ABSTRACT

Name of Trainee: Lev Gorfinkel (lev.gorfinkel@yale.edu)
Mentors: Dr. Niketa Shah (niketa.shah@yale.edu)
Type of Trainee: Resident

Title: Bone Marrow Transplant Using Fludarabine-Based Reduced Intensity Conditioning Regimen with in-Vivo T-Cell Depletion in Patients with Fanconi Anemia
L., Gorfinkel; C., Keenan; C., Demsky; F., Pashankar; G., Kupfer; and N.C, Shah.
Yale University School of Medicine

Background: Fanconi Anemia (FA) is the most common cause of the inherited bone marrow failure (BMF) syndromes and is characterized by bone marrow failure and cancer predisposition. The only cure for BMF in FA remains bone marrow transplant. Due to DNA instability in FA, reduced intensity conditioning has been used to diminish late complications including secondary malignancies. Most FA conditioning regimens in mismatched and unrelated donor transplants rely on total body irradiation (TBI), which increases the risk of secondary malignancies. Most of the non-TBI conditioning regimens use an Ex Vivo T cell depletion approach, but this is not feasible at all programs. The objective was to evaluate the success of bone marrow transplant in patients with FA using non-TBI conditioning regimens with In-Vivo T cell depletion approach.

Design/Methods: Stem cell transplant using non-TBI based conditioning was performed on two siblings with Fanconi Anemia and homozygous 2bp deletion in the FANCG gene. The first sibling underwent matched unrelated donor transplant at 7 years of age with a bone marrow (BM) graft with fludarabine, alemtuzumab, busulfan, cyclophosphamide conditioning and cyclosporine (CSA) and mycophenolate as Graft Versus Host Disease (GVHD) prophylaxis. The second sibling underwent match sibling donor at 6 years of age with cord and BM grafts using fludarabine, alemtuzumab, cyclophosphamide for conditioning and CSA for GVHD prophylaxis.

Results: The first sibling had engraftment on D+12, there were no signs of acute GVHD and at 23 months post-transplant has no signs of chronic GVHD. The second sibling had engraftment on D+14, there were no signs of acute GVHD and at 13 months post-transplant has no signs of chronic GVHD. Major complications for both siblings included BK viremia and viruria.

Conclusions: Conditioning regimens without radiation can lead to successful engraftment without development of GVHD and may reduce risk of developing secondary neoplasms, even with unrelated donor transplants. As FA is a rare disease, future studies should focus on pooling together BMT data to change current conditioning regimens.

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