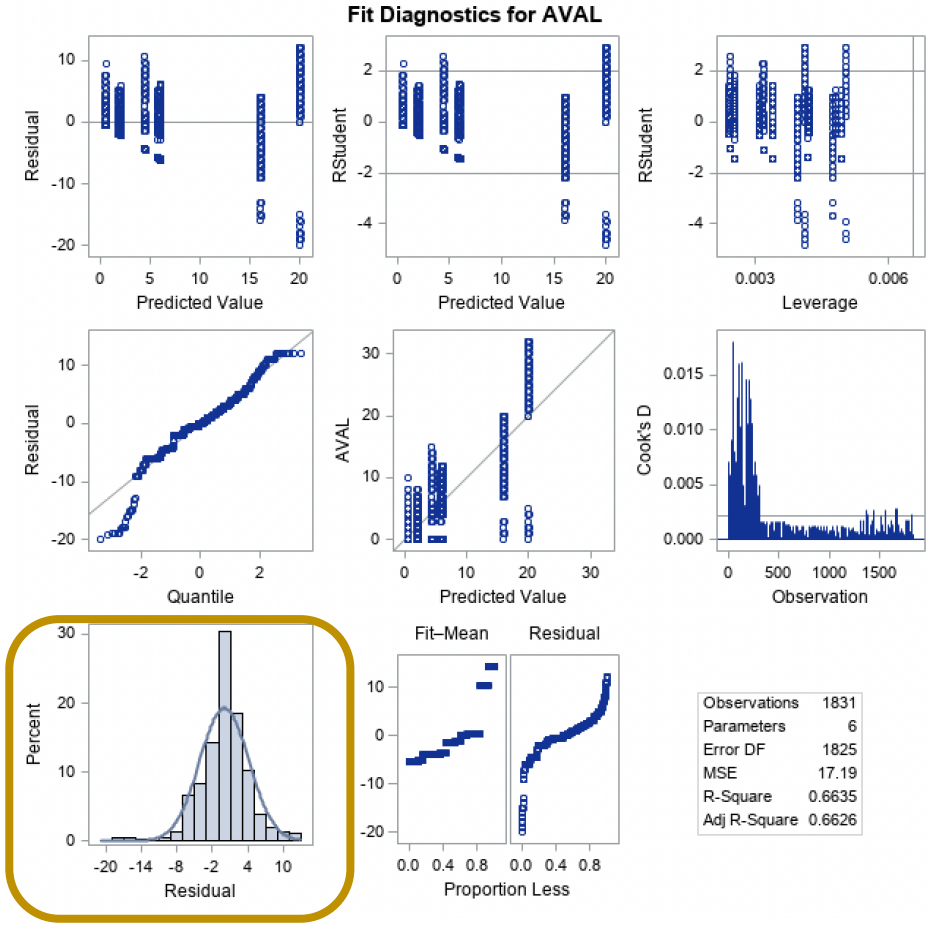
treatment,

baseline body weight group

dichotomous baseline PASI score by median

No obvious violation of assumptions

Check assumptions



Supplemental analysis: linear mixed effect model

Response:

continuous endpoint PASI

(% reduction from baseline in PASI score))

Covariates:

treatment,
baseline body weight group
dichotomous baseline PASI score by median

Randomized experiments

No obvious correlation

Check correlations

supplemental analysis: linear mixed effect model to analyze repeated measure of continuous endpoint

The REG Procedure

Number of Observations Read	1831
Number of Observations Used	1831

Correlation

Variable	arm2	arm3	arm4	weightgrp	basemedian	PASI_change
arm2	1.0000	-0.3129	-0.3137	0.0164	0.0083	0.1022
arm3	-0.3129	1.0000	-0.5008	-0.0095	-0.0352	0.1121
arm4	-0.3137	-0.5008	1.0000	0.0132	0.0484	0.2878
weightgrp	0.0164	-0.0095	0.0132	1.0000	-0.0304	-0.0034
basemedian	0.0083	-0.0352	0.0484	-0.0304	1.0000	0.5821
PASI_change	0.1022	0.1121	0.2878	-0.0034	0.5821	1.0000

Supplemental analysis: linear mixed effect model

Response:

continuous endpoint PASI
(% reduction from baseline in PASI score))

Covariates:

treatment,
baseline body weight group
dichotomous baseline PASI score by median

Overall model is significant

All covariate except weight group are significant

ANOVA table and hypothesis testing of

supplemental analysis: linear mixed effect model to analyze repeated measure of continuous endpoint

The REG Procedure
Model: MODEL1
Dependent Variable: PASI_change

Number of Observations Read	1831
Number of Observations Used	1831

Analysis of Variance

Source	DF	Sum of Squares	Mean Square	F Value	Pr > F
Model	5	103906	20781	824.9	<.0001
Error	1825	45999	25.20487		
Corrected Total	1830	149905			

