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Overall survival in myelofibrosis treated with allogeneic hematopoietic cell transplant is impacted by reversal of marrow fibrosis: a single institution experience from Oregon Health & Science University

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Keywords

Human, Hematopoietic Stem Cell Transplantation, Primary Myelofibrosis, Splenomegaly, Graft vs Host Disease, Janus Kinase Inhibitors, Logistic Models

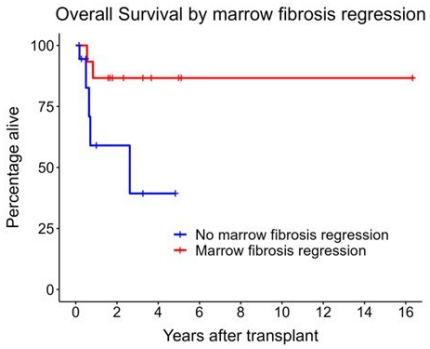
Abstract

Allogeneic hematopoietic cell transplantation (allo HCT) is the only curative therapy for patients with intermediate-2 or high risk myelofibrosis (MF). We sought to examine the impact of pre-HCT splenomegaly, splenic RT, and marrow fibrosis on overall survival (OS). Subjects with primary or secondary MF who underwent allo HCT using matched related (n=10) or unrelated (n=24) donor grafts, PBSC (n=33) or marrow (n=1), between 2005 and 2021 were identified. Median follow-up was estimated by reverse Kaplan-Meier (KM). Marrow fibrosis regression (defined as any decrease in grade) and GVHD were considered time-varying predictors. Time-to-engraftment and OS were modeled by Cox regression, while post-HCT death rates were estimated via the extended KM method. Logistic regression was used to model fibrosis regression by a specified time point. Our data on engraftment, GVHD, and survival are comparable to that reported by the CIBMTR with this analysis demonstrating a strong correlation between aGVHD, lack of marrow fibrosis regression, and increased risk of death. Novel strategies, such as the use of peri-HCT JAK inhibition and T cell depletion (in-and ex-vivo), may provide rapid marrow remodeling and improve OS in MF patients.

Table 1: Patient, disease, and treatment characteristics and post-HCT GVHD

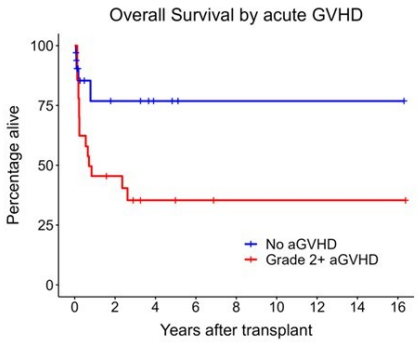
Patient or disease feature	Summary statistics: n=34 (%)
Age at allo HCT, median (range)	62 (41 – 73) years
KPS	
90	11 (32.4 %)
80	20 (58.8 %)
70	3 (8.8 %)
HCT-CI	
0-2	15 (44.1 %)
3-7	19 (55.9 %)
Primary MF	21 (61.8 %)
Secondary MF	13 (38.2 %)
DIPSS score	
Intermediate-1 risk	2 (5.9 %)
Intermediate-2 risk	20 (58.9 %)
High risk	10 (29.4 %)
N/A	2 (5.9 %)
JAK2 mutation	
Yes	20 (58.9 %)
No	10 (29.4 %)
N/A	4 (11.8 %)
Pre allo HCT ruxolitinib	
Yes	22 (64.7 %)
No	11 (32.4 %)
N/A	1 (2.9 %)
Pre allo HCT Spleen size	
≤ 20 cm	20 (58.8 %)
> 20 cm	14 (41.2 %)
Pre allo HCT Splenic RT	
Yes	15 (44.1 %)
No	19 (55.9 %)
Pre allo HCT marrow fibrosis	
Grade 1	5 (14.7 %)
Grade 2	8 (23.5 %)
Grade 3	21 (61.8 %)
Conditioning Regimen: GVHD prophylaxis	
MAC; CNI/MTX +/- prednisone (n=1 on T-cell modified trial, Tac only)	8 (23.5 %)
RIC; CNI/MTX +/- prednisone	22 (64.7 %)
NMA; Cyclo/MMF	4 (11.8 %)
Acute GVHD	
None	11 (32.3 %)
Grade 1	3 (8.8 %)
Grade 2	6 (17.6 %)
Grade 3-4	13 (38.2 %)
Engraftment syndrome	1 (2.9 %)
Chronic GVHD	
None	19 (55.9 %)
Limited	5 (14.7 %)
Extensive	9 (26.5 %)
cGVHD but unknown extent	1 (2.9 %)

Figure 1: Marrow remodeling as predictor of post-HCT death



KM curves by regression status up to D+365; n=24 patients

Figure 2: acute GVHD as predictor of post-HCT death



KM curves by aGVHD status (time-varying); n=33 patients