

## Innovations in Immune-Oncology Early-Phase Trial Designs: Theory, Practice and Next Steps

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### **ABSTRACT**

The explosion of immunotherapeutic (I-O) agents for cancer treatment has challenged the current assumptions of early-phase trial designs. The goal of determining the maximum tolerated dose (MTD) is no longer desirable because novel agents are characterized by reduced toxicity profiles, to the point of being essentially safe within the therapeutic dose range. Recent phase I trials for single-agent or combination therapy have focused on detecting signals of antitumor activity, pharmacokinetic / pharmacodynamics (PK/PD) relationships, or on assessing feasibility and utility of biological correlative assays. This presentation will discuss challenges brought by the new I-O agents and propose a novel statistical design for incorporating immunological endpoints into the dose-selection process. The design uses a likelihood framework to assess safety and employs randomization to skew patient allocation to the most promising/efficacious doses. The proposed methodology will be illustrated via the R package *iAdapt* and *Shiny* app that enable the user to assess the design performance under various scenarios and to facilitate trial conduct in real time.