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Title: Results of a Phase 1 Trial of Treg Adoptive Cell Transfer (TRACT) in de novo living donor kidney transplant recipients. J Leventhal[1], A LeFever[2], A Skaro[1], L Gallon[1], J Mathew[1], D Stare[1], and G Johnson[3]. [1]Northwestern University, Chicago, United States; [2]Northwestern Memorial Hospital, Chicago, United States and [3]TRACT Therapeutics, Inc., Chicago, United States.

Body: Therapeutic cell transfer using regulatory T cells (Tregs) in solid organ transplant recipients holds the promise of reducing the need for drug based immunosuppression (IS) and improving long term graft survival. In late 2014 we initiated a Phase 1 trial of autologous, polyclonally expanded Tregs in living donor kidney transplant recipients (KTx) (NCT 02145325, IND 15898). This is a nonrandomized dose-ranging study with 3 tiers of cell dosing (0.5, 1, and 5 x 10E9 cells infused, n=3 subjects/tier). Enrolled subjects underwent a nonmobilized leukopheresis at least 2 weeks prior to KTx. This leukopheresis product was cryopreserved for later isolation and manufacturing of Tregs. We have demonstrated the ability to isolate and manufacture phenotypically "pure", functional, GMP grade Tregs from a cryopreserved pheresis product in support of our IND. Briefly, we enrich for natural Tregs through sequential negative (CD8, CD19) and positive (CD25) immunomagnetic selection (CliniMACS, MIltenyi BioTec). The enriched natural Tregs undergo a 3 week expansion culture using CD3/CD28 Exp-Act® beads (Miltenyi Biotec), IL2, and sirolimus. Resultant cells need to meet the following release criteria: > 70% viable; > 70% CD4+ CD25+; < 10% CD8+ and CD19+; <3000 Exp-Act® beads/10E8 cells; endotoxin < 5.0EU/kg; negative aerobic, anaerobic and fungal sterilities, negative mycoplasma and negative gram stain, > 50% suppression of T effector proliferation in vitro. KTx recipients receive alemtuzumab induction to achieve lymphodepletion (deemed important for the later effectiveness of TRACT) and are begun on tacrolimus and mycophenolate based IS. Subjects are converted from tacrolimus to sirolimus at 30 days post KTx to provide an IS milieu conducive to the survival of infused Tregs. Tregs are infused day +60 post-KTx.

9 subjects have been enrolled and 9 subjects have received TRACT. We have successfully isolated and expanded Tregs from all collected pheresis products. All manufactured product has met release criteria. There have been no serious adverse events attributable to TRACT in any subject. Protocol biopsies performed after TRACT have not shown rejection. There have been no infectious complications. Immunophenotypic analysis of subjects shows a significant (9-20 fold) increase in % of circulating $CD4^{+}CD127^{-}CD25^{High}$Foxp3 cells in peripheral blood post TRACT. **Conclusion: TRACT using autologous polyclonally expanded Tregs appears safe. Plans for a Phase 2 trial are complete.**