Thirty-five percent of survivors were transplanted with related donor cells, 25% with unrelated donor cells, and 40 percent had an autologous transplant. Age at time of transplant ranged from 6 months to 69 years. Median age was 42.

The year of the survivor's most recent transplant ranged from 1981 to 2006 with a median of 2002. Sixty-three of the respondents had two or more transplants.

Issues of concer, rating by frequency with which they were cited, are shown in Table 1.

Psychological health of the survivor (71%), monitoring long-term complications (70%), chronic GVHD (74% allogeneic related-donor transplant, 81% allogeneic unrelated-donor transplant) and fatigue (66%) were the top issues cited by survivors. Other major concerns were cognitive problems (49%), psychological health of the family (47%), educating local doctors about long-term follow-up care (43%), health insurance (42%), secondary cancers (42%) and sexuality (41%).

Spouses expressed greater concern than survivors about financial problems (43% vs. 30%), psychological health of the family (59% vs. 47%), and caregiver burnout (44% vs. 29%). Survivors had greater concern than spouses about cognitive problems (49% vs. 37%), secondary cancers (42% vs. 24%) and infertility (22% vs. 8%).

Spouses of survivors who were transplanted with unrelated donor cells expressed concern more frequently than other spouses about the psychological health of the survivor, fatigue, psychological health of the family, and marital difficulties.

Ninety-one percent of respondents said they would be interested in an educational forum to help them cope with survivorship issues.

The growing number of HSCT survivors requires a fresh look at how to equip patients and families to live well post-transplant. The results of this survey have been used to design of a one-day Transplant Survivors Symposium, April 14, 2007 in Chicago IL. Between 200 and 300 survivors and their families are expected to attend. Symposium proceedings will be available to non-participants via the web, on CD, and in print.

*Issues of Concern to HSCT Survivors and Spouses*

| Issue | Survivors | Spouses |
|---|---|---|
| Psychological Health of Survivor | 71% | 78% |
| Monitoring Long Term Complications | 70% | 67% |
| Fatigue | 66% | 70% |
| Cognitive Problems | 49% | 37% |
| cGVHD | 47% | 49% |
| Psychological Health of Family | 47% | 59% |
| Educating Local Physicians About Survivor Needs | 43% | 37% |
| Health Insurance | 42% | 44% |
| Secondary Cancers | 42% | 24% |
| Sexuality | 41% | 37% |
| Employment | 36% | 35% |
| Immunization | 36% | 30% |
| Life Insurance | 33% | 32% |
| Financial Problems | 30% | 43% |
| Caregiver Burnout | 29% | 44% |
| Dental Problems | 26% | 21% |
| Resume Relations w/ Family & Friends | 24% | 17% |
| Infertility | 22% | 8% |
| Complementary/Alternative Medicine | 20% | 13% |
| Marital Difficulties | 20% | 25% |
| Pain Control | 19% | 24% |
| Young Adult Issues | 7% | 5% |
| Sibling Needs | 5% | 3% |
| Behavioral Problems | 2% | 3% |
| Delayed Growth | 1% | 2% |

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### P53 MUTATIONS IN SECONDARY MALIGNANCIES AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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We previously demonstrated frequent genomic alterations measured by microsatellite instability (MSI) in non-malignant and malignant epithelial tissues of pts who underwent aHCT (Blood 2006;107:3389-3396). Transplant survivors have a high risk of developing secondary cancer, especially squamous cell carcinomas. The p53 gene plays a pivotal role in maintaining genome integrity and in the development of cancer. We hypothesized that besides the alterations in microsatellite regions also p53 mutations occur after aHCT and may play a role in malignant transformation and development of secondary cancer. Therefore, we performed mutation analysis of the p53 gene on malignant cells isolated from paraffin-embedded tumor biopsies from 4 pts that developed secondary epithelial malignancies 2-12 years post aHCT and on non-neoplastic buccal cells obtained from 4 otherwise healthy pts 3-5 years following aHCT. Buccal cells from 3 healthy individuals and HaCat cells with a known p53 heterozygous mutation were used as negative and positive controls, respectively. DNA extraction was followed by proofread-PCR with specific primers for the exons 5-8. Each PCR product was cloned in a pUC vector and transfected in Escherischia coli chemocompetent cells. Sequence analysis was performed on 8-12 clones per exon per patient. p53 mutations were not found in the buccal cells of the aHCT healthy recipients. p53 mutations were evident in 2 out of 4 tumor specimens. One patient with a squamous cell carcinoma developed 2 years post aHCT was found to harbour a single p53 mutation in exon 8. This p53 mutation was evident in 10 out of the 10 clones tested, suggesting that 100% of the malignant cells were mutated. In the second patient with an underlying malignancy of the tongue, two different mutations (exons 5 and 8) in 50% of the isolated cells were detected. Despite the small size of the sample (4 pts), p53 mutations seem to occur frequently (50%) in secondary malignancies after HCT. We didn't find p53 mutations in nonmalignant epithelial cells of the oral cavity. However, given the low sensitivity of the applied methodology (detection of a mutation if it affects more than 40% of the tissue cells) we cannot exclude that indeed p53 mutations are already present in a lower percentage of non-neoplastic cells before overt malignant transformation occurs. Results regarding the presence of p53 mutations in nonmalignant tissues affected with chronic GvHD will be presented in the meeting.

