misfold, form fibrils and deposit in vital organs causing malfunction and death. HDM/SCT can produce hematologic remissions and prolong survival. HDM/SCT was developed for the treatment of AL at Boston University Medical Center in 1994. In 1996, treatment was moved to the outpatient setting. The program has been FACT-accredited since 2000. To date, we have performed 496 SCTs. 95% of patients are offered outpatient treatment. While patients with severe cardiac involvement are not candidates for HDM/SCT, patients with less severe cardiac disease can undergo HDM/SCT, with impatient cardiac monitoring. The CP begins with an extensive multidisciplinary team evaluation involving members from hematology, nephrology, cardiology, pulmonology, neurology, psychiatry, nursing, nutrition, clinical research and the amyloid program. The evaluation involves 3 days of visits which assess organ involvement, performance status, support network including their ability to physically and emotionally adhere to an outpatient treatment program as well as to post-transplant follow-up, and candidacy for a research protocol. Weekly meetings are held to discuss evaluation results and determine eligibility before a patient can be scheduled. Once treatment begins, daily rounds, including toxicity evaluations, physical exams, medication review and reinforcement of the treatment plan are conducted. Oral and written instructions are provided regarding expected toxicities, symptom management and emergency contacts. Prophylactic treatment with antiemetic, antibacterial, antiviral, antifungal and growth factors are used. The most common reasons for hospitalization is febrile neutropenia. Severe diarrhea, vomiting, diarrhea, dehydration may also necessitate hospitalization. CPs and SOPs were developed early on in the program and are adhered to with a mechanism to document any deviations. CPs are reviewed annually for revisions based on current peer-reviewed literature and program experience. Educational short courses are held regularly for staff to insure adherence to CPs and SOPs. In summary, outpatient HDM/SCT is a feasible treatment option for patients with AL amyloidosis, provided treatment is conducted in an experienced center.

**102 AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION MAY REVERSE RENAL FAILURE IN PATIENTS WITH MULTIPLE MYELOMA**


**Background:** Approximately 20% of patients with multiple myeloma (MM) have renal failure at diagnosis, and about 7% are dialysis-dependent. These patients may potentially benefit from high-dose chemotherapy and autologous hematopoietic stem cell transplantation (auto SCT). However, many of these patients are considered ineligible for auto SCT due to concerns about increased treatment-related toxicity. We evaluated the outcome of 46 patient with MM and renal failure, defined as serum creatinine ≥2 mg/dl sustained for >1 month, who received auto SCT at our institution.

**Methods:** Forty-six patients with a median age of 56 years (range: 29–72) received auto SCT between September 1997 and August 2006. Median serum creatinine and creatinine clearance (CrCl) at auto SCT were 2.9 mg/dl (range 2.0 – 12.5) and 33 ml/min (range 8.7 – 63), respectively. Ten patients (22%) were dialysis-dependent.

**Results:** Median follow up in surviving patients was 34 months (range 5–81). Complete (CR) and partial responses (PR) were seen in 9 (22%) and 22 (53%) of the 41 evaluable patients, with an overall response rate of 75%. Two patients (4%) died within 100 days of auto SCT. Grade 2–4 Non-hematological adverse events were seen in 18 patients (39%) and included cardiac arrhythmias, pulmonary edema, hyperbilirubinemia. Median progression-free (PFS) was 22.8 months and median overall survival OS has not yet been reached. Kaplan-Meier estimates of 3-year PFS and OS were 36% and 64%, respectively. Thirty patients (62.5%) are still alive after a median follow up of 34 months, and 18 patients (39%) are alive and progression-free. Significant improvement in renal function, defined as an increase in GFR by 25% above baseline, was seen in 17 patients (37%). None of the 10 dialysis-dependent patients became dialysis independent. A pre-transplant creatinine level of ≥3 mg/dl was associated with a significantly shorter overall survival (p = 0.05, HR 2.8).

**Conclusions:** Auto SCT was safe and feasible in selected patients with MM and renal failure, and was associated with a significant improvement in renal function in approximately one-third of the transplanted patients.

