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MOBILIZATION WITH CHEMOTHERAPY COMPARED TO G-CSF ALONE: AN ANALYSIS OF RESOURCE USE AND COST IN AUTOLOGOUS STEM CELL TRANSPLANT PATIENTS

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Objectives: The most common mobilization regimens for autologous stem cell transplant (ASCT) are granulocyte-colony stimulating factor (G-CSF) alone or in combination with chemotherapy. Chemotherapy plus G-CSF has been shown to mobilize more cells than G-CSF alone but often at the expense of costly side effects. The purpose of this study was to evaluate resource use and cost during mobilization for patients mobilized with chemotherapy plus G-CSF vs. G-CSF alone.

Methods: Patients 18 years of age or older with evidence of ASCT between January 1, 2000 and December 31, 2006 were identified from a nationally-representative database of private payer medical and pharmacy claims. Patients had to receive apheresis within 60 days prior to ASCT and have a history of multiple myeloma, non-Hodgkin's lymphoma, or Hodgkin's disease; patients also were required to be continuously enrolled in one health plan for at least 90 days pre-ASCT and have no evidence of a prior ASCT. Using claims data, patients were classified into one of two mobilization regimens: G-CSF alone or chemotherapy with G-CSF. Total resource use and direct medical costs were calculated from the time of administration of the mobilization regimen to the first apheresis day; paid claims were used as a proxy for costs and expressed in 2006 US$.

Results: 235 ASCT patients were identified; 172 (73%) were mobilized with G-CSF alone and 63 (27%) with chemotherapy and G-CSF. Total mobilization costs were 27% higher among patients mobilized with chemotherapy versus those mobilized with G-CSF alone ($39,686 vs. $31,251, $P = 0.020$). Patients mobilized with chemotherapy had higher inpatient hospital costs ($8,225 vs. $5,854, $P = 0.056$), more use of growth factor ($9,217 vs. $6,948, $P = 0.003$), and higher pharmacy costs ($5,343 vs. $1,484, $P<0.001$) than patients mobilized with G-CSF alone. Rituximab comprised 48% of pharmacy costs in the chemotherapy and G-CSF group, while the remaining costs were due to chemotherapy drugs, MESNA, and anti-emetics. Excluding rituximab and G-CSF, patients mobilized with chemotherapy had pharmacy costs that were $1,645 higher than patients mobilized with G-CSF alone.

Conclusion: ASCT patients mobilized with chemotherapy had higher total mobilization costs than patients mobilized with G-CSF alone. This significant difference in costs was due to more costly hospitalizations and greater use of G-CSF and other pharmaceuticals in patients mobilized with chemotherapy.

Total Mobilization Costs for Chemotherapy and G-CSF vs. G-CSF Alone

	Chemotherapy and G-CSF	G-CSF Alone		
	Mean (SD)	Mean (SD)	% Difference	*P*-value
Total Mobilization Costs	$39,686 (31,188)	$31,251 (31,750)	27%	0.020
Inpatient	$8,225 (19,214)	$5,854 (18,312)	41%	0.056
Outpatient	$16,901 (17,085)	$16,965 (19,772)	0%	0.971
Pharmacy	$14,560 (12,067)	$8,432 (13,502)	73%	<0.001
- G-CSF	$9,217 (7,069)	$6,948 (10,514)	33%	0.003
- Rituximab	$2,547 (6,228)	$332 (1,625)	667%	<0.001
- Other retail pharmacy	$2,797 (2,923)	$1,152 (2,644)	143%	<0.001

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CD34+ CELL YIELD ON DAY 1 OF APHERESIS PREDICTS TOTAL CD34+ CELL MOBILIZATION, NEUTROPHIL RECOVERY, AND SURVIVAL AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION FOR LYMPHOMA

