

complications. We reports here 33 Korean PNH patients who underwent allotransplantation.

Aims: To understand the impact of allotransplant in Korean PNH patients, we retrospectively analyzed medical charts of 33 PNH patients from national registry in Korea.

Results: Patient ages ranged from 15 to 56 years (median 29 years, male 14, female 19). Classic PNH were 12 patients and PNH with bone marrow disease were 21. Median LDH level at the time of diagnosis was 1159 IU/L (297 ~ 7699). The source of stem cells were bone marrow in 13 patients and peripheral blood in 20 patients. Sibling donor were 23 and unrelated donor were 10. Conditioning regimens consisted of BuCy or Cy/TBI (n = 14), fludarabine containing reduced intensity regimen (n = 18), or other. All patients attained successful leukocyte engraftment (median 13 days, range 10~30 days) and platelet engraftment (median 17 days, range 11~48 days). Grade II~IV acute GVHD were in 19 patients (skin 13, liver 3, gut 3). Grade II~IV chronic GVHD were in 13 patients (limited 10, extensive 3). With a median follow-up of 82.6 months (range, 19.5 ~160.2 months), 26 patients are alive with CR. Seven patients were died after transplantation due to pulmonary hemorrhage (n = 2), sepsis (n = 2), GVHD/multi organ failure (n = 2), or massive thromboembolism (n = 1). Patients with reduced intensity conditioning regimen had a better survival than patients with conventional conditioning regimen (p = 0.027). There were no survival differences between classic PNH patients and PNH patients with BMD. There were also no differences between two groups categorized by PNH clone sizes, stem cell sources, and PNH related symptoms.

Conclusion: Our data demonstrates that reduced intensity conditioning regimen is suitable for allogeneic stem cell transplantation of PNH patients.

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A RANDOMIZED PHASE III TRIAL INVESTIGATING 2 Gy TBI VS. Flu/2 Gy TBI CONDITIONING FOR HLA-MATCHED RELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION (HCT): TEMPO OF CD3 AND NK CELL ENGRAFTMENT DETERMINES RELAPSE AND PROGRESSION FREE SURVIVAL IN PATIENTS WITH HEMATOLOGIC

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Nonmyeloablative conditioning with fludarabine (Flu) and 2 Gy TBI with MMF/CSP postgrafting immunosuppression results in reliable allogeneic engraftment. A retrospective analysis of pts conditioned with 2 Gy TBI alone prior to receiving PBSC from HLA-matched related donors showed that rejection primarily occurred in pts who pre-HCT had not received intensive chemotherapy. Addition of Flu (30 mg/m²/d x 3 d) in a subsequent cohort seemed associated with increased nonrelapse mortality (NRM). Here, we report results of a phase III randomized multi-institutional trial that asked whether Flu was needed in heavily pretreated pts to assure sustained engraftment of HLA-matched related grafts. Immunosuppression included MMF (28 d) and CSP (180 d). Eighty-five pts with AML (n = 15), NHL (n = 32), MM (n = 9), CLL (n = 9), MDS (n = 4), and HL (n = 16) were randomized to be conditioned with either 2 Gy TBI alone (TBI; n = 44) or Flu/2 Gy TBI (Flu/TBI; n = 41) with stratification by transplant center, disease risk and prior high dose HCT. Pts received G-PBMC containing a median of 7.9 x10⁶ CD34 and 3.6 x10⁸ CD3 cells/kg. The median age was 55 (range, 17-73) years. Forty-five had failed previous autologous (n = 41) or allogeneic (n = 4) high-dose HCT. The primary endpoint was NRM with secondary endpoints of survival, relapse/progression, GVHD and rejection. Median follow-up was 4.6 (range, 0.6-7) years.

