(DFS) was 28 months in AA and 17 months in non-AA (p = NS). Five patients (all non-AA) died, 4 of 5 due to progression of disease. Response rates of AA patients treated with novel agents followed by ASCT were then compared to 38 consecutive historical AA patients receiving conventional induction chemotherapy followed by ASCT at our center. After utilizing novel agents the ORR in AA patients increased from 56% to 89% (p = 0.02). Median DFS also improved from 21 to 28 months (p = 0.43). Our findings demonstrate that despite the AA population having double the incidence of multiple myeloma, AA patients respond well to novel agents followed by ASCT. These results also suggest that differences in long term survival between AA and non-AA MM patients observed in previous studies could be due to limited access to care rather than biologic causes.

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EARLY AND LATE COMPLICATIONS ASSOCIATED WITH BUSULFAN, CYCLOPHOSPHAMIDE, AND ETOPOSIDE (BU/CY/VP-16) CONDITIONING FOLLOWED BY ALLOGENEIC OR AUTOLOGOUS STEM CELL TRANSPLANTATION IN RELAPSED/REFRACTORY NON-HODGKIN'S LYMPHOMA

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Introduction: Stem cell transplantation (SCT) is a treatment option for relapsed/refractory Non-Hodgkin's lymphoma (NHL) patients. Busulfan, cyclophosphamide, and etoposide (Bu/Cy/VP-16) has been investigated as a conditioning regimen for allogeneic (alloSCT) and autologous (auSCT), but its spectrum of early (<1 year) and late (> 1 year) complications are not well characterized. We investigated the complications experienced by patients at the Northwestern University transplanted with this regimen.
Methods: We performed a retrospective analysis of all relapsed/refractory NHL patients who received SCT at our center with Bu/Cy/VP-16 conditioning from 3/2003-6/2011.
Results: 25 patients with relapsed/refractory NHL who had SCT with Bu/Cy/VP were identified. Median age was 49 (range: 28-71). 13/25 (52%) patients had alloSCT and 12/25 (48%) had auSCT. Median follow-up was 12 months (range: 5 days-96 months). Progression free survival was 71 ± 10 % (95% confidence interval (CI): 53-95%), overall survival was 77 ± 9% (95% CI: 61-98%), and disease free survival was 85% overall. At less than 100 days post SCT, 4/25 (16%) patients died, 2 alloSCT and 2 auSCT. Causes included progressive disease, sepsis, and respiratory failure. Peri-transplant morbidity (<100 days post-transplant) most commonly included neutropenic fever (22/25, 88%), mucositis (16/25, 64%), and elevated liver enzymes (19/25, 76%), cardiovascular complications (8/25, 32%), pneumonitis (7/25, 28%), and bacteremia (6/25, 24%). At 1 year follow-up, 9/21 (43%) had persistently elevated liver enzymes, 8/21 (38%) had pneumonitis, and 2/21 (9.5%) had BOOP. At greater than 1 year, 3/13 (23%) had persistently elevated liver enzymes and 3/13 (23%) had BOOP. In the alloSCT population, 10/11 (91%) had acute graft versus host disease (GVHD) and 6/11 (55%) had chronic GVHD.
Conclusions: We conclude that Bu/Cy/VP-16 is a highly effective conditioning regimen for NHL. Toxicity is not insignificant, as 100 day mortality was 16%. At least 2 of the 4 deaths occurred because of progressive disease, so selection of patients whose disease is responsive to pre-transplant therapy would reduce the 100 day mortality. Common peri-transplant complications included neutropenic fever, mucositis, and elevated liver enzymes. Given the high efficacy of this regimen with moderate long-term toxicity, in chemotherapy responsive patients it can be considered as a viable conditioning option prior to SCT.

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MYELOABLATIVE DOSES OF BUSULFAN AND FLUDARABINE AS CONDITIONING FOR ALLOGENEIC STEM CELL TRANSPLANTATION IN NON-HODGKIN'S LYMPHOMA

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Mortality associated with myeloablative conditioning has limited its application in non-Hodgkin's lymphoma (NHL). Myeloablation with pharmacokinetically-targeted busulfan and fludarabine (t-i.v. BuFlu) has been shown to be safe and effective in acute leukemia and MDS, however there is very limited data in lymphoma. We assessed retrospectively the outcomes of a consecutive series of 60 patients (pts) diagnosed with NHL who underwent allogeneic hematopoietic cell transplant (allo-HCT) with t-i.v. BuFlu between 12/2004 and 8/2010. Thirty-seven pts were male and median age was 54 yrs (range 27-68 yrs). Histologies included *de novo* or transformed diffuse large B-cell lymphoma (DLBCL; n = 12), follicular lymphoma (FL; n = 17), mantle cell lymphoma (MCL; n = 9), lymphoblastic lymphoma (LBL; n = 8), peripheral T-cell lymphoma (PTCL; n = 13) and marginal zone B-cell lymphoma (n = 1). Median number of treatment lines was 3 (range 1-8). Median time from diagnosis to transplant was 32 months (range 4.5- 177.5 months). At transplant, 28 (47%) pts were in CR, 22 (37%) in PR and 10 (16%) had SD/PD. Average daily busulfan AUC was targeted based on pts age, concurrent comorbidities, or eligibility for a Bu dose escalation trial: 3500 µmol x min/L in 13 pts, 5300 in 41 pts and more than 5300 in 6 pts. Rituximab 375 mg/m2 on days +1 and +8 was added in 21 of 49 pts with CD20+ lymphomas. GVHD prophylaxis included tacrolimus and methotrexate (n = 39), mycophenolate (n = 8) or sirolimus (n = 13). Thirty-two pts received grafts from matched sibling donors, 21 from matched unrelated, and seven from mismatched (one antigen/allele) unrelated donors. The cumulative incidence of grade 2-4 and grade 3-4 acute GVHD at day 100 was 74% and 20% respectively. The cumulative incidence of moderate-severe chronic GVHD at 2 years was 62%. Progression free survival (PFS) at 3 years was 47.8% for all pts. Overall survival (OS) and CI of relapse at 3 year was 55.2% and 26.9% respectively. OS and PFS were superior for pts with FL and LBL. Patients in CR at transplant had an OS and CI of relapse at 3 years of 60.7% and 10.7% respectively. NRM at day 100 and 3 year was 10% and 25.3% for the whole group. Main causes of death were relapse (40%), infection (25%) and GVHD (14%). In conclusion, in our series outcomes were better in patients with LBL and FL. NRM was lower than historically reported with BuCy or TBI based conditioning regimens but relapse continues to be the main cause of failure.

Table. Progression free survival, Overall survival and Cumulative incidence of relapse and Non-relapse mortality according to Histologic Type

	Follicular n = 17	T cell n = 13	DLBC n = 12	Mantle n = 9	Lymphoblastic n = 8	All n = 60
PFS						
1 yr	70.5	30.7	33.3	55.6	62.5	51.7
3 yr	64.7	23.1	33.3	27.8	62.5	47.8
OS						
1 yr	70.5	53.8	41.7	55.6	100	63.2
3 yr	64.7	46.1	41.7	55.6	66.7	55.2
CI RELAPSE						
1 yr	5.9	38.5	33.3	22.2	37.5	25.0
3 yr	5.9	46.2	33.3	22.2	37.5	26.9
CI NRM						
100 day	11.8	23.1	0	11.1	0	10.0
1 yr	29.4	30.8	33.3	22.2	0	23.3
3 yr	29.4	30.8	33.3	22.2	0	25.3