Recruitment Case Study: PRO data analysis from a clinical trial database Background

• The client is a big pharma company with a prostate cancer drug already approved for metastatic cancer.

• The company wants to move the drug into the non-metastatic cancer arena. • Having completed a full clinical development program, the client is planning to report the Phase 3 clinical trial results and submit a filing for regulatory approval with the EMA (European Medicines Agency). • The trial compared patients receiving the drug with patients receiving standard of care (SoC).

• The primary endpoint is metastatic free survival. Among the secondary endpoints, patient reported outcomes (PRO) were included. • Patient-reported outcomes were assessed through different instruments. We mention below some of those: o European Organization for Research and Treatment of Cancer Core Quality of Life questionnaire (EORTC QLQ-C30) o European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Prostate 25 (EORTC QLQ-PR25) o EuroQoL Group-5 Dimension-5 Level Instrument (EQ-5D-5L) • The client wants to include a PRO label claim in their EMA submission and asked you to perform the analyses on the PRO-related endpoints. For the current task, it will be assumed that the client is only interested in the global health status (GHS)/ quality of life (QoL) part of the EORTC QLQ-C30. The outcome variable reflecting GHS/QoL takes values from 0-100; higher score indicates better quality of life. The PRO instruments will be collected at the timepoints as per the table below:

PRO assessment schedule

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Scale/Timepoint | Baseline | Week 4 | Week 8 | Week 12 |
| GHS/QoL | x | x | x | x |

Information: A PRO is a measurement based on a report that comes from the patient (i.e., study subject) about the status of patient’s health condition without amendment or interpretation of the patient’s report by a clinician or anyone else. A PRO can be measured by self-report or by interview, provided that the interviewer records only the patient’s response. Symptoms or other unobservable concepts known only to the patient (e.g., pain severity or nausea) can only be measured by PRO measures. PROs can also assess the patient perspective on functioning or activities that may also be observable by others.

Task

The attached excel file (Data for case study Greece\_20220303) includes GHS/QoL measures from this clinical trial for the 3 post-baseline timepoints. There is a description of the variables in the “Info” sheet. Prepare a 15-min presentation (MS PowerPoint) using the data from the attached excel file in which you will address the following using any software that is appropriate for the analysis. For all analyses assume that the significance level is α=0.05.

Part 1

a) Present descriptive statistics and appropriate visualization illustrating the change from baseline in GHS/QoL for both treatment groups across all time points. Interpret the results.

b) Build an appropriate statistical model by modeling both the mean, the variance and the covariance between measurements, in which you will examine if there is any difference in the GHS/QoL scores between patients receiving client’s prostate cancer drug (i.e., drug X) and patients receiving standard of care (i.e., SoC) at Week 12. Consider both marginal and random effects models in the process of model building.

Part 2

Examine if there is a difference in the GHS/QoL between patients receiving drug X and those on SoC across all available timepoints.

Part 3

Provide appropriate interpretations of the meaning of the variance and covariance parameters of the estimated covariance and correlation matrix of observations, using the model at Part 1 b.

Part 4

Suppose that a change from baseline of 5 (or more) points indicates an improvement in the GHS/QoL scale. a) Create a new binary variable to classify patients based on their improvement or no improvement status at Week 4. b) Present descriptive statistics and appropriate visualization illustrating improvement and nonimprovement status for both treatment arms at Week 4. c) Analyze improvement to see if the probability of improvement at Week 4 is different between those patients receiving drug X and those on SoC. d) Consider the same analysis at weeks 8 and 12 separately. How do your inferences change compared with those obtained at week 4?