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.

## 143
COMPARISON OF MULTIPLE MYELOMA PATIENTS TREATED WITH AUTOGOUS 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 5×109/kg CD34 cells. All patients were given 200 mg/m² of Melphalan (HEL) 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/mm³. 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 CD34 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).

### Results

<table>
<thead>
<tr>
<th>Variables/Drug Group</th>
<th>Thal Dex (N=11)</th>
<th>VAD (N=38)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>59.8 (53.6, 66.0)</td>
<td>56.5 (52.9, 60.2)</td>
<td>0.38</td>
</tr>
<tr>
<td>Days of apheresis</td>
<td>2.18 (1.46, 2.91)</td>
<td>2.00 (1.68, 2.32)</td>
<td>0.60</td>
</tr>
<tr>
<td>CD34 yield</td>
<td>7.95 (4.05, 11.8)</td>
<td>7.82 (6.34, 9.30)</td>
<td>0.74</td>
</tr>
<tr>
<td>Viability Day 1</td>
<td>84.3 (76.8, 91.8)</td>
<td>80.6 (73.2, 88.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Viability Day 2</td>
<td>85.0 (78.3, 91.7)</td>
<td>90.8 (88.1, 93.5)</td>
<td>0.06</td>
</tr>
<tr>
<td>Viability Day 3</td>
<td>82.4 (71.8, 93.0)</td>
<td>84.0 (74.7, 93.3)</td>
<td>0.83</td>
</tr>
<tr>
<td>Days to ANC Engraftment</td>
<td>14.1 (13.3, 14.9)</td>
<td>13.7 (13.1, 14.2)</td>
<td>0.36</td>
</tr>
<tr>
<td>Days to PLT Engraftment</td>
<td>18.5 (15.9, 21.2)</td>
<td>19.8 (17.3, 22.3)</td>
<td>0.82</td>
</tr>
<tr>
<td>Number of PLT Transfusions</td>
<td>3.91 (1.61, 6.21)</td>
<td>3.74 (2.61, 4.87)</td>
<td>0.84</td>
</tr>
<tr>
<td>Number of RBC Transfusions</td>
<td>4.54 (3.00, 6.09)</td>
<td>3.00 (2.39, 3.61)</td>
<td>0.03</td>
</tr>
<tr>
<td>Mobilization Regimen (%G)</td>
<td>100</td>
<td>76</td>
<td>0.10</td>
</tr>
<tr>
<td>Death &lt;100 days</td>
<td>0</td>
<td>0</td>
<td>1.00</td>
</tr>
<tr>
<td>Mucositis II-IV &lt;30 days</td>
<td>25</td>
<td>13.5</td>
<td>0.36</td>
</tr>
<tr>
<td>Sepsis &lt;30 days</td>
<td>16.7</td>
<td>2.7</td>
<td>0.12</td>
</tr>
<tr>
<td>Pneumonia &lt;30 days</td>
<td>8.3</td>
<td>2.7</td>
<td>0.40</td>
</tr>
<tr>
<td>Karnofsky Score</td>
<td>95.83</td>
<td>94.48</td>
<td>1.00</td>
</tr>
</tbody>
</table>

## 144
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.

### Materials and Methods:

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/m², 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/m² 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 (>4×10⁹ CD34+ cells/kg in one single collection), 7 slow mobilizers (<1.5×10⁹ 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 and Karnofsky Score.
prior to mobilization and progression free survival as well as overall survival. Conclusion: We conclude that 1) degree of plasma cell BM infiltration before mobilization did not predict for transplant outcomes and 2) increased plasma cell BM infiltration before mobilization adversely affect the efficiency of stem cell mobilization. Thus, pre-transplant cytoreductive therapy improves stem cell collection efficiency but did not affect the transplant outcomes.

145

ID/KLH ACTIVE IMMUNOTHERAPY (FAVID®) FOLLOWING HIGH DOSE THERAPY (HDT) AND AUTOLOGOUS STEM CELL TRANSPLANTATION (ASCT) FOR NON-HODGKIN’S LYMPHOMA (NHL)

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Sixteen patients with NHL were treated in a pilot study evaluating the feasibility, safety and potential efficacy of patient specific idiotype immunization (Id/KLH Active Immunotherapy) following HDT and ASCT. Favid was administered along with GM-CSF. Two patients continue in active therapy; 1 mantle cell lymphoma (MCL) and 1 transformed NHL (TL) and are not reported here. Of the remaining 14 patients, 8 had MCL, 4 had follicular lymphoma (FL), 1 had small lymphocytic lymphoma (SLL) and 1 had TL. The median number of prior regimens for all patients was 3 (range 1-10). For MCL patients, the median number of prior regimens was 2.5 (range 1-4) which included CHOP and hyperCVAD/- rituximab (R). FL patients received a variety of regimens including fludarabine, CVP, CHOP, R alone or in combination and Zevalin. All MCL and FL patients received HDT with BEAM except 1 who received CEB. The TL patient received Bexarx, Cy/VP-16. Idiotype immunizations were begun 3 months following HDT/ASCT. Of the 6 patients with MCL who achieved a CR following transplant, 5 remain in continuing CR (CCR) between 27 and 60 months post-transplant. The 6th patient relapsed after 40 months. Of the 3 patients with FL who obtained a CR, 2 continue in CR at 41-58 months post-transplant. The 3rd FL patient died from MDS at 34 months. Of the 5 MCL patients with a continuing CR, 4 developed cellular anti-Id and anti-KLH responses and one was not tested. The patient who relapsed after 40 months also had both anti-Id and anti-KLH cellular responses. Of the 3 FL patients who obtained a durable CR, 2 developed anti-Id and anti-KLH cellular responses and the 3rd was not tested. Id/ KLH Active Immunotherapy was well tolerated with injection site reactions being the most commonly reported adverse effects. GM-CSF related myalgias were also commonly reported. We conclude that Id/KLH Active Immunotherapy following HDT and ASCT for MCL and FL is feasible, safe, associated with idiotype specific immune responses and may be associated with prolonged remissions, even in patients heavily pretreated with very immunosuppressive regimens.

146

USE OF A NOVEL ORGANIC ARSENIC (ZIO-101) AFTER AUTOTRANSPLANTATION FOR MULTIPLE MYELOMA

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Background: Autotransplants are commonly used to treat multiple myeloma; unfortunately most recipients relapse. Subsequent therapy is often difficult because of limited bone marrow reserve. ZIO-101, a new organic arsenic, is active against human myeloma cell lines in vitro and in SCID mice with human myeloma xenografts. ZIO-101 is active in phase-1 trials in multiple myeloma and has little bone marrow toxicity. Because of these features, ZIO-101 is a good candidate for therapy of multiple myeloma after an autotransplant.


Subjects: N=13. Median age, 57 y (range, 41-78 y); 5 were male. All had advanced myeloma: median N prior therapies, 6 (range, 2-12). 6 received ≥1 prior autotransplants.

Dosimetry: 4 cohorts received 25 courses of ZIO-101 with a starting dose of 78 mg/m2/d IV and a maximum administered dose (MAD) of 420 mg/m2/d. 2 schedules were studied: (1) daily for 5 consecutive d every 4 w; and (2) twice weekly for 3 w every 4 w. Median N cycles was 2 (range, 1-10). Adverse events at doses <300 mg/m2/d were modest and there was no clinically-important bone marrow toxicity or QTc-prolongation. Estimated maximum tolerated dose (MTD) is 300-420 mg/m2/d.

Activity: Activity was seen including subjects receiving a prior autotransplant. Details will be presented.

PK: Studies at 420 mg/m2/d showed a tmax = 1 h (SD ± 0.9), Cmax = 1.06 μg/mL (SD ± 0.07 μg/mL), t1/2 = 17.8 h (SD ± 1.4 h) and AUC0-∞ = 25.9 μg h/mL (SD ± 0.8 μg h/mL).

Conclusions: ZIO-101 is safe in persons with multiple myeloma at doses ≤300-420 mg/m2/d (MTD) and may be especially useful posttransplant because of modest bone marrow suppression.

147

IMPROVED OUTCOME OF PATIENTS WITH MANTLE CELL LYMPHOMA (MCL) IN FIRST REMISSION (CR1) AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Introduction: MCL, accounts for 5% of non-Hodgkin lymphoma and is characterized by t(11;14) translocation leading to Cycin D1 over expression. It is currently considered incurable, with a median overall survival (OS) of 3 to 4 years from diagnosis. Results of hematopoietic stem cell transplant (HSCT) are mixed, with earlier studies showing no survival advantage over conventional chemotherapy, but more recent studies, suggesting better outcome. The optimal timing of HSCT for patients (pts) with MCL is not known.

Methods: Between 2/1994 and 5/2006, 70 consecutive pts with MCL underwent an autologous (auto) (n = 56) or allogeneic (allo) [n = 14 (11-myeloablative; 3-reduced intensity regimens-RIC)]. Most pts had stage IV disease 50/70 (71%). 46/70 (66%) pts had bone marrow (BM) involvement. Conditioning regimen for auto HSCT consisted mainly of CBV (cyclophosphamide, BCNU and etoposide). Allo HSCT regimens included ablative (cyclophosphamide/V彭16 ± TBI); or RIC (fludarabine/busulfan or fludarabine/ TBI). GVHD prophylaxis consisted of cyclosporine (CSA) and methylprednisolone/methotrexate or CSA/mycophenolate mofetil. 56 pts received BM, 10 peripheral blood (PB) and 4 (BM/PB).

Results: Median age at transplant was 56 years (yrs) (range 35-67). Median follow up was 2.1 yrs (range, 0.01-9.1). 50% of the pts had at least 2 prior therapies prior to transplant. 55/70 pts had a response after transplant (52-complete remission, and 3 partