



The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Low Disease Relapse and High Survival in Non-Myeloablative Two-Step Haploidentical Transplant, Results of a Prospective Trial

Xia Bi, MD¹, Dolores A. Grosso¹, John L. Wagner, MD¹, Joanne Filicko-O'Hara, MD², William O'Hara, PharmD³, Neal Flomenberg, MD¹, Usama Gergis, MD MBA⁴

¹Bone Marrow Transplant and Cellular Therapy, Thomas Jefferson University Hospital, Philadelphia, PA

²Bone Marrow Transplant and Cellular Therapy, Sidney Kimmel Cancer Center of Thomas Jefferson University, Philadelphia, PA

³Department of Pharmacology, Thomas Jefferson University Hospital, Philadelphia, PA

⁴Thomas Jefferson University, Philadelphia, PA

Introduction

We previously developed a two-step approach that separates the lymphoid and myeloid portions of the graft, allowing a consistent T cell dosing and sparing the stem cells from the effect of cyclophosphamide. The two-step approach demonstrated safety and efficacy in patients treated with a myeloablative conditioning protocol. Here, we extended our 2-step platform to older and less fit patients and explored the effects of using a high dose of T cells on disease relapse and transplant outcomes.

Methods

Patients received fludarabine 30mg/m² IV daily for 3 days, from day -10 to day -8. Two hundred cGy total body irradiation (TBI) was given on day -7. This was increased to 400 cGy TBI in 2 doses after 13 patients had been treated. A fixed dose of 2 x 10⁸/kg CD3+ T cells was given on day -6, followed 2 days later by cyclophosphamide 60mg/kg IV daily on day -3 and day -2. Tacrolimus and mycophenolic acid were started on day -1, followed by infusion of CD34-selected stem cells on day 0.

Results

Thirty-three patients with hematologic malignancies were treated (Table 1). Majority were haploidentical transplants (91%), and the rest were matched related donors. Median age was 68 (range, 33-76) years, with 64% patients >65 years old. Median follow-up was 31 months (range, 0-76 months). Median HCT-comorbidity score was 4 (range, 0-9). Forty-seven percent had high or very high-risk disease risk index. Twenty-seven percent had prior autologous transplant.

Overall survival was 75% at 1 year and 50% at 3 years. The cumulative incidence (CI) of non-relapse mortality (NRM) and relapse were 22% and 31% at 3 years. However, the CI of relapse was much lower for patients treated with 400 cGy TBI versus those treated with 200 cGy TBI (6% vs 54%, *p* = 0.017) (Figure 1), while NRM was similar (25% vs 15%, *p* = 0.348). This contributed to a very high survival of 69% in patients who received the higher dose of TBI at 3 years, with median OS not reached.

The median time to neutrophil and platelet recovery was 11 and 17 days, respectively. The median donor CD3+ T cell chimerism at day +28 was 100% (range, 71% to 100%). The CI of grade II acute graft-versus-host-disease (GVHD) was 23% and 27% at 100 days and 6 months, respectively. The CI of chronic GVHD was 8% at 3 years. There were no grade III or IV acute GVHD, no severe chronic GVHD and no deaths attributable to acute or chronic GVHD. There were 13 deaths in the study, of which 7 died from disease relapse, 3 died from toxicity related to treatment regimen, and 2 died from infection.

Conclusions

The NMA two-step approach allo-SCT showed a low disease relapse rate and high survival in patients treated with 400 cGy TBI, despite a generally older and more medically compromised patient population.

Disclosures Gergis: Jazz: Consultancy, Honoraria, Other: Travel Support, Speakers Bureau; *Astellas*: Speakers Bureau; *Kite, a Gilead Company*: Honoraria, Other: Travel Support and other relationship, Speakers Bureau; *Gamida*: Consultancy, Current equity holder in publicly-traded company; *Iovance*: Current equity holder in publicly-traded company; *Novartis*: Honoraria; *Thomas Jefferson University*: Current Employment; *Incyte*: Honoraria, Other: Travel Support, Speakers Bureau.

Table 1 Patient, Disease, Transplant, and Graft characteristics

Patients' characteristics	Total
Number of patients	33
Median age at HCT, (range)	68 (33-76)
<= 65 years	12 (36)
> 65 years	21 (64)
Sex, N (%)	
Male	19 (58)
Female	14 (42)
Race	
Caucasian	22 (67)
African American	8 (24)
Hispanic	3 (9)
HCT-CI	
0	1 (3)
1-2	4 (12)
>=3	28 (85)
Performance status	
90-100%	26 (79)
80%	7 (21)
Disease-specific characteristics	
Diagnosis, %/disease status at transplant, n	
AML	18% CR1, n=6; CR>=2, n=3; R/R, n=3
MDS	27% marrow evidence of MDS, n=9; MDS-NED, n=2
Ph+ ALL	3% CR1, n=1
MM	12% VGPR, n=4; PR, n=1
NHL	3% Hodgkin-CR2, n=1; 3% Hodgkin-multiply relapsed, n=1; transformed LBCL-NED, n=2
Disease risk index score	
Low	4 (5)
Intermediate	41 (48)
High	38 (44)
Very high	3 (3)
Transplant-related characteristics	
Prior auto transplant	9 (27)
Donor age, median (range)	45 (20-64)
Donor type, N of patients (%)	
Haploidentical	30 (91)
Matched related	3 (9)

Figure 1 Cumulative incidences of relapse and NRM based on whether patients received 2GY TBI versus 4GY TBI.

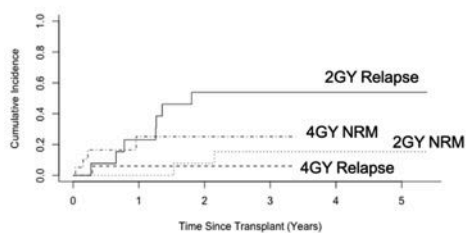


Figure 1

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