

Model-based Phase I Designs with Incorporation of Individualized Dosing Using Toxicity Scores from Multiple Treatment Cycles

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Abstract: In the era of molecularly targeted agents (MTAs) and immunotherapies, several aspects of phase I designs need to evolve in order to adapt to the changing nature of cancer therapies and to expedite their clinical translation. We have previously developed novel phase I designs to incorporate evaluation of early efficacy, in addition to clinician-assessed toxicity scores from multiple treatment cycles, for identification of tolerable and efficacious doses for subsequent investigation. To extend our previous work, we introduced a dose algorithm that allows patients in subsequent treatment cycles to be treated with an individualized dose that is tailored to their specific tolerance and the cumulative adverse effects of the drug. The proposed method provides a comprehensive statistical framework for the personalized dose modification in subsequent treatment cycles. The design is calibrated with respect to specific operating characteristics. We conduct extensive simulations to assess the performance of the proposed design with comparison to our previous published work.