Mobilization for Autologous Stem Cell Transplantation in Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma: A Single Institution Experience

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Persons aged 18-75 years			
	European American	African American	Other
US Census data 2007-2010, 8 counties of WNY	90%	9.5%	<1%
NYS DOH Cancer Registry, 2005-2010 cases of acute and chronic leukemia, lymphoma and myeloma in 8 counties of WNY	91%	8%	<1%
Total Referrals to BMT program at RPCI 2005-2011	90.5%	7%	2.5%
Total Referrals to BMT program at RPCI 2005-2011, and resided in 1 of 8 counties in WNY	90%	8%	2%
All patients who received a BMT at RPCI 2005-2011	92%	6%	2%
Received a BMT at RPCI, 2005-2011 and resided in 1 of 8 counties in WNY	91%	7%	2%
Proportion of BMT referrals who participated in biospecimen research, 2005-2011	95%	95%	88%
Proportion of BMT referrals who participated in survey research, 2005-2011	70%	37%	67%

Health (DOH) Cancer Registry and 2007-2010 U.S. Census Data. From 2005-2011, 1106 patients aged 18-75 years were referred to our center for BMT consultation, the majority of whom (74%) reside in the 8 counties of Western NY (WNY). The Table compares the race of BMT patients, referrals, cancer cases and general population estimates. Reasons for not receiving a BMT differed by race with European Americans (EAs) mostly due to patient decision (20%) and African Americans (AAs) mostly due to death before BMT (16%). We further examined patient characteristics which might influence referral for BMT consultation and utilization of BMT by conducting a retrospective cohort study of the 1106 BMT referrals who participated in our Databank and Bio-Repository (DBBR) biologic specimen banking (one-time blood sample collection) and epidemiologic questionnaire (written at 9th grade level, 45 minutes to complete). As shown in the Table, participation in biospecimen research did not vary by race, however AAs were significantly less likely to participate in survey research than EAs and other races. While the minority rates of referrals and BMT may appear low, they reflect the race distribution of the cancer cases and general population in WNY. AAs are equally likely to participate in biospecimen banking, but further study is needed to elucidate reasons for lower participation in survey research.

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Maximum Tolerated Dose of Lomustine in Combination with Etoposide, Cytarabine and Melphalan in a Short Conditioning Regimen in the Transplantation of Hematopoietic Stem Cells in Patients with Lymphoma

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The maximum tolerated dose (MTD) of lomustine when used in combination with etoposide, ara-C, and melphalan (LEAM) in a conditioning regimen prior to autologous hematopoietic stem cell transplantation (HSCT) for lymphoma is unknown. We performed a phase 1 clinical trial with traditional 3+3 design to determine the MTD of lomustine administered on D-4 followed by etoposide (1 g/m2 D-3), ara-C (4g/m2 D-2), and melphalan (140 mg/m2 D -1). Dose-limiting toxicity (DLT) was defined as grade 3 or 4 non-hematologic or infectious toxicity, delayed engraftment beyond D+30 or death from any cause. The initial dose of lomustine was 200 mg/m2 (L200 cohort), increased by 200 mg/m2 at each subsequent cohort (L400, etc). Because L400 exceeded MTD, a third cohort was created with 300 mg/m2 of lomustine (L300). Fourteen subjectes entered the trial being 9 with Hodgkin lymphoma, 2 with mantle cell lymphoma, 1 with diffuse large B-cell lymphoma, 1 with follicular lymphoma and 1 with peripheral T-cell lymphoma. Subjects were either in PR (n=6) or CR (n=8) after the most recent salvage theapy. Median age of subjects was 36 years. Six patients were treated with L200 (1 DLT, death by sepsis), two patients were treated with L400 (2 DLT, grade 4 gastrointestinal toxicity) and 6 patients were treated at an intermediate dose of 300 mg/m2 (L300, 1 DLT, neurological grade 4, reversible) and L300 was declared the MTD. A median number of 6.91 CD34 cells/kg (range 1.37-18.8) were infused. The average duration of neutropenia (neutrophils <500/mm3) was 7.8 days, lower than the historical control of 13 days with cyclophosphamide, BCNU, and etoposide (CBV) conditioning. Neutrophils and platelet engraftment occurred on average at day 10 and 12 respectively. We concluded that 300mg/m2 is the MTD of lomustine in combination with etoposide, ara-C and melphalan (LEAM) conditioning in autologous-HSCT in patients with lymphoma. More detailed toxicity profile and anti-lymphoma activity will be obtained from ongoing expansion of the L300 cohort. LEAM is a simple conditioning regimen with rapid dosing, consequent short period of neutropenia and acceptable toxicity.

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Mobilization for Autologous Stem Cell Transplantation in Hodgkin's Lymphoma and Non-Hodgkin's Lymphoma: A Single Institution Experience

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Background: Plerixafor (Mozobil) plus G-CSF is an FDA-approved strategy to mobilize hematopoietic stem cells (HSCs) in patients (pts) with NHL and Multiple Myeloma. We report our institutional experience mobilizing HSCs with and without plerixafor in pts with NHL and HL.

Methods: We collected data on all NHL (n=85) and HL (n=44) pts who underwent mobilization without chemotherapy between 2010 and 2012 at Ohio State University under IRB approved protocols. Our standard is plerixafor on day 4 of G-CSF in pts who received radiation, ≥10 cycles of chemotherapy, are ≥age 60, or on day 5 to pts who had a CD34 count of <10/μL that morning. Our target CD34+ cell yield is >5x10^6 /kg recipient weight, with a minimum of >2x10^6 /kg. Factors associated with sufficient mobilization were evaluated using univariate logistic regression models as well as graphical analyses.

