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722.ALLOGENEIC TRANSPLANTATION: ACUTE AND CHRONIC GVHD, IMMUNE RECONSTITUTION

Graft-Versus-Host Disease (GvHD) Prophylaxis after Haploidentical Peripheral Blood Stem Cell Transplantation (haplo-PBSCT) Using Abatacept in Combination with Post-Transplant Cyclophosphamide (PTCy)

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Background: Multiple studies demonstrated the efficacy of PTCy in achieving successful multiple-HLA-antigen mismatched (haploidentical) donor transplantation. However, acute GvHD (aGvHD) remains a major cause of morbidity and mortality after transplantation. Furthermore, many patients (pts) experience severe cytokine release syndrome (CRS) immediately after haplo-donor transplantation, which may be a greater risk after haplo-PBSCT. We hypothesized that adding co-stimulation blockade with abatacept (Abat) starting before transplantation to a standard GvHD prophylaxis regimen of PTCy, tacrolimus, and mycophenolate mofetil in haplo-PBSCT would be safe and effective in aGvHD prevention and decrease the incidence of cytokine release syndrome (CRS) associated with use of this cell source.
Methods: This retrospective study included 50 recipients of haplo-PBSCT between 1/1/20, and 3/31/23, who received standard PTCy GvHD prophylaxis with (PTCY/Abat, n=22) or without (PTCy, n=28) the addition of Abat at a planned dose of 10 mg/kg/dose IV on days -1, +5, +14 (n=10) and +28 (n=12). Choice of donor, conditioning regimen, and use of Abat were per physician discretion. The PTCy GvHD regimen and pre- and post-transplant care of all pts were as previously described (Baker et al. Biol Blood Marrow Transplant. 2016;22:2047-55). Survival development of aGvHD or chronic GvHD (cGvHD), and engraftment success and kinetics were evaluated. CRS (Lee, et al. Blood 2014;124:188-95), aGvHD (Magic criteria, Harris et al. Biol Blood Marrow Transplant. 2016;22:4-10) and cGvHD (NIH consensus criteria, Jagasia et al. Biol Blood Marrow Transplant 2015;21:389-401) were scored per citations.
Results: In total, 22 pts received PTCy/Abat. Ten pts did not receive day +28 Abat for insurance reasons. Twenty-eight pts received PTCy without abatacept. Pt characteristics and CRS grading are described in the Table. Although distributions of diagnosis, sex, and pt or donor ages were similar between cohorts, there was some imbalance, particularly in higher use of TBI myeloablative conditioning regimen for PTCy cohort (Table). The median follow-up of survivors is 10 months. In this analysis we found a non-significant trend to lower incidence (65% vs 88% p=0.079) and severity of CRS for PTCy/Abat recipients vs PTCy recipients (Table). Only 1 of 20 evaluable PTCy/Abat recipients developed grade 2 CRS vs 6 of 26 PTCy pts. PTCy/Abat recipients achieved faster ANC engraftment (median: 15 days, 95% CI: 14-16 vs 17 days, 95% CI: 16-18; p<0.0001 (Figure 1A)) and platelet recovery (median: 15 days, 95% CI 13-22 vs 24 days 95% CI 19-29; p=0.002). No pt in either group developed 1 o or 2 o graft failure. Median peripheral blood CD3 chimerism at day +28 was 100% (range, 57-100%) for PTCy/Abat pts and 100% (range, 85-100%) for PTCy pts. The cumulative incidence of any aGvHD was 71% for PTCy/Abat pts vs 73% for PTCy pts, (p=0.9). Grade II or III aGvHD occurred in 13/21 and 1/21

evaluable PTCy/Abat pts, and 12/26 and 3/26 evaluable PTCy pts, respectively. No grade IV or liver aGvHD occurred in either group. The median time of onset of aGvHD was 54 days for PTCy/Abat pts and 36 days for PTCy pts (p= 0.08). The cumulative incidence of any grade cGvHD trended higher in the PTCy/Abat group (81% vs 50% p=0.052). Also, the PTCy/Abat group had a higher incidence of severe grade cGvHD (6/13 vs 2/10 evaluable pts). The 200-day cumulative incidence of relapse was 35% for PTCy/Abat and 11% for PTCy (p=0.2). No statistically significant differences in overall survival, or relapse-free survival (Figure 1B) were detected for these two populations.

Conclusions:The addition of Abat starting before haplo-PBSCT did not interfere with the aGvHD and engraftment protective effects of PTCy in this cohort. Abat initiated before PBSC infusion may reduce the risk and severity of CRS and was associated with earlier neutrophil and platelet recoveries. Although the incidence of aGvHD did not differ between the two groups, time of onset trended later among PTCy/Abat recipients. Larger pt populations will be needed to determine more accurately the effects of adding Abat to PTCy on relapse risk and cGvHD incidence and severity.

Disclosures Rowley: *ReAlta Life Science:* Consultancy; *SIRPant Immunotherapeutics:* Membership on an entity's Board of Directors or advisory committees. **Suh:** *Kite Pharma:* Membership on an entity's Board of Directors or advisory committees.

OffLabel Disclosure: Abatacept- currently FDA approved for acute GVHD prevention in matched unrelated and mismatched unrelated donor transplants. In our study, we used Abatacept for acute GVHD prevention in the haploidentical transplant setting

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