Characteristics of early phase trial designs for immunocology and comparisons of common designs

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Abstract: Many new developments in cancer treatment in the modern era involve using patients’ own immune system to fight cancer. Therapeutic options under this framework such as immune checkpoint inhibitors and monoclonal antibodies are all success examples of immunotherapy. These agents have demonstrated promising clinical activity across many disease indications but also present new challenges in the design and analysis of the early phase clinical trials for those agents. In this presentation, we will describe several unique characteristics of these therapy options including different toxicity profiles and mechanisms of action for which the classic statistical assumptions typically associated for cytotoxic agents may no longer be applicable. We will also review a few popular designs in the literature, including the 3+3, continuous reassessment method (CRM), Bayesian optimal interval (BOIN) design, and Keyboard design, and evaluate how varying design parameters, such as number of dose levels, target toxicity rate, maximum sample size, and cohort size, could impact the performances of each design through simulations. We will focus on parameter specifications that are commonly used in real world clinical trials of immunotherapy agents. Our preliminary results indicate that 3+3 tends to have the worst performance while BOIN and Keyboard perform similarly to the CRM.