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723.CLINICAL ALLOGENEIC AND AUTOLOGOUS TRANSPLANTATION: LATE COMPLICATIONS AND APPROACHES TO DISEASE RECURRENCE | NOVEMBER 13, 2019

Outcomes Following Second Allogenic Haematopoietic Cell Transplantation in Patients with Myelofibrosis: A Retrospective Study on Behalf of the Chronic Malignancies Working Party of EBMT

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Introduction:

The only curative treatment for myelofibrosis (MF) remains allogenic haematopoietic cell transplantation (allo-HCT) although the risks of non-relapse mortality (NRM), relapse and graft rejection need to be taken into consideration. Therapeutic approaches following relapse after allo-HCT include symptom-directed management, chemotherapy, JAK2 inhibitors, adoptive immunotherapeutic approaches with donor lymphocyte infusion (DLI) and, in a minority, a second allo-HCT. Frequently, due to the advanced age of the recipient, early relapses, and numerous complications, 2nd allo-HCT can only be considered in a limited number of patients. Few studies evaluating the role of 2nd allo-HCT in MF following 1st relapse or primary/secondary graft rejection have been published to date.

Methods and results:

Patient selection was performed by identifying adult patients who underwent 2nd allo-HCT for MF between 2010-2017: 216 patients were analyzed; 64% were male, 78% had primary MF (PMF) and 22% secondary MF (sMF). Median age at the time of 2nd allo-HCT was 57 years, and median time from 1st allo-HCT was 8 months. Of this cohort, 56% of patients received a 2nd allo-HCT for relapse, 31% for graft failure and the reason was missing in 13%. A greater proportion was transplanted within 1 year from 1st allo-HCT (61 %) whilst 39% had 2nd allo-HCT > 1 year. A reduced Karnofsky performance status (KPS<90) was noted in 50% of patients. Conditioning regimens were reduced-intensity (RIC) in 72% and myeloablative (MAC) in 19% of patients, respectively. Donors were related in 38% and unrelated in 62%. T-cell depletion was reported in 46% of patients. In 31% of patients, the same donor as utilized for the first allo-HCT episode was recruited, whilst an alternative donor was utilized in 54% of cases. Sustained engraftment was achieved in 69% of the cohort, with a significant proportion of patients experiencing either primary (13%) or secondary (12%) graft failure, details were lacking for 13%. Median follow-up was 40 months and for the entire cohort the 2-year overall survival (OS) was 49%. Univariate analysis of

gender, age (older or younger than 55 yrs), disease type (pMF vs sMF), donor type (same vs alternative, matched vs unrelated), conditioning intensity (MAC vs RIC) and ATG exposure did not highlight any significant effects on OS rates. Of note, patients undergoing a 2nd allo-HCT for graft failure showed significantly worse outcome compared to those transplanted for relapse with a 2-year OS of 34% and 52%, respectively (p=0.02). In addition, performance status had a significant effect on OS; those with a KPS<90 had an OS of 40% compared to those with a KPS≥90 (61%, p=0.03). Patients transplanted ≤12 months from 1st allo-HCT had significantly worse 2-year OS compared to those transplanted later (43% for ≤12 months, 57% for >12 months, p=0.02). The 2-year relapse-free-survival (RFS) for the entire cohort was 44%. Only time elapsed from the 1st allo-HCT to 2nd was significantly associated with 2-year RFS (41% for ≤12 months, 49% for >12 months, p=0.05). Of note, the 2-year OS and RFS were comparable following use of the same or a different donor. The 2-year cumulative incidence of relapse and NRM were 22 and 34%, respectively. The time interval from 1st to 2nd allo-HCT appeared to be highly significant for NRM with patients transplanted ≤12 months having a higher 2-year NRM compared to those transplanted >12 months (40 vs 24%, respectively, p=0.008). A trend for higher NRM was the reason for 2nd allo-HCT: patients transplanted for graft rejection had a 2-year NRM of 45% compared to 31% for those with relapse (p=0.06).

Conclusions:

This analysis supports the utilization of a 2nd allo-HCT for patients with MF who have presented with graft failure or relapse following a 1st allo-HCT. In univariate analysis, overall outcome appears worse in patients being transplanted after graft failure as well as for those transplanted within 1 year after 1st allo-HCT, due to increased NRM. Of note, the use of either the original or a different donor are associated with similar outcomes. Further work is required to elucidate other risk factors, GVHD rates and to define the optimal conditioning regimen in this setting.

Table.

	Patients (number = 216)
Median age, years (range)	57.3 (26.1, 76.0)
Median follow-up, months (IQR)	40 (17, 72)
Sex, male (%)	64
Time from diagnosis to 2nd allo-HCT, median, years (range)	3.65 (0.4, 47.3)
Time from 1st allo-HCT to 2nd, median, months (IQR)	8.0 (3.4, 20.7)
Reason for 2nd allo-HCT, n° (%)	
Relapse	121 (56)
Graft failure	67 (31)
Missing data	28 (13)
Myelofibrosis subtype, n° (%)	
Primary	168 (78)
Secondary	48 (22)
Disease status at 2nd allo-HCT, n° (%)	
CR	19 (9)
Stable disease	21 (10)
Relapse/progression	128 (59)
Other/missing data	48 (22)
Karnofsky status, n° (%)	108 (50)
<90	108 (50)
≥90	78 (36)
Missing data	30 (14)
Donor, n° (%)	
Related	82 (38)
Unrelated	133 (61.5)
Missing	1 (0.5)
Donor at 2nd allo-HCT compared to first, n° (%)	
Same donor as at first	66 (31)
Alternative donor	116 (54)
Missing data	34 (15)
Conditioning intensity, n° (%)	
Standard	41 (19)
Reduced	156 (72)
Missing	34 (16)
ATG, n°(%)	
Yes	100 (46)
No	104 (48)
Missing data	12 (7)
Overall survival (OS), % (SE)	
2-year OS	49.2 (3.6)
5-year OS	36.1 (4.0)
Relapse free survival (RFS), % (SE)	
2-year RFS	44.5 (4.1)
5-year RFS	36.3 (4.4)
Relapse, % (SE)	
2-year relapse	21.6 (3.4)
5-year relapse	26.0 (3.9)
Non relapse mortality (NRM), % (SE)	
2-year NRM	33.9 (3.7)
5-year NRM	37.7 (4.2)

Disclosures

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Author notes

*Asterisk with author names denotes non-ASH members.