

Dose-finding in Adoptive Cell Therapy Trials

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12:00 Noon Eastern time, Tuesday, November 9, 2021

ABSTRACT

Dose-finding clinical trials in oncology have historically served as initial safety trials to identify the maximum tolerated dose (MTD). Participants are sequentially assigned to doses based on accumulating safety data. In the development of adoptive cell therapies, dose feasibility presents a new design challenge. Adoptive cell therapy involves extracting cells from a patient, expanding them in culture up to a pre-specified number of cells, and infusing these cells back into the patient. Each dose level being studied is defined by the number of cells infused per kilogram recipient weight into the trial participant. The issue of dose feasibility arises when the desired number of cells is not reached in the expansion process. Consequently, dose assignments for some patients may deviate from the planned dose according to the dose-finding algorithm. The study objective in early development becomes identifying an MTD with high feasibility of being administered. This talk describes a new dose-finding method that adaptively accounts for safety and feasibility endpoints in guiding dose allocation. We illustrate the proposed methodology in a single simulated trial and evaluate its operating characteristics through extensive simulation studies. A design that incorporates feasibility, as a function of the quantity and quality of the product manufactured and safety, will impact which doses are carried forward for further testing of efficacy in middle development.