A ADAPTIVE DOSE-FINDING APPROACH FOR CORRELATED BIVARIATE BINARY AND CONTINUOUS OUTCOMES IN PHASE I ONCOLOGY TRIALS

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By incorporating efficacy into a dose-finding design, one essentially introduces the question, ‘What efficacy endpoint should be used to evaluate antitumor activity?’ Researchers often define antitumor activity with binary outcome categories (e.g., response or nonresponse) on the basis of a threshold for tumor shrinkage as a continuous variable. This discrete outcome has been used in many studies that have proposed incorporating both efficacy and toxicity in dose-finding methods for phase I trials. However, data on categorization of continuous variables by any threshold often result in a considerable loss of information, which consequently reduces statistical efficiency. In overcoming this issue, a mixed model of continuous efficacy and binary toxicity in phase I oncology trials is required. In this study, we developed a novel adaptive dose-finding approach for inclusion of correlated bivariate binary and continuous outcomes in designing phase I oncology trials. For this approach, binary toxicity and continuous efficacy outcomes are modeled jointly with a factorization model. The basic strategy of the proposed approach is based primarily on the Bayesian method. We based the dose escalation/de-escalation decision rules on the posterior distributions of both toxicity and efficacy outcomes. We compared the operating characteristics of the proposed and existing methods through simulation studies under various scenarios. We found that the recommendation rate of the true recommended dose (RD) in the proposed method was more favorable than that in the existing method when the true RD was relatively at the tail end among the tested doses. It was similar to that of the existing method when the true RD was relatively at the top end.