

Data Studio

1:30–3:00pm, Wednesday, 1 April 2020

Videoconference: <https://stanford.zoom.us/j/229096257>

Investigator: Robert Lowsky Blood and Marrow Transplantation

Investigator: Ying Lu Biomedical Data Science

Title: A Novel Dose-Finding Method for a Phase 1 Clinical Trial of
Kidney Graft Immune Tolerance Induction

Summary:

Currently in the United States, over 100,000 patients undergoing dialysis for renal failure are on a wait list for transplantation because it offers the best chance for a near-normal lifestyle and improved life expectancy. Recipients of donor kidneys require lifelong adherence to combinations of immune suppression (IS) medications to prevent immune-mediated rejection of the graft.

The unmet medical needs in solid organ transplantation are to eliminate this lifelong adherence to combinations of IS medications with their serious side effects and to prevent immune-mediated rejection. We are planning a Phase 1 clinical trial to study whether conditioning the recipient using total lymphoid irradiation (TLI), anti-thymocyte globulin (ATG), and a single very low dose of total body irradiation (svldTBI) followed by an infusion of vertebral body (VB) hematopoietic cells (HCs) will result in persistent mixed chimerism after a standard-of-care deceased donor kidney transplant. We expect that persistent mixed chimerism will result in IS drug minimization/cessation and lead to an acquired immune tolerance of the graft.

One of the primary objectives is to identify the safe and effective dose of svldTBI (range 40–120 centiGray) that will support persistent mixed chimerism. We are developing a novel dose finding method that is an extension of the modified Toxicity Probability Interval design version 2 (mTPI-2). This method allows escalation and de-escalation according to a pre-tabulated decision table. Our method is based on the Bayesian probability interval of toxicity and efficacy that employs a simple beta binomial hierarchical model to find the safe and effective svldTBI dose in the interval of efficacy for mixed chimerism.

Statistical Questions

Our statistical questions concern both the theory and methodology that we are developing for this novel dose-finding method.

For more information about Data Studio:

<https://med.stanford.edu/dbds/programs/data-studio.html>