Abstract: P1923

Title: UPFRONT MATCHED UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SEVERE IDIOPATHIC APLASTIC ANEMIA AND REFRACTORY CYTOPENIA OF CHILDHOOD IN PEDIATRIC PATIENTS. A STUDY OF THE SPANISH PEDIATRIC GROUP FOR HEMATOPOIETIC CELL TRANSPLANTATION AND CELL THERAPY (GETH-TC)

Abstract Type: e-Poster Presentation

Topic: Bone marrow failure syndromes incl. PNH - Clinical

Background:

Hematopoietic stem cell transplantation (HSCT) from a matched sibling donor (MSD) is the standard of care for children with severe idiopathic aplastic anemia (SAA) and refractory cytopenia of childhood (RCC). When an MSD is lacking, immunosuppressive therapy (IST) has historically been recommended. However, IST associates high failure rates and clonal evolution risk. The outcomes of matched unrelated donor (MUD) HSCT following immunosuppressive therapy (IST) are inferior compared to MSD. Front-line MUD-HSCT may improve outcomes compared to IST and rescue MUD-HSCT after IST failure.

Aims:

The aim of this study is to assess the role of upfront MUD-HSCT for pediatrics patients with SAA/RCC who lack an MSD.

Methods:

We performed a retrospective multicenter observational study of pediatric patients diagnosed with either SAA or RCC and treated with MUD-HSCT as first line in the absence of MSD. All patients were treated in hospitals in Spain affiliated to the pediatric Spanish Group for HSCT (GETH-TC).

Results:

19 patients (16 males/3 females) with SAA (17) and RCC (2) underwent an upfront MUD-HSCT (10/10). Median age at diagnosis was 11 years (1-17). No one had cytogenetic anomalies. Median time from diagnosis to HSCT was 102 days (61-258). Most patients had a good performance status (Lansky >70). Two had fungal infections before HSCT. Conditioning regimen consisted of fludarabine plus cyclophosphamide in SAA-patients (n=17), and busulfan/treosulfan, fludarabine +/- thiotepa in RCC-patients (n=2). All received lymphodepletion with thymoglobulin. GVHD prophylaxis was cyclosporine/methotrexate in most cases. Bone marrow (BM) was the prevalent source. Median cell dose for BM was 4x108 CNT/kg (1.72-8.8) and for peripheral blood 13.5x106 CD34+/kg (7.3-12.3). All patients engrafted. Thirteen achieved complete donor chimerism, 5 mixed chimerism and 1 secondary graft failure 11 months post-transplant. Four presented poor graft function (PGF) and 8 post-HSCT immune cytopenias (IC). Eleven experienced bacterial infections, two with severe septic shock requiring Pediatric Intensive Care Unit admission. No cases of post–HSCT fungal infection occurred, and while viral reactivations were common, no patient developed viral disease. Endothelial complications included veno-occlusive disease (n=2) and transplant-associated microangiopathy (n=2). Five developed grade 2 acute GvHD, and 2 mild/moderate chronic GvHD. No transplant-related mortality was observed. After a median follow-up of 20 months, overall survival was 100%, event-free survival 94.7% (CI 84-100) and cGvHD/graft failure-free survival 89% (CI 75-100).

Summary/Conclusion:

In our experience, upfront MUD-HSCT shows promising outcomes in terms of OS, EFS, chronic GVHD. Managing mixed chimerism, PGF and IC is critical. A more extended follow-up is required to assess late sequelae and substantiate these findings. Upfront MUD-HSCT is an alternative treatment option for pediatric

AHBMF patients lacking an MSD.

Keywords: Allogeneic bone marrow transplant, Allogeneic stem cell transplant, Childhood, Severe aplastic anemia