Table. Transplant outcomes after HLA-matched related donor HCT in patients conditioned with 2 Gy TBI only or with fludarabine 90 mg/m²

	TBI (n = 44)	Flu/TBI (n = 41)	P
Rejections (number of pts)	2	0	0.50
GVHD			
Grade II-IV acute @ 120 d, %	34	46	0.23
Grade III-IV acute @ 120 d, %	9	7	0.82
Chronic @ 3 years	49	71	0.21
Donor chimerism			
T-cell day 28, %, median	61	90	<0.0001
T-cell day 84, %, median	68	92	<0.0001
NK-cell day 28, %, median	75	96	0.0005
Nonrelapse mortality @ 3 years, %	17	14	0.35
Relapse/progression @ 3 years, %	51	33	0.04
Relapse mortality @ 3 years, %	32	22	0.10
Overall survival @ 3 years, %	52	65	0.09
Progression-free survival @ 3 years, %	32	53	0.03

No significant differences between arms were observed for NRM (3 year; TBI 17%, Flu/TBI 14%), grade II-IV acute (TBI 34%, Flu/TBI 46%) or chronic GVHD (TBI 49%, Flu/TBI 71%). Rejection was only observed in 2 TBI pts. The 3 year survival was 52% and 65% in TBI and Flu/TBI pts (p = 0.09), respectively, with a higher incidence of relapse/progression (TBI 51%, Flu/TBI 33%, p = 0.04) and relapse related mortality (TBI 32%, Flu/TBI 22%, p = 0.10), translating into a significantly lower progression-free survival (TBI 32%, Flu/TBI 53%, p = 0.03) in TBI pts. Compared to TBI pts, the CD3 donor chimerisms on d28 and d84 were significantly higher in Flu/TBI pts as was the NK cell chimerism on d28. Even though low rates of rejection and similar incidences of NRM were observed in both arms, Flu/TBI pts had better progression free survival. In view of the significantly higher CD3 and NK donor chimerism in Flu/TBI pts, the result of this randomized trial demonstrate the importance of Flu in augmenting the graft versus tumor effect, by ensuring prompt and durable high level donor engraftment early post-transplant.

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ADENOVIRUS VIREMIA IN PATIENTS WITH CLINICAL SYMPTOMS AFTER T-CELL DEPLETED HSCT: RATES OF ADENOVIRUS DISEASE AND OUTCOMES

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Background: Invasive ADV infections are a known cause of mortality in HSCT. High or rising ADV viral loads are thought to be a predictor of ADV disease. T-cell depletion (TCD) reduces the risk of graft vs host disease, but has been associated with an increased incidence and complications of certain viral infections. We examined the outcomes of patients found to have ADV viremia after TCD HSCT at our institution.

Method: A retrospective review was conducted on 401 adult and pediatric patients who received TCD HSCTs at MSKCC from Jan 2006 through March 2011. Follow up ranged from (6 months - 5 years). Quantitative ADV PCR in whole blood was evaluated by the treating physicians based on clinical symptoms. ADV viremia was defined as at least 1 positive study of $\geq 1,000$ copies/ml or >2 consecutive positive studies of ≥ 500 copies/ml/ ADV PCR. Definitions were: early ADV viremia - first positive ADV PCR at < 180 days post HSCT, and high viral load (HVL) as $\geq 10,000$ copies/ml. ADV Disease: Definite: presence of typical adenovirus nuclear inclusions on histopathology, and/or positive culture from sterile site (other than blood), or both. Probable adenovirus: ADV viremia and associated clinical symptoms without other identifiable causes).

Results: The 401 TCD HSCTs included 23.7% children, 90% peripheral blood stem cell grafts, and 63.1% unrelated donors, median age 47.5 yrs (range 0.1-73 yrs). Thirty five (8.7%) patients were diagnosed with ADV viremia at a median of 93 days (range 15 - 674) post HSCT. The incidence of diagnosed ADV viremia in this group was higher in pediatric vs adult pts (15.3 vs 6.2%). ADV was detected in 35/401 (8.7%) (6.2% adult and 15.3% pediatric) pts a median of