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IMPACT OF DISEASE AND MOBILIZING AGENTS ON INITIAL AND RE-MOBILIZATION FAILURE

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Background: High-dose chemotherapy with autologous stem cell transplantation (ASCT) is a common treatment strategy in lymphoma and myeloma, but no standard approach for the mobilization of peripheral hematologic stem and progenitor cells has been established. Levels of circulating CD34+ cells, a surrogate marker for mobilization efficiency, vary widely between pts, and may be influenced by disease state, prior therapy, and/or mobilization regimen. **Methods:** The Washington University (St. Louis, MO) transplantation database includes clinical parameters from 407 MM, 562 NHL, and 164 HD pts who received an ASCT (1995-2006). A retrospective analysis of this large (1133 pts) population was conducted to determine factors associated with mobilization efficiency. Mobilization failure was defined as collection of $< 2 \times 10\text{^}6$ CD34+ cells/kg within 5 apheresis days. Statistical analysis included ANOVA with Scheffe Test to determine differences in mobilization between the various mobilization regimens (G-CSF, G-CSF/chemotherapy, G-/GM-CSF, G-CSF/AMD3100). **Results:** All pts were included in the analysis; 87% received G-CSF alone as the initial mobilization regimen. Mobilization failure rates are summarized in Table 1. NHL and HD pts had a 4-fold higher failure rate than MM pts. G-CSF/chemo increased the median CD34+ yield compared to G-CSF alone, although no obvious impact on the failure rate was noted in this relatively small group of pts. Remobilization was associated with high failure rates in NHL (79.2%), HD (77.1%), and MM (73.3%). Pooled collections were $<2 \times 10\text{^}6$ CD34+/kg in 33.6%, 37.1%, and 36.7% of failed mobilizers, resp. G-CSF mobilization failures remobilized with G-CSF plus AMD3100 collected significantly more CD34+ cells than G-CSF-failures remobilized with either G-CSF, G/GM-CSF or G-CSF/chemo (1-way ANOVA: $F(3, 233) = 27.878$, $F0.5(3, 233).05 = 2.643$, $p < .0001$). The compared groups did not significantly differ in initial mobilization efficiency with G-CSF (as determined by ANOVA and Scheffe Test). **Conclusions:** The mobilization failure rate is substantially higher in NHL and HD pts than MM pts. Pts who fail initial mobilization are likely to fail a 2nd mobilization, regardless of disease state. As the combination of chemotherapy to G-CSF may not be sufficient to reduce failure rates, alternative mobilization strategies are needed to improve HSPC collection, particularly in NHL/HD pts and failed mobilizers.

First mobilization failures (< 2×10^6 CD34+/kg)

	Mobilization regimen	N	Failures	Median yield (x10^6)	Median yield (x10^6)
NHL	G-CSF	471	26.5%	2.89	2.76-3.04
	G-CSF/Chemo	35	22.9%	4.68	2.8-8.53
	All*	564	28.7%		
HD	G-CSF	130	26.2%	3.01	2.75-3.37
	G-CSF/Chemo	12	16.7%	5.38	2.35-9.52
	All*	165	24.8%		
MM	G-CSF	386	6.5%	4.62	4.16-4.98
	G-CSF/Chemo	17	5.9%	8.52	4.46-16.3
	All*	409	6.6%		

*Incl. pts mobilized w. alternative regimens

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AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANT USING BUSULFAN, ETOPOSIDE, HIGH DOSE ARA-C, AND G-CSF PRIMING AS CONDITIONING REGIMEN IN PATIENTS WITH ACUTE MYELOID LEUKEMIA IN FIRST COMPLETE REMISSION

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Introduction: Conditioning regimens for autologous stem cell transplantation (ASCT) in patients with acute myeloid leukemia (AML) using more specific drugs for myeloid malignancies, such as high-dose Ara-C (HD/Ara-C) and etoposide, have been increasingly proposed as an alternative the classic BUCY schedule. **Objectives:** To analize safety and efficacy of a conditioning regimen combining busulfan, etoposide, HD/Ara-C, and G-CSF priming for patients with AML in first complete remission (CR1) undergoing ASCT. **Patients:** 147 patients with AML in CR1 after induction and consolidation therapy with idarubicin or daunorubicin and Ara-C following a '3+7' schedule (PETHEMA LMA99 trial) underwent ASCT. They were 65 male and 82 female with a median age 46 years. The median WBC and platelet counts at presentation were 2×10^9/L (range, 0.04-193) and 59×10^9/L (range, 7-578), respectively. According to the MRC criteria, 125 patients with available karyotype (85%) were classified as follows: 24 patients (19%) with standard risk, 87 patients (70%) with intermediate risk, and 14 patients (11%) with high risk. Conditioning regimen consisted of busulfan 1 mg/kg/6 hours on days -8 to -5, etoposide 20 mg/kg/day on days -4 and -3, Ara-C 3 g/m^2/12 hours on days -3 and -2, and G-CSF 10 μg/kg/day on days -9 to -2. **Results:** Median time from diagnosis to ASCT was 6 months. Median time to neutrophil count recovery above 0.5×10^9/L was 12 days (range, 5-90) and days of hospital stay was 29 days (range, 11-94). Thirty-two percent of patients had bacteremia, 9.5% documented infection without bacteremia , and 21% clinically documented infection without microbiological documentation. The most relevant extrahematological toxicity was gastrointestinal toxicity grade ≥3 (36%). Event-free survival (EFS) at 4 years was 53%. Cytogenetics was the only variable associated to EFS: 62% for standard-risk group, 52% for intermediate-risk group, and 24% for high-risk group ($P = 0.0066$). Five patients died due to ASCT (transplant-related mortality, 3.4%). Four of them died before day +100 mainly due to infections, while the remaining patient died of pulmonary thromboembolism 31 months after ASCT. **Conclusions:** The conditioning regimen combining busulfan, etoposide, HD/Ara-C, and G-CSF priming shows a high antileukemic efficacy in patients with AML in CR1. This regimen shows a moderate toxicity profile and low transplant-related mortality. Citogenetics was the only prognostic factor identified for EFS.

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ARSENIC TRIOXIDE WITH ASCORBIC ACID AND HIGH-DOSE MELPHALAN FOR AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MULTIPLE MYELOMA

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Backround: Arsenic trioxide (ATO) has been shown to be synergistic with melphalan both in vitro and in vivo. We conducted a phase