Homework for MS Participants

in the

2020 UConn Statistics Virtual Biopharmaceutical Summer Academy

Phase II

Disclaimer:

The examples and references are created based on publicly available open-source information. It is for educational purpose only. The presentations reflect the views of the speakers based on their understanding of the open source information and have not been evaluated by the owner of the products or Boehringer Ingelheim. The names of the actual products mentioned may be the trademarks of their respective owners. The materials cannot be used for promotional activities. They are not intended to diagnose, treat, cure or prevent any disease.

Disclaimer of data:

The data is simulated and is not real data from clinical study. They are for educational purpose only.

Once completed, please send your presentation to us along with a write-up to explain what you have done and what is the story that you want to tell us through them. The final presentation will be on the last day of the academy.

The homework has two parts: Trial-design part and the data analysis part.

Trial-design part

1. Sample size calculation: For the first exercise, assume that the trial will have two arms: one arm of test drug with a dose of 210 Q2W and placebo arm. Please calculate required sample size to detect a significance difference in PASI 75 at week 12 between treatment arm and placebo arm assuming

a. 1:1 randomization
b. 2:1 randomization

Placebo arm is assumed to have an affect size of 10%. For test drug arm assume 3 different effect size: 20%, 30% and 50%.

2. Sample size calculation based on MCP-MOD.

We postulate that the 210 mg Q2WK dose of test drug will have 20% higher PASI 75 efficacy than etanercept, the 140 mg Q2WK and 280 mg monthly doses will have etanercept-like efficacy, and the 70 mg Q2WK dose will have half the efficacy of etanercept. Based on PASI 75 response rates in past etanercept studies, these assumptions translate into PASI 75 response rates at week 12 equal to 56%, 47%, 47%, 23.5% and 10% for 210 mg Q2WK dose, 140 mg Q2WK, 280 mg Q4WK, 70 mg Q2WK and placebo respectively.

Sample R –code will be provided.

Data analysis part

<u>Baseline characteristic/ demography (Do all the analysis by treatment group/ different dose group)</u>

3. Summarize and compare baseline characteristics (age, Sex, weight, PASI, SPGA) of the patients between the test drug arms: placebo, 70 mg, 140 mg, 210 mg and 280 mg. provide a summary of the findings.

Note: Use ADSL datasets.

Analysis of Efficacy (Do all the analysis by treatment group/ different dose group)

4. Analysis of primary and secondary endpoints: Provide summary of efficacy analysis.

Suggest including, but not limited to, below analysis:

a. Include graphical display of improvement in PASI score over time (~~baseline, week 2, week3, …., week 6~~) for all treatment groups. Do this for PASI 50, 75, 90 and 100. Also do this for sPGA score.

Note: Use ADPA dataset. Baseline value is recorded under column "BASE" in ADPA dataset.

b. Provide summary of efficacy results, for PASI 50, 75, 90 and 100 scores, at week 12. Also do this for sPGA score.
5. Is there any effect of baseline characteristic on primary and secondary endpoint: PASI score or sPGA score?
6. Please provide any other findings for example: association between primary, secondary endpoints, findings in base line characteristics etc.

Analysis of Safety (Do all the analysis by treatment group/ different dose group)

7. Summarize overall adverse event by preferred term, highest grade (severity) and treatment.

   Suggestion: Summarize adverse events by number of patients with highest grade and not by instances of an adverse events. For example, if patient1 experienced diarrhea with two grade 2 instances and one grade 3 instance then count this patient one time only for grade 3 diarrhea. If the adverse events are in the dataset has severity (mild, moderate, severe etc.) instead of grades 1-2-3-4 then use the same logic as grades.

   Use ADAE dataset for this exercise.