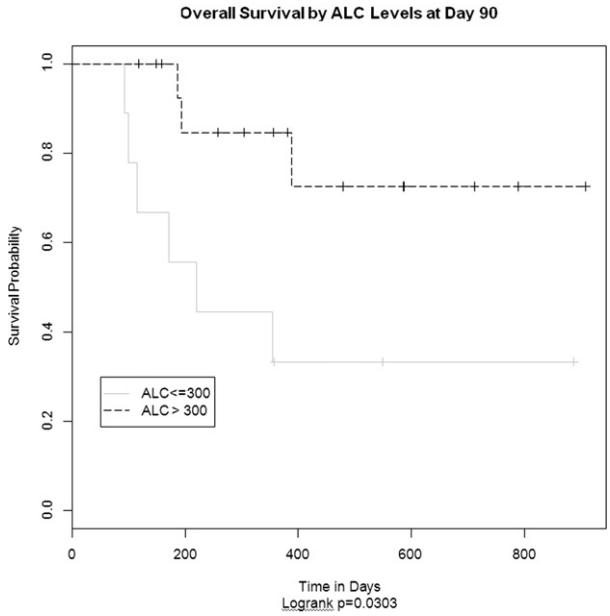

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Immune Reconstitution Following Reduced Intensity Stem Cell Transplantation for Non-Malignant Disorders in Children

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Introduction: Myeloablative stem cell transplants (SCT) for nonmalignant disorders (NMD) are complicated by early and late treatment-related toxicities. We used a novel reduced intensity conditioning (RIC) regimen with early administration of alemtuzumab to achieve donor engraftment with lower toxicities in NMD. Delayed immune reconstitution (IR) and severe/fatal late infections have been previously described with RIC using alemtuzumab peri-SCT. Early administration in our protocol is designed to selectively deplete host immunity with minimal effects on post-transplant IR. We report the kinetics of IR and infection patterns in the first year post-SCT with this approach.

Methods: HSCT was performed for marrow failure, genetic diseases or immune disorders with alemtuzumab (day -22 to -19; 33 mg if $<$ 10 kg; 48 mg if $>$ 10 kg), fludarabine (day -8 to -4; 150 mg/m^2), and melphalan (day -3; 140 mg/m2) followed by infusion of matched related (MRD) or matched unrelated (MUD) marrow/PBSC. GVHD prophylaxis included a calcineurin inhibitor (6-9 m), short course methotrexate (days 1, 3 and 6) and short course prednisone (28 d). Stable engraftment ($>$ 20% donor) occurred in 89% of patients. Lymphocyte numbers, proliferation, and immunoglobulin levels were measured at 3, 6 and 12 m. We evaluated 35 MRD and 31 MUD recipients with immune studies collected at a minimum of two time periods after SCT and tracked cumulative incidence of bacterial, viral and fungal infections.

Results: Lymphocyte, NK, CD4 and CD8 T cell numbers and immunoglobulin levels normalized by 6 months post SCT in both groups. MUD SCT resulted in slower IR than MRD. Notably, MUD recipients had lower B cells after 6 months though immunoglobulin levels were normal. The kinetics of recovery of immune function correlated with incidence of infections, which were highest until day 100 and declined after day 180.

Conclusions: SCT following RIC with early administration of alemtuzumab resulted in successful donor marrow engraftment and rapid IR within 6 months in contrast to previous experience. Only B cell recovery was noted to be slower in MUD compared to MRD transplants. This RIC regimen supports early immune recovery with reduced and more localized infectious complications after the first 6 months. These results provide a context for refining infection surveillance, antibiotic prophylaxis, revaccination and return to normal lifestyle devoid of infectious complications.

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Early Lymphocyte Recovery Predicts Superior Overall Survival After Unmanipulated Haploidentical Blood and Marrow Transplantation for MDS and Acute Myeloid Leukemia Evolving From MDS

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Early lymphocyte recovery has shown to be associated with superior survival in patients with hematological malignancies following umanipulated haploidentical blood and marrow transplantion (HBMT), but its effect on clinical outcomes in patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) evolving from MDS is