Results: Most pts were male (56%) and Caucasian (91%), the median Karnofsky (KPS) score prior to transplant was 90 (range: 70-100); those who received plerixafor (n=88) tended to have lower KPS vs. G-CSF alone (n=41; p=.07). Median age of the cohort was 54 years (range: 19-76), with HL pts younger than NHL pts (median: 37 vs. 60 years). Ability to collect $>2x10^6$ /kg CD34+ cells on day 1 was highly associated with achieving a total yield of $>5x10^6$ /kg CD34+ cells (OR=41.6; p<.001). Both collection goals were significantly associated with earlier time to ANC engraftment (p<.001). In the 88 pts who received plerixafor (75 NHL pts), the median number of doses was 2 (range: 1-3); 76% received their first dose on day 4 (range: 4-7). Patients who received day 4 plerixafor had significantly lower CD34 counts on day 4 than those that received G-CSF alone (p<.001). Plerixafor use was highly associated with $>2x10^6$ /kg on first collection (p=.03), but not with the total number of collections or the ability to achieve a total yield of $>5x10^6$ /kg CD34+ cells. However, whether or not pts got plerixafor on day 4 vs. later was significantly associated with sufficient total CD34+ cell yield (37% vs. 10%; p=.016).

Conclusions: Pts who received planned plerixafor on day 4 were more likely to achieve the target yield despite having risk factors for mobilization failure. Routine use of plerixafor in lymphoma pts who are less likely to be poor mobilizers may lead to fewer apheresis procedures, faster engraftment, and shorter hospital stays. The potential economic benefits of this strategy warrant further investigation.

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Pegylated Filgrastim Is Comparable with Filgrastim As Support for Autologous Hematopoietic Stem Cell Transplantation

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Objetives: G-CSF has shown to shorten time to neutrophil engraftment in autologous peripheral blood hematopoietic stem cell transplantation (Auto-HSCT). Two filgrastim pharmacological presentations exist for clinical use, non-pegylated and pegylated. Our aim was to compare clinical outcomes in using as support Peg-Filgrastim (PEG-F)or Filgrastim (F) in a group of adults undergoing autologous HSCT.

Methods: From 2010 to 2012, 69 adult patients underwent Auto-HSTC in our BMT unit. Attending physician decided the allocation to PEG-F or F. Other support measures were standardized in all patients. An independent reviewer collected data from medical records. Descriptive analyses were carried-out as well as Kaplan-Meier survival estimates.

Results: From 69 included subjects, 50 received PEG-F and 19 F. Median age was 46 vs 54 for PEG-F vs. F (P=.05). There was no difference by gender, body weight, diagnoses, conditioning regimen, or CD34+ cells infused. Most common diagnoses were Multiple Myeloma (48%) and Hodgkin lymphoma (28%). In concordance with diagnoses, Melphalan (52%) and BEAM (46%) were the conditioning regimens most commonly used. Median CD34+ (x106)/Kg preserved were 4.3 for PEG-F vs. 3.9 for F, (P=.61). Median initiation of PEG-F was 7 days after cell infusion compared to 3 days for F; P<.01. We did not have transplant mortality death. Neutropenic fever was equal among groups (58% vs 47%). Median number of days to achieve 500 neutrophils was 12 vs 11 (PEG-F vs F); P<.01. All patients showed neutrophil and platelet engraftment.

Conclusions: We did not find clinically relevant differences among the effects of the two pharmacological filgrastim presentations. We also found that 4 day difference in starting the drug only represented 1 day of delay in neutrophil engraftment without clinical repercussions. Now, we considered changing our clinical practice by introducing PEG-F for all patients, taking into consideration ease of application and economical consideration.

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BEAM Vs Melphalan Based Conditioning Therapy for Second Autologous Stem Cell Transplant (ASCT) for Multiple Myeloma (MM)

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Background: Salvage ASCT is increasingly utilized for eligible MM patients (pts). High dose melphalan (HDM) is the standard conditioning used for 1st ASCT. Despite concerns for resistance, HDM is predominantly used as conditioning regimen for 2nd / or salvage ASCT. BEAM (Carmustine, etoposide, Ara-C and Melphalan) has shown superior PFS and OS compared to HDM during 1st ASCT for MM pts. We conducted a single institution retrospective analysis to evaluate response and toxicity with BEAM conditioning in 2nd ASCT.

Methods: Thirty two pts who received 2nd ASCT for MM (2007-2013) were identified. Sixteen pts received HDM (140-200mg/m^2; Group A) and an equal number received BEAM (carmustine 300 mg/m2, etoposide 100 mg/m2, cytarabine 100 mg/m2, and melphalan 140 mg/m2; Group B). Patient characteristics, toxicity and response at day 100 were collected and compared between the 2 groups. Fischer's

Table 1
Data Summary

Variables	Group A, N=16	Group B, N=16
Age* (yrs)	58 (39-72)	58 (49-68)
KPS* (%)	70 (60-80)	70 (60-80)
Creatinine Clearance pre 2nd ASCT* (ml/min)	76 (42-129)	108 (44-218)
CR pre- 2nd ASCT [n (%)]	2 (12)	3 (14)
CD34+ cells infused for 2nd ASCT* (x 10^6 cells/kg)	3.35 (2.2-10.7)	3.12 (2.79-12.04)
Febrile Neutropenia [n (%)]	10 (63)	16 (100)
In-patient stay for 2nd ASCT* (days)	15 (12-24)	23 (19-51)
CR at Day +100 post 2nd ASCT [n (%)]	2¶ (14)	7ξ (47)

KPS- Karnofsky's Performance score
CR- Complete response
ASCT- Autologous Stem cell transplant
* Values are median with range in parenthesis
¶Day +100 response data not available for 2 patients in Group A
ξ Day +100 response data not available for 1 patient in Group B