# LYMPHOMA/MULTIPLE MYELOMA

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### LOW DOSE THALIDOMIDE MAINTENANCE IN MYELOMA PATIENTS AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION

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Autologous stem cell transplantation has become the gold standard for treatment of patients with multiple myeloma under the age of 65, and improves survival for these patients. It is evident that all patients will progress after transplantation. At this time it is not clear what is the best induction regimen prior to high dose chemotherapy and ASCT. Thalidomide has been proven to impact on plasma cell growth through multiple mechanisms. At our institution we used thalidomide (50-100 mg) after ASCT as a maintenance program along with a bisphosphonate (Zometa or Aredia). We reviewed 68 myeloma patients

who were transplanted at our facility between 2001 and 2005. 30 patients were placed on a thalidomide maintenance program. Patients received various cytoreductive regimens prior to stem-cell collection. 27 patients who received thalidomide were in partial remission prior to ASCT; 3 patients were in complete remission and none were refractory. Of the 38 patients who did not receive maintenance 35 were in partial remission, 2 were in complete remission and 1 was refractory. All patients except 2 received a preparative regimen including melphalan 200 mg per meter squared. 24 patients received thalidomide maintenance with 100 mg daily and 6 patients received 50 mg daily. The dose given depended on prior tolerability of the drug and history. Thalidomide was started between 120 and 150 days post ASCT. Patients needed to have an ANC above 1000 and platelets above 100 as well as resolution of transplant related toxicities. 13 patients needed a decrease in thalidomide because of neuropathy. One of these 13 patients also suffered from decreased GI motility and bezoar.

The average time to progression was 32.5 months in the thalidomide group and 19 months in the patients who did not receive the drug. Patients who received thalidomide after transplant had improved median time to progression (36 months) compared to patients who did not receive thalidomide (15 months). Low dose thalidomide maintenance in combination with bisphosphonates seemed to improve progression free survival in myeloma patients after stem cell transplantation.

| Results Variables/Drug Group | Thal Dex (N=11) | VAD (N=38) | p-value |
|---|---|---|---|
| Age (years) | 59.8 {53.6, 66.0} | 56.5 {52.9, 60.2} | 0.38 |
| Days of apheresis | 2.18 {1.46, 2.91} | 2.00 {1.68, 2.32} | 0.60 |
| $CD_{34}$ yield | 7.95 {4.05, 11.8} | 7.82 {6.34, 9.30} | 0.74 |
| Viability Day 1 | 84.3 {76.8, 91.8} | 80.6 {73.2, 88.0} | 0.63 |
| Viability Day 2 | 85.0 {78.3, 91.7} | 90.8 {88.1, 93.5} | 0.06 |
| Viability Day 3 | 82.4 {71.8, 93.0} | 84.0 {74.7, 93.3} | 0.83 |
| Days to ANC Engraftment | 14.1 {13.3, 14.9} | 13.7 {13.1, 14.2} | 0.36 |
| Days to PLT Engraftment | 18.5 {15.9, 21.2} | 19.8 {17.3, 22.3} | 0.82 |
| Number of PLT Transfusions | 3.91 {1.61, 6.21} | 3.74 {2.61, 4.87} | 0.84 |
| Number of RBC Transfusions | 4.54 {3.00, 6.09} | 3.00 {2.39, 3.61} | 0.03 |
| Mobilization Regimen (%G) | 100 | 76 | 0.10 |
| Death <100 days | 0 | 0 | 1.00 |
| Mucositis II-IV <30 days | 25 | 13.5 | 0.36 |
| Sepsis <30 days | 16.7 | 2.7 | 0.12 |
| Pneumonia <30 days | 8.3 | 2.7 | 0.40 |
| Karnofsky Score | 95.83 | 94.48 | 1.00 |

