University of California, Irvine
Statistics Seminar

Optimizing Natural Killer Cell Doses for Heterogeneous Cancer Patients Based on Multiple Event Times

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(Bldg. #314 on campus map)

A sequentially adaptive Bayesian design is presented for a clinical trial of cord blood derived natural killer cells to treat severe hematologic malignancies. Given six prognostic subgroups defined by disease type and severity, the goal is to optimize cell dose in each subgroup. The trial has five co-primary outcomes, the times to severe toxicity, cytokine release syndrome, disease progression or response, and death. The design assumes a multivariate Weibull regression model, with marginals depending on dose, subgroup, and patient frailties that induce association among the event times. Utilities of all possible combinations of the nonfatal outcomes over the first 100 days following cell infusion are elicited, with posterior mean utility used as a criterion to optimize dose. For each subgroup, the design stops accrual to doses having an unacceptably high death rate, and at the end of the trial selects the optimal safe dose. A simulation study is presented to validate the design's safety, ability to identify optimal doses, and robustness, and to compare it to a simplified design that ignores patient heterogeneity.

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