

Estimation of personalized maximum tolerated dose (pMTD) by incorporation of patient' s genomic profiles and all toxicity information in cancer Phase I clinical trial

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Abstract: Estimation of personalized maximum tolerated dose (pMTD) is the first critical step toward personalized medicine which can maximize the therapeutic effect of treatment for individual patient. To estimate pMTD, we propose to fully utilize the patient' s biomarkers that can predict susceptibility to specific adverse events and response as covariates in a cutting-edge Bayesian adaptive and optimal cancer Phase I clinical trial design called EWOC-NETS. The methodology of incorporating patient' s biomarker information in the estimation of pMTD for novel cancer therapeutic agent will be fully elaborated. Simulation studies demonstrate that utilization of biomarkers in EWOC-NETS can estimate pMTD while keeping its original merits: such as ethical constraint of overdose control and full utilization of all toxicity information to improve the accuracy and efficiency of pMTD estimation. A real cancer Phase I clinical trial will be presented to illustrate the utilization of genomics information for the estimation of pMTD.