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### COMPARISON OF MULTIPLE MYELOMA PATIENTS TREATED WITH AUTOLOGOUS STEM CELL TRANSPLANT HAVING RECEIVED THAL DEX OR VAD

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**Background and Rationale**

Thalidomide Dexamethasone (Thal Dex) is one of the standard preparation treatments for auto-transplant in patients with Multiple Myeloma (MM). We evaluated 49 patients with MM to determine whether outcomes differed between those receiving Thal Dex and those receiving Vincristine, Doxorubicin, and Dexamethasone (VAD).

**Materials and Methods**

A retrospective assessment was performed of MM patients who were transplanted at Inova Fairfax Hospital from 1997-2005. All patients received either VAD or Thal Dex as primary therapy and in preparation for auto-transplant. All patients had Karnofsky performance scores of ≥80% and all were apheresed using a high volume technique and ideal body weight for calculations with G-CSF (G) or G+GM-CSF, with goal of $5\times10^6$/kg $CD_{34}$ cells. All patients were given 200 mg/m$^2$ of Melphalan (MEL) over two days and were treated with growth factor support G beginning day +4 though ANC recovery of 1000. Blood product replacement was standardized to transfuse for hemoglobin >8 gm/dl or platelet counts of >10,000/mm$^3$. Viability was performed using flow cytometry and propidium iodide. Continuous variables were analyzed as means and 95% confidence intervals, but p-values were produced using a Wilcoxon Rank Sum Test for non-normally distributed data. Categorical variables were analyzed using a Fisher's Exact Test.

**Discussion**

In MM patients with comparable pretransplant performance status being equal, there were no statistical differences in $CD_{34}$ yield, cell viability, days of apheresis, platelet transfusions, engraftment, complications, or mobilization regimen between those receiving VAD and those receiving Thal Dex. However, patients receiving Thal Dex appeared to require more RBC blood product support (p=0.03).

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### AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) FOR PATIENTS WITH MULTIPLE MYELOMA (MM): IMPACT OF THE DEGREE OF PLASMA CELL BONE MARROW INFILTRATION ON MOBILIZATION KINETIC AND TRANSPLANT OUTCOMES

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**Background:** The recommended treatment for younger patients (pts) with newly diagnosed symptomatic MM is ASCT after some form of cytoreductive therapy. One of the goals of the cytoreductive therapy is to reduce the tumor bulk, in particular, decrease the plasma cell bone marrow (BM) infiltration to less than 10-30% prior to stem cell collection. However, the utility of this approach is controversial. **Objective:** To evaluate the impact of the degree of plasma cell bone marrow (BM) infiltration on mobilization kinetic and transplant outcomes. **Method:** We conducted a retrospective study on all pts with MM who underwent ASCT at our institution between 1/99 and 12/03. Stem Cell mobilization regimen consisted of the combination of Cyclophosphomide 1.5-3g/m$^2$, GM-CSF (5mcg/kg) starting on Day #3 and G-CSF (5mcg/kg) on Day#7 until targeted CD 34 count achieved. The median age at ASCT was 55 (range 41-73). All pts received melphalan 200mg/m$^2$ as conditioning regimen. The pts were grouped according to degree of plasma cell infiltration on BM biopsy performed before mobilization. Group 1 had plasma cell infiltration of <10% (n=26), group 2 had 10-29% involvement (n=27) and group 3 had >30% plasma cell infiltration (n=16). **Results:** Sixty-nine patients were included in the study; 43 were rapid mobilizers (>4× $10^6$ CD34+ cells/Kg in one single collection), 7 slow mobilizers (<1.5 × $10^6$ CD34+ cells/kg over 4 collections or more) and 19 normal mobilizers (all other patients). The median days of apheresis was 1 (range 1-6). Ordinal logistic regression model identified that for each 10 point (10%) increase in plasma cell BM infiltration prior to mobilization, it is 1.27 times more likely to be in the next slower mobilization group (p value =0.0449). Age did not influence the mobilization kinetic. The median progression-free survival and overall survival for the entire cohort were 28.5 and 45 months respectively. There was no relationship found between plasma cell involvement