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# POSTER ABSTRACTS

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

### Outcomes after RIC and Abatacept-Based Acute and Chronic Gvhd Prophylaxis in Allogeneic Transplantation for Sickle Cell Disease - Can Calcineurin Inhibitor Use be Curtailed?

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**Introduction:** Sickle cell disease (SCD) progression can be curtailed by successful allogeneic transplantation from suitable donors. Allogenic transplantation with reduced intensity immune suppressive conditioning (RIC) from sibling or unrelated donors was considered acceptable with the availability of an Human Leucocyte Antigen (HLA)-matched (8/8 loci) or minimally mismatched (7/8) donor on NCT00920972 and in 2018 the study was modified to include abatacept for acute and chronic graft-versus-host disease (GVHD) prophylaxis based on the incidence of severe chronic GVHD noted (13-38%) and the benefits described with abatacept1-3. An interim review of trial results following the modification of GVHD prophylaxis is presented.
**Methods:** Patients with symptomatic SCD who were <21 years of age were enrolled on appropriate study cohorts based on the level of donor match. Cohort 1 included HLA matched donors and cohort 3 included donors mismatched at 1 of 8 major HLA loci (-A, -B, -C, -DRB1) by high resolution typing. Conditioning included alemtuzumab (distal: day -22 to -19), fludarabine (days -8 to -4) and melphalan (day -3). Thiotepa (day -4) was included for mismatched donors. GVHD prophylaxis included tacrolimus (day -1 and tapered 6-9 months later), methotrexate (days +1, 3 and 6) and abatacept (days -1, +5, 14, 28, 60, 90, 180, 270 and 365)4. Though the half-life of the drug is ~30 days, the interval was adjusted after day 100 to every 90 days to curb allogeneic T cell proliferation following complete elimination of the drug. No previous data exists on this approach. Outcomes tracked were GVHD, mortality and graft rejection (GR) (<25% donor myeloid cells/disease recurrence)
Results: Nine related donor transplants (4-18 years, median 9y) and 9 unrelated donor transplants (URD) (7-20 years, median 16y) (5 mismatched) were undertaken consecutively after the addition of abatacept to the standard GVHD regimen. The duration of follow-up ranged from 2-59 months (median 44m). GR was noted in 2 patients. One patient with primary GR subsequently rejected a second graft after myeloablative conditioning. Another patient with secondary GR received a CD34-selected boost post-ATG unsuccessfully but stabilized after a flu/cy/ATG regimen and another CD34-selected boost. The most recent engraftment analysis in 17/18 patients is 98% (range, 46 to 100) for myeloid and 94.5% (range, 56 to 100) for lymphoid lineage cells. No patient developed > grade 2 acute or any chronic GVHD in the MSD group. In the URD group 1 patient each developed >grade 2 aGVHD and extensive cGVHD. Of evaluable patients, one remains on systemic immune suppression therapy >18 months post-transplant. The only mortality noted was after 2 subsequent transplants in the patient with GR. Seventeen patients remain disease free post-transplant. Disease free survival (DFS) is 94%. GVHD-free-DFS is 89%. The incidence of viral reactivation was 65% and 17% before and after day +100 respectively. Immune reconstitution was noted to normalize beyond 6-9 months.
**Conclusion:** Transplant is beneficial in SCD, and an expansion of donor sources can help to increase the number of patients rendered disease-free. GVHD risks preclude consideration of allogeneic transplantation. A GVHD-free cure rate of >88% despite risk factors such as age and HLA-mismatch following RIC and abatacept-based GVHD prophylaxis is encouraging for allogeneic transplantation options for children and adolescents with SCD. Long-term follow-up is in progress.
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**Disclosures** No relevant conflicts of interest to declare.

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