Application of Item Response Theory Model for Mayo Score in Ulcerative Colitis in Early Signs of Efficacy Trials

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Objectives: Traditional approaches to power studies in Ulcerative Colitis (UC) generally use the Mayo Score while disregarding the underlying nature of the subcomponent domains. The goal of this work was to determine if Item Response Theory (IRT) [1] could improve the power and maintain the type I error in typical Early Signs of Efficacy (ESOE) trials within this population and assess its imprecision and bias in estimation of remission rate.

Methods: A database of Phase 2 and 3 studies was utilised, providing a total number of 1693 patients. Data of each item were modeled as fixed effects using two parameter logistic model, a single UC latent variable was used to describe the patient-specific disease progression time course and a drug effect was estimated. Estimation following stochastic simulation from the final model or bootstrapping was used to assess power, type I error, bias and imprecision of the remission rate.

Results: The final IRT model contained 5 ordered categorical submodels describing both local and central endoscopy, stool frequency, rectal bleeding, and Physician Global Assessment subscores. Overall, simulated percentage of subjects in remission was in good agreement with the observed percentage. For a drug effect equivalent to 20% of subjects in remission and 30 patients per cohort in a 1:1 randomized to active versus placebo trial, the power and type I error [95% CI] to detect the drug effect was 98.8% and 6.8[3.68-9.92]%, respectively. Bias and root MSE of the remission rate was found to be 3.1 and 7.9%, respectively.

Conclusions: The application of IRT provided characterisation of the individual items and prediction of the composite Mayo scores. This approach showed increased power to detect drug effect while preserving the type I error. The utility of IRT models in predicting the UC remission rate by utilising the relationship of items to the underlying latent disease variable based on total prior available data, is also highlighted.