ASA-BI-NESS Statistics Webinar Series

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November 7, Thursday 10:30-11:30 am EST

For more information regarding upcoming webinar schedule, please contact medecc.us@boehringer-ingelheim.com

Title

Extensions of the TEQR and mTPI designs including non-monotone efficacy in addition to toxicity in dose selection

Abstract

With the emergence of immunotherapy and other novel therapies, the traditional assumption that the efficacy of the study drug increases monotonically with dose levels will not always hold true. Therefore, dose-finding designs such as mTPI (modified toxicity probability interval design) and TEQR (toxicity equivalence range design) that evaluate only toxicity data in determining the optimal dose may not be adequate. Hence, this webinar will cover three new early phase designs that we have proposed to consider efficacy in addition to safety in selecting the optimal dose. The first two designs are the extended TEQR and mTPI designs – in these designs, the optimal dose for safety and efficacy is determined by applying isotonic regression to the observed toxicity and efficacy rates, once the early phase trial is completed. The third design is the 2D TEQR design, the frequentist counterpart of an existing Bayesian design called the TEPI (Toxicity Efficacy Probability Interval) design. We conduct simulation studies to investigate the operating characteristics of our proposed designs for various underlying toxicity and response rates and compare them to existing designs. We found that the extended mTPI design selects the optimal dose for safety and efficacy more accurately than the other designs considered for most of the scenarios explored. Although for the same sample size and cohort size, the frequentist 2D TEQR design is less accurate than the Bayesian TEPI design in selecting the optimal dose, the accuracy of optimal dose selection of the 2D TEQR design can be increased, in many cases, with a moderate increase in cohort size.

Professional Biography

Revathi Ananthakrishnan works as a Biostatistician at Celgene on designing, analyzing and interpreting immuno-oncology trials. She has a broad interdisciplinary background of Mathematics, Statistics, Physics and Biology. She did her PhD in (Bio)Physics and post-doc in Biomathematics. After her post-doc, she started working as a clinical trials Biostatistician in Industry, and did her PhD in Biostatistics while working in Industry. She is interested in various aspects of Oncology clinical trials and clinical trial methodology, especially in the design of early phase Oncology trials. She has worked on several early phase Oncology trials as well as trials for regulatory submission for solid tumors and blood cancers.

Sponsored by

- American Statistical Association (Boston, Connecticut, Florida, New Jersey, Princeton/Trenton, and Washington chapters)
- Boehringer Ingelheim Pharmaceuticals, Inc. (Biostatistics and Data Sciences Department)
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For interested participants

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