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IMPACT OF DARATUMUMAB AND BELATACEPT ON HLA ANTIBODIES IN KIDNEY TRANSPLANT CANDIDATES WITH 100% CPRA: EARLY RESULTS OF ATTAIN (ITN090ST)

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Background and Aims: Despite high allocation priority, <10% of kidney transplant candidates with cPRA 100% can find a compatible donor. Current desensitization strategies are ineffective due to antibody rebound. Adding costimulation blockade to plasma cell (PC) depletion prevents antibody rebound in nonhuman primates by countering nodal B cell and Tfh expansion.
Method: ATTAIN is a pilot, phase I/II trial of daratumumab, a CD38 mAb used in multiple myeloma, plus belatacept, a high affinity CTLA4-Ig, to desensitize kidney transplant candidates with cPRA ≥99.9%. Enrolled subjects receive daratumumab (6 doses: 8 mg/kg) and belatacept (4 doses: 10 mg/kg) over 10 weeks with bone marrow and blood assessments pre-and post-treatment. The primary efficacy endpoint (PE) is a composite of (1) elimination of ≥1 HLA antibody specificity, (2) ≥50% reduction in the MFI of ≥3 HLA antibody specificities, or (3) kidney transplant from a previously incompatible donor. Target accrual is 15, enrolled in 2 cohorts (5+10).
Results: Cohort 1 (n = 5, mean age 44, 60% with previous transplant) has been enrolled and treated, with 5-31 weeks follow-up to date. The treatment was tolerated well in all 5 patients who showed a significant reduction in most HLA antibodies after treatment without manifestation of rebound. 3 of 5 participants reached the PE and 5 of 5 had >50% bone marrow (BM) PC depletion. One patient received a kidney transplant from a previously incompatible deceased donor and is doing well at 7 months post-transplant without rejection or rebound of HLA antibody. Treatment was temporarily paused in 3 subjects due to AEs (acute cholecystitis and COVID, upper GI bleed, fevers); no cases of opportunistic infection or malignancy occurred.
Conclusion: A novel HLA desensitization regimen consisting of PC depletion with Daratumumab and costimulatory blockade with Belatacept appears safe and successful in the ongoing ATTAIN clinical trial. In the initial subject, this regimen led to transplant without HLA antibody rebound or acute rejection. Longer follow-up and additional subjects are needed to confirm these promising results. ATTAIN (NCT04827979) is a trial conducted by the Immune Tolerance Network and sponsored by NIAID (award UM1AI109565).

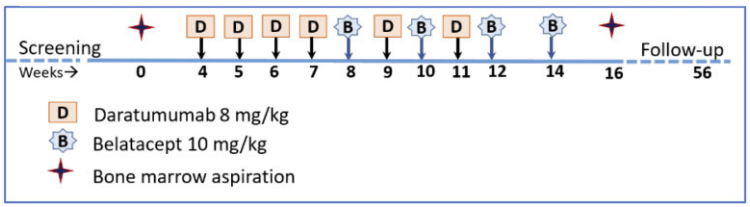

Figure 1: Study regimen.

Figure 2: Change in HLA antibodies with treatment.