The Statistical Design and Analysis of Pharmacogenetic Studies in Clinical Trials

Chintu Desai
Associate Director, Biostatistics
Biogen Idec

*(Submitted for oral presentation)*

**Abstract:** Pharmacogenetics is the study of how genetic factors may affect the efficacy and safety of a therapeutic agent. To date, pharmaceutical drug trials have largely incorporated pharmacogenetic investigations as a supplement to the main study objectives. As such, the approach is subject to statistical issues regarding study design, power and efficient analysis. The design and analysis of clinical trials specifically for pharmacogenetic endpoints forms the basis of this talk.

Perhaps the most important issue in current pharmacogenetic studies is lack of power to detect treatment differences. Contributing factors include, but are not limited to, patient availability, rare variants and small effect sizes. In addition, a pharmacogenetic variant cannot always be treated as merely another intrinsic covariate if the genetic groups are not well balanced or the genetic pathway is complex. Currently, adequately powered study designs tend to require sample sizes which may not be practical for commercial clinical trials. Therefore the challenge is to develop study designs which are feasible.

The presentation will be based upon one part of a research project, proposing a potential study design to be used in a pharmacogenetic setting, which we have named the Subgroup Extension Design. The concept is to investigate a multi-layered hypothesis, specifically whether there is a clinically meaningful therapeutic effect in a disease cohort, either overall or in a subgroup based upon a genetic separator. The design aspects including results of investigations into different clinical scenarios and implications for the analysis of study data will be discussed.