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Lymphoma patients who mobilize CD34+ cells poorly have inferior outcomes after autologous stem cell transplantation (ASCT). Identifying poor mobilizers early may allow intervention (e.g., adding plerixafor) to improve mobilization. We retrospectively compared CD34+ cell yields on day 1 (D1) of autologous stem cell collection with the total CD34+ cell yield and with ASCT outcomes including neutrophil (ANC) recovery >500 cells/ul, nonrelapse mortality (NRM), relapse-free survival (RFS), and overall survival (OS). Patients (n = 411) underwent ASCT at a single center from 1998 through 2007. Diagnoses were Hodgkin lymphoma (n = 83), aggressive B-cell NHL (n = 196), indolent B-cell NHL (n = 64), mantle cell NHL (n = 37), or T-cell NHL (n = 31). All were mobilized with etoposide 2 g/m2 and filgrastim 10 ug/kg. After WBC recovery to 1000/uL, leukapheresis commenced for ≥2 days and up to 5 days, to a target dose of ≥7 (minimum ≥2) million CD34+ cells/kg. Conditioning for ASCT was high-dose busulfan, cyclophosphamide, and etoposide. Median follow-up among 248 survivors is 42 months. Causes of death were relapse (66%), NRM (28%) and unknown (6%). Total CD34+ cell yield was median 8.82 million/kg (range, 2 to 162) in 3 days of apheresis (range, 2 to 20). Median D1 yield was 1.98 million CD34+ cells/kg (range, 0 to 120). The D1 yield was strongly correlated with total CD34+ cell yield ($R = 0.87$, $P<0.001$) and days of apheresis required ($R = -0.87$, $P<0.001$). Higher D1 yield (by patient quintiles) was associated in univariable analyses with faster ANC recovery after ASCT ($P<0.001$), lower NRM ($P = 0.03$), better OS ($P = 0.03$, $P = 0.001$, and $P<0.01$ for quintiles 3, 4, and 5 vs. quintile 1), and better RFS ($P<0.01$ and $P = 0.04$ for quintiles 4 and 5). In multivariable analyses, D1 yield and Karnofsky performance status (KPS) were prognostic for NRM; D1 yield, KPS, lymphoma histology, number of prior chemotherapy regimens, and pre-ASCT disease status were prognostic for RFS; and D1 yield, age, KPS, histology, number of prior regimens, and number of days of apheresis were prognostic for OS. These data extend our prior observation that stem cell mobilization is associated with ASCT outcomes in lymphoma patients. The D1 CD34+ cell yield predicts the total CD34+ cell yield, ANC recovery after ASCT, NRM, and survival. Poor mobilizers are identifiable on D1 of CD34+ cell collection and represent a patient subgroup in which to test interventions to improve mobilization and potentially other ASCT outcomes.

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DAY 15 INTERLEUKIN 15 LEVELS AFFECT NATURAL KILLER CELL RECOVERY AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION

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Recently, we reported in a prospective study (Porrata et al. Biology of Blood & Marrow Transplantation 2008;14(7):807–16) that the absolute number of natural killer (NK) cells at day 15 post-autologous stem cell transplantation (ASCT) affects survival. Factors affecting NK cell recovery at day 15 post-ASCT are not completely understood. Interleukin-15 (IL-15) is a cytokine associated with NK cell differentiation and homeostasis. Thus, we studied the role of day 15 IL-15 on NK cell recovery post-ASCT. From February 2002 to February 2007, 50 non-Hodgkin lymphoma (NHL) patients enrolled in the study. We identified higher levels of day 15 IL-15 compared with normal controls and pre-ASCT IL-15 levels [normal IL-15 levels: median = 0 pg/ml (range: 0–3.37 pg/ml); pre-ASCT IL-15 levels: median = 0.09 pg/ml (range: 0–229.42 pg/ml); and day 15 IL-15: median = 5.48 pg/ml (range: 0–36.94), $p < 0.0001$)]. ROC curve and AUC analysis showed that day 15 IL-15 was a significant marker for NK cell recovery (AUC = 0.87, $p < 0.0001$). The best cut-off level was 9.5 pg/ml. Groups (≤9.5 or >9.5 pg/ml) were balanced in regard to histology ($p = 0.48$); gender ($p = 0.8$); stage ($p = 0.7$); LDH ($p = 0.5$); disease status prior to ASCT ($p = 0.9$); performance