

Adaptive Designs in Dose-finding Oncology Drug Combination Trials

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When two drugs are combined as a mixture in the drug development, the toxicity rate for the combo dose is expected to be higher than the individual drug and there can be several combo doses having the same toxicity rate, i.e. the MTD is not unique. It is crucial to identify all /some of the combos with the same toxicity rate and then carry the most efficacious combo to the later phase trial. In this case, the traditional 3+3 design may not be able to locate all the MTDs. So we generalize some of the adaptive design schemes that have been implemented for locating MTD for single drug to drug combination studies as well as the zone-based adaptive design. A simulation study will be conducted to compare the performance of traditional 3+3 design, zone based adaptive design, and model based adaptive designs for different scenarios and a recommendation will be provided.

Key words: Combo dose, MTD