Dose Escalation with Overdose Control using a Quasi-Continuous Toxicity Score in Cancer Phase I Clinical Trials

Zhengjia (Nelson) Chen

Department of Biostatistics and Bioinformatics
Emory University

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GEMS classroom, 3rd Floor in Shriner's Building
Coffee, water, and cookies will be provided

Abstract

In cancer Phase I clinical trials, 3+3 design is still used for its simplicity, but it has limitations such as inaccuracy of maximum tolerated dose (MTD) and inflexibility. Escalation With Overdose Control (EWOC) is a Bayesian adaptive design which can overcome these limitations and control the probability of overdosing. However, like other Phase I designs, EWOC treats toxicity response coarsely as a binary indicator (Yes vs No) of dose limiting toxicity (DLT) although patient usually has multiple toxicities and a lot of useful toxicity information is discarded. We establish a novel scoring system to treat toxicity response as a quasi-continuous variable and utilize all toxicities of patients. Our system consists of generally accepted and objective components (a logistic function, grade and type of toxicity, and whether the toxicity is DLT) so that it is relatively objective. We couple our system with EWOC to develop a new design called Escalation With Overdose Control.
using Normalized Equivalent Toxicity Score (EWOC-NETS) by replacing the binary indicator of DLT and the target probability of DLT with a Normalized Equivalent Toxicity Score (NETS) and a Target NETS (TNETS), respectively. Simulation studies and its application to real trial data demonstrate that EWOC-NETS can treat toxicity response as a quasi-continuous variable, fully utilize all toxicity information, and improve the accuracy of MTD and efficiency of Phase I trial. A user-friendly software of EWOC-NETS is under development and will be available in the future.