**Dose Escalation with Over-dose and Under-dose Control**

**Using a quasi-continuous toxicity score in Phase I/II Clinical Trials**

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**Abstract**

Escalation with overdose control (EWOC) is a Bayesian adaptive design for selecting dose levels in cancer phase I clinical trials and has been carried out for many years. However, the toxicity response was treated as binary indicator of dose limiting toxicity (DLT) and underdose control was not considered in this design. Chen et al. (2010) proposed a novel toxicity scoring system to fully utilize patients’ toxicity information using a normalized equivalent toxicity score. Chen et al. (2015) extended EWOC to Phase I/II clinical trials by controlling for under-dosing (EWOUC) to provide at least minimum efficacy of drug. In this paper, we developed EWOUC-NETS based on these two methods to combine their advantages. Additionally, we further extended this study by treating efficacy outcome as also continuous and recommended dose (RD) was chosen based primarily on Bayesian method. The dose escalation decision rules were based on the posterior distribution of both toxicity and efficacy outcomes. We compared the operation characteristics of the proposed and existing methods through simulation studies under five scenarios. We found that EWOUC-NETS with continuous efficacy outcome effectively increased the efficacy with similar DLT rate.

**Introduction**

One of the most important steps in drug development is Phase I cancer clinical trials. Evaluating a new drug’s toxic effect on patients and Phase I trials are conducted to