REQUEST FOR PROPOSALS

Liver Transplant Tolerance Trials

Background

Liver transplant tolerance is an unmet need. Liver transplant recipients enjoy good patient and graft survival; however, risks of long-term immunosuppression such as infection, malignancy, and metabolic side effects of CNIs contribute to morbidity in the long-term. Immunosuppression withdrawal (ISW) can be successful in approximately 15% of carefully selected liver transplant recipients. However, there are currently no biomarkers to predict the success or failure of this approach. Interventions or biomarkers that meaningfully increase the rate of successful ISW are essential to improve outcomes.

Research Objectives and Scientific Scope

The objective of this RFP is to support phase I/II multicenter interventional clinical trials of tolerance in adult liver transplant recipients. We are looking for a combination of potential interventions to increase the likelihood of successful ISW from the current 15% baseline to >40%. These interventions could include: 1) pharmacologic and/or cellular therapies expected to independently improve the likelihood of success of ISW, and/or 2) candidate biomarkers that predict successful ISW. Study populations may include de novo liver transplant candidates/ recipients or long-term patients with functioning transplants. Criteria for the operational tolerance endpoint must include a liver biopsy demonstrating histologic stability, in addition to stable liver enzymes and absence of rejection at 1 year post-ISW.

Proposals must be based on a testable mechanistic hypothesis, ideally supported by preliminary data, and include a description of the mechanistic assays that will be performed on samples from study subjects and, if appropriate, contemporaneous or historical controls (such as stored samples from subjects enrolled in prior ITN liver transplantation trials: A-WISH and OPTIMAL). Given the early clinical trial phase, we anticipate proposals that enroll 10-50 patients. Priority will be given to proposals that have a clear and strong mechanistic hypothesis. Evidence to support dosing and safety of the proposed intervention in humans must be provided in the proposal.

Applications including the following will be considered non-responsive and will not be reviewed:

- Observation-only trials
- Animal models
- Xenotransplantation

Eligibility and Application process

The ITN is fully open to reviewing compelling transplant tolerance clinical trial proposals from the general transplant research community, even if they do not fall into the specific area outlined above.

The proposals should be very brief, ideally a single page. The early proposal review process will focus on evaluating the conceptual framework of the proposed trial and its significance and suitability for further development; it does not require submission of a detailed clinical protocol. Review will potentially be an iterative process.

Please direct all proposal submissions and any questions concerning this RFP to Philip Bernstein, Director Strategic Review and Planning: submissions@immunetolerance.org
This RFP will remain open, but we will begin reviewing letters of interest by January 15th 2027.