**103 CYTOREDUCTIVE REGIMEN CONTAINING RAMINUSTINE (MCNU), CARBOPLATIN, ETOPOSIDE AND CYCLOPHOSPHAMIDE (MCEC) BEFORE AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION (PBSCT) FOR RELAPSED OR REFRACTORY LYMPHOMA**

Asakura, Y., Tanoue, R., Kim, S.-W., Azuma, T., Kato, T., Kato, T., Baba, M., Yamasaki, T., Hattori, A., Sato, K., Nakamura, T., Watanabe, T., Kobayashi, Y., Tominai, K., Takane, Y. National Cancer Center Hospital, Chuo-ku, Tokyo, Japan

MCNU, a derivative of nitrosourea that was developed in Japan, shows good penetration into CSF and might be expected to decrease CNS relapse of lymphoid malignancies when used before transplantation. However, its feasibility and efficacy have not been extensively analyzed in adult patients with lymphoma. We retrospectively evaluated an MCEC regimen which consisted of MCNU (200 mg/m²) on days -8 and -3, carboplatin (300 mg/m²) on days -7 through -4, etoposide (500 mg/m²) on days -6 through -4 and cyclophosphamide (50 mg/kg on days -3 and -2) in 68 patients with lymphoma (median age 48 yr; range, 20–65 yr) who underwent autologous PBSCT at our institution between Jan. 1999 and Feb. 2008. The diagnosis included DLBCL (N = 33), FL (14), including 6 transforms, T-cell lymphoma (12), and HL (9). The median time from diagnosis to PBSCT was 20 months (2–198 mo), and the median number of prior chemotherapy regimens was 3 (2–7). 97% had ECOG PS ≤2, 41% had prior XRT, 4% had bulky disease, 62% had stage III-IV disease, 28% had IPI at relapse of H/H-I. The disease status at PBSCT was 1st CR/PR in 15%, ≥2nd CR/PR in 72%, and NC/SD in 13%. Grade (G) non-hematological toxicities (CTCAE ver. 3.0) included elevated transaminase (1), hyponatremia (1) and hypokalemia (1). G1 and CNS toxicities consisted of G3 mucositis (10), G3 diarrhea (27) and G2 seizure (1). There were no G4 cardiac, pulmonary or renal toxicities except for one who died of treatment-related MOF. The cumulative incidence of relapse at 2 yrs was 49 %. Of 33 relapses, 2 occurred newly in the CNS without any previous history. With a median follow-up of 24 months (3–80) after PBSCT for surviving patients, the 2-yr OS and PFS were 68% (95% CI 55–81%) and 50% (95% CI 38–63%), respectively. In univariate analyses, T-cell phenotype (p < 0.01), bulky disease (p < 0.01), disease status other than CR/PR (p < 0.01), stage III-IV (P = 0.03), IPI (H/H-I, p < 0.01) and treatment without rituximab (p < 0.01) were unfavorably associated with OS. Multivariate analysis confirmed that T-cell phenotype (HR 1.85; 95% CI 0.85–2.86, p < 0.01), bulky disease (HR 3.02; 95% CI 1.26–6.79, p < 0.01), disease status (HR 1.95; 95% CI 0.89–3.91, p = 0.01), IPI (HR 2.66; 95% CI 1.19–4.14, p < 0.01) and treatment without rituximab (HR 4.12; 95% CI 1.14–7.10, p < 0.01) were unfavorably associated with OS. The results suggested that autologous PBSCT with the MEC regimen is a feasible and effective treatment option for relapsed/refractory lymphoma.

**104 TIMING OF HIGH DOSE MELPHALAN (HDM) AND OUTCOMES FOR AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) IN PATIENTS WITH MULTIPLE MYELOMA (MM)**

Mahendra, A., Bolwell, B., Rybicki, L., Siboeck, R., Polhman, B., Andresen, S., Earl, M., Bean, R., Copelan, E., Kaldy, M.1 Cleveland Clinic, Cleveland, OH; 2 Cleveland Clinic, Cleveland, OH

