Model-Assisted Designs for Dose Optimization in Oncology Drug Development

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Abstract

Traditional oncology drug development program is based on cytotoxic chemotherapies. The underlying assumption is that the higher the dose, the more efficacious the drug is. The paradigm is to find the maximum tolerate dose (MTD) or the recommended Phase 2 dose (RP2D) in Phase I studies followed by testing the drug efficacy at MTD or RP2D in Phase II studies. This paradigm, however, may not be suitable for molecularly targeted agents and immunotherapies because higher dose can lead to higher toxicity but may not result in higher efficacy. In 2022, US FDA launch "Project Optimus" to reform the dose optimization and dose selection paradigm in oncology. In this talk, I will introduce the model-assisted designs, which incorporate Bayesian modeling with good statistical operating characteristics, yet easy to implement by listing precalculated boundaries to find the optimal biological dose (OBD). Three designs based on the Bayesian Optimal INterval (BOIN) design: the one-stage BOIN12 design, the two-stage utility-based U-BOIN design, and the TITE-BOIN12 design for late-onset toxicity and efficacy will be discussed. These three designs are effective in finding the OBD. Examples will be given. User-friendly free software will be demonstrated. Model-assisted designs follow the new KISS principle: Keep It Simple and Smart and are ideal for drug development.

Keywords: Bayesian Optimal Interval (BOIN) Design; Optimal Biological Dose; Project Optimus