Root MSE	5.02045	R-Square	0.6931
Dependent Mean	14.89732	Adj R-Sq	0.6923
Coeff Var	33.70031		

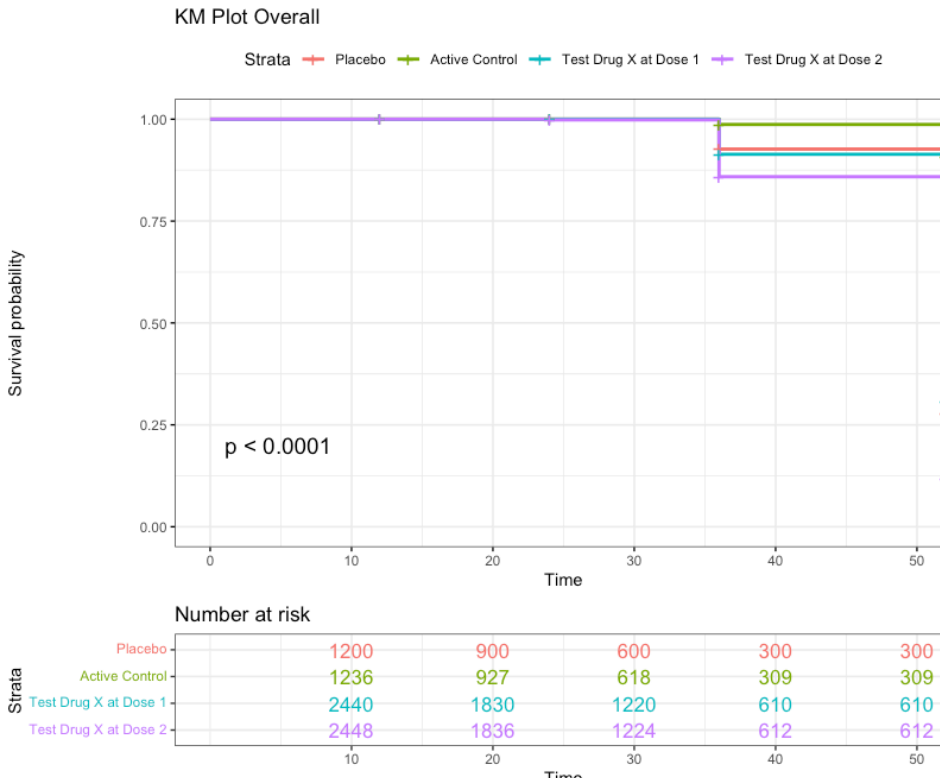
Parameter Estimates

Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	-1.87424	0.31600	-5.93	<.0001
arm2	1	13.85175	0.40714	34.02	<.0001
arm3	1	13.54811	0.35058	38.65	<.0001
arm4	1	15.18475	0.35076	43.29	<.0001
weightgrp	1	0.01241	0.24691	0.05	0.9599
basemedian	1	10.21357	0.23530	43.41	<.0001

Kaplan-Meier Curves

- Using the dichotomous baseline PASI score (0 or 1) as current status and then using the visit variable “AVISIT” to be “Time” (converted to weeks) to plot the proportion of the patients with PASI 75 for all treatments

In general, it is observed that Drug X does relatively well in predicting the survival of patients staying in the trial



Log Rank

In general, due to the p-value being very small in both models, one would reject the null hypothesis of saying that the survival curves of the treatments are identical to one another. That is, each of the treatment's survival curve is different from one another

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Call:
survdiff(formula = Surv(adpa_new$Weeks, adpa_new$PCHGCA1N) ~
    as.factor(TRTP) + strata(as.factor(CHG)), data = adpa_new)

                                 N Observed Expected (O-E)^2/E (O-E)^2/V
as.factor(TRTP)=Active control  1200      254    292.0      4.95     17.47
as.factor(TRTP)=Placebo         1236       33     26.5      1.60      5.45
as.factor(TRTP)=Test drug 140mg 2440      511    572.0      6.50     30.03
as.factor(TRTP)=Test drug 210mg 2448      702    609.5     14.03     70.76

 Chisq= 81.6  on 3 degrees of freedom, p= <2e-16
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Call:
survdiff(formula = Surv(adpa_new$Weeks, adpa_new$PCHGCA1N) ~
    as.factor(TRTP) + strata(BASE), data = adpa_new)

                                 N Observed Expected (O-E)^2/E (O-E)^2/V
as.factor(TRTP)=Active control  1200      254      244       0.4     1.004
as.factor(TRTP)=Placebo         1236       33      250     188.1   470.005
as.factor(TRTP)=Test drug 140mg 2440      511      499       0.3     0.944
as.factor(TRTP)=Test drug 210mg 2448      702      507      74.7   239.223

 Chisq= 552  on 3 degrees of freedom, p= <2e-16
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