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Comparison of Peripheral Blood Vs. Bone Marrow Chimerism after a Reduced Intensity Conditioning Allogeneic Stem Cell Transplant

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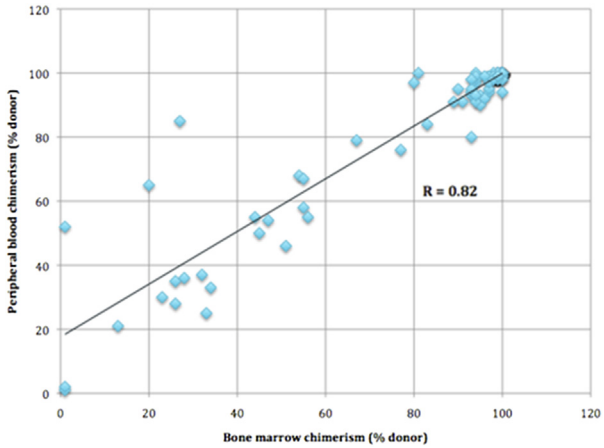
Introduction: Post allogeneic HSCT chimerism analysis of bone marrow (BM) and peripheral blood (PB) has been used to monitor engraftment and to detect early disease recurrence. Mixed chimerism is occasionally encountered early after RIC HSCT. The sensitivity of PB chimerism to detect mixed BM chimerism remains to be determined. Our aim is to determine the sensitivity of PB chimerism studies in predicting BM mixed chimerism post RIC allogeneic HSCT and to determine the clinical relevance of early detection.

Methods: We did a retrospective review of chimerism data from PB and BM samples from patients undergoing RIC allogeneic HSCT from matched related, matched unrelated and haploidentical donors. Chimerism data was collected every 3 months during the first year post HSCT. Only samples drawn up to 5 days apart were included in the analysis.

Results: We analyzed 200 pairs of BM and PB samples in 89 patients with median age of 58 years (range 22-77). Of these, 132 pairs demonstrated </= 1% recipient cells in both specimens (Marrow -, Blood -, M-B-), 45 pairs demonstrated >1% recipient cells in both specimens (M+B+), 4 pairs had a BM sample which showed </= 1% recipient cells and a PB sample which showed >1% recipient cells (M-B+) and 19 pairs had a BM which showed >1% recipient cells and a PB sample which showed </= 1% recipient cells (M+B-). The ability of PB specimens to detect mixed BM chimerism showed: 70% sensitivity, 97% specificity, positive predictive value of 92%, and negative predictive value of 87%. The 19 M+B- specimens were from 16 patients (characteristics in *Table 1*). Of these 16 patients, 4 relapsed (two at the time of M+B-, one 22 days post-M+B-, and one 45 months post-M+B-) and 6 ultimately died (4 of relapse, 1 of infection, 1 of graft vs. host disease). M+B- seen early post transplant (median D+30) was not associated with relapse, while later detection was associated with relapse (median D+137). The patients in the M+/B- group who relapsed had acute leukemia (3/4) and multiple myeloma (1/4).

Table 1
Demographics

	All patients	Patients with M+/B-	% M+/B-
Total patients	89	16	18%
Female	42	8	19%
Male	47	8	17%
Diagnosis			
AML	26	4	15%
NHL	18	2	11%
MM	11	2	18%
CLL	7	4	57%
ALL	6	2	33%
Aplastic anemia	5	0	0%
Other	16	2	13%
Transplant type			
Matched unrelated	16	2	13%
Matched related	28	4	14%
Haploidentical	45	10	22%
Status			
Alive	49	10	20%
Deceased	40	6	15%



Conclusions: PB chimerism had a high specificity; yet, it was insufficiently sensitive (70%) to detect mixed BM chimerism in patients undergoing RIC allogeneic HSCT. Though numbers are small, peripheral blood samples best predict marrow chimerism in patients with aplastic anemia rather than in malignancies originating in the BM (leukemias and myeloma). Continued bone marrow sampling is thus required, with the possible exception of patients transplanted for aplastic anemia or malignancies not originating in the BM.

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Low Dose Thymoglobulin Result in Improved Outcomes after Allogeneic Unrelated Hematopoietic Stem Cell Transplantation (HCT) for Patients with Acute Myeloid Leukemia/ Myelodysplastic Syndrome Conditioned with Intravenous Busulfan and Fludarabine

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Low Dose Thymoglobulin Result in Improved Outcomes after Allogeneic Unrelated Hematopoietic Stem Cell Transplantation (HCT) for Patients with Acute Myeloid Leukemia/ Myelodysplastic Syndrome Conditioned with Intravenous Busulfan and Fludarabine.

Intravenous Busulfan/Fludarabine (Bu/Flu) based conditioning regimens have resulted in lower treatment related mortality (TRM) after allogeneic HCT in both reduced and full intensity dosing in AML/MDS . The addition of thymoglobulin to such regimens to minimize the risk of graft versus host disease after unrelated donor (MUD) HCT has been linked to the increased concerns of relapse risk.

Method: In order to study the impact of addition of low dose thymoglobulin to Bu/Flu regimens in MUD recipients, the medical records of 38 consecutive AML/MDS patients who underwent MUD HCT with BU/Flu and low dose thymoglobulin were retrospectively reviewed. All the patients received single daily dose of iv Bu 3.2 mg/kg for 2 days (RIC, Bu2-Flu) or 4 days (FIC, Bu4-Flu) based on age, older or younger than 65 respectively. Fludarabine was given as a single daily dose of 40 mg/Kg for 4 days. Graft versus host