HDM is the most widely used preparative regimen for ASCT in MM. The timing of HDM prior to transplantation has varied between studies. HDM is given on day −2 (2 days prior to stem cell injection) in some and on day −1 in others. At our institution, HDM was initially given on day −2. Considering Melphalan undergoes rapid hydrolysis in plasma with a short half-life in the order of 60–90 minutes, administration on day −1 seemed feasible and...
our protocol was modified. We report a single-institution experience using HDM as a preparative regimen in 40 consecutive pts with MM receiving melphalan on day –2 or day –1. Between July 2003 and May 2008, 40 pts with MM underwent HDC with ASCT using HDM either on day –2 (n = 13) or day –1 (n = 27) in sequential cohorts. The two groups were similar with respect to age, gender, ISS stage, number of prior chemotherapy regimens, prior radiation therapy, FEV1 and DLCOs pre transplantation. The median CD34+ dose (×10^6 /kg) was 5.82 (range, 2.78–13.68) in the group treated with HDM on day –2 and 3.36 (range, 2.06–10.71) in the group treated with HDM on day –1 (p<0.001). Pts treated with HDM on day –2 recovered granulocytes at a median of day 11 (range, 10–12) whereas pts treated on day –1 recovered by day 13 (range, 11–17 post-transplant (p<0.001); this difference remained significant after adjusting for CD34+ dose (p<0.001). Pts achieved platelet counts more than 20,000/µL at a median of 12 days (range, 10–27) post-transplant in the group receiving HDM on day –2 and by 13 days (range, 8–19) in the group treated on day –1 (p = 0.74). Pts receiving HDM on day –1 had worse mucositis as measured by the oral mucositis assessment scale (p = 0.027). In the group receiving HDM on day –2, 12 pts (92%) are alive with a median follow up of 7 mths (range, 3.8–18.7). In the group receiving HDM on day –1, 24 pts (89%) are alive with a median follow up of 27.8 mths (range, 1.2–55.4). There was no significant difference observed in the median relapse-free survival (p = 0.56) or overall survival (p = 0.48) between the two groups. Melphalan has a short half-life on the order of 60–90 minutes and hence administration on day –1 seems feasible. However, our data indicates that the time to granulocyte engraftment is shorter in pts receiving HDM on day –2, time to platelet engraftment is similar and severity of mucositis is lower. These data suggest that administration of HDM on day –2 may improve hematopoietic recovery and decrease mucositis.

### 105

**A MD3100: SUCCESSFUL MOBILIZATION IN PATIENTS WHO FAIL STANDARD MOBILIZATION WITH GOOD TRANSPLANT OUTCOME AND NO SIGNIFICANT TOXICITY**

Kanakarat, G.T., Beveridge, R., Eichna, D., Scherer, D., Sampal, K., Salam, A., See, G.B., Lucy Nam, M.H., Mintz, K., Souab, M., Oroh, G. INOVA Fairfax Hospital, Fairfax, VA

AMD3100 reversibly inhibits the binding of SDF-1 to CXCR4, which normally regulates the migration of hematopoietic stem cells (HSC) from the bone marrow. Used in conjunction with G-CSF, rapid mobilization of CD34+ HSC into the peripheral bloodstream can be achieved. In addition to the standard mobilization protocol with G-CSF, AMD3100 is administered through a compassionate-based protocol at 240 µg/kg in the evening before the first day of pheresis and every evening preceding subsequent days of pheresis. At our institution, we report use of the drug when patients have failed to collect 3.0 million CD34 stem cells in patients with hematologic malignancies for ASCT using amifostine 740 mg/m² (day T-2 and T-1) and melphalan (Mel) 200 mg/m² (day T-1). During this same 2006–2008 time period, we performed a total of N = 46 autologous PSC transplants in MM patients age 38–71 yr using the same mobilization and ASCT regimen; median (range) CD34+ cell dose infused was 8.8 (3.5–23.1) ×10^6/kg. Exposure to immunomodulatory agents may affect blood T-regulatory cells (T-reggs), cells that protect the host from autoimmune disease by suppressing self-reactive cells. The leukapheresis products collected after PSC mobilization from such patients may contain low concentrations of T-reg cells. Further, Mel-containing regimens are associated with a higher incidence of GVHD in the allogeneic setting (A Shimoni et al. Leuk 21: 2109, 2007). Although rapid-autologous GVHD has potentially a serious complication of ASCT. Despite absence of rash, this condition should be considered in the differential diagnosis of MM pts with otherwise unexplained GI symptoms or hepatic dysfunction in the post-ASCT period. We hypothesize that the combination of exposure to immunomodulatory agents before PSC collection and use of Mel in ASCT predispose select pts to spontaneous autologous acute GVHD.

### 107

**FEASIBILITY OF CD34-POSITIVE STEM CELL MOBILIZATION BY ADMINISTRATION OF AMD3100 SIX HOURS PRIOR TO LEUKAPHERESIS**

Chari, A.1, Vendical, M.1, Clark-Garvey, S.1, Schwartz, J.2, Sleoty, R.3, Dinguid, D.1, Savage, D.1 NYPH - Columbia University Medical Center, New York, NY; NYPH - Columbia University Medical Center, New York, NY

AMD3100, an inhibitor of the SDF-1 chemokine interaction with the CXCR4 receptor, has allowed successful mobilization of CD34 stem cells in patients with hematologic malignancies for whom traditional GCSF-based mobilization regimens have failed. As part of a Compassionate Use Protocol (CUP), we have been able to collect adequate stem cells in seven such patients. Based on pharmacokinetic and pharmacodynamic data, the recommended time of the subcutaneous administration of 240 mcg/kg of AMD3100 is 10–11 hours before the start of apheresis (in addition to standard GCSF administration timing). After treating three patients on this schedule, we found this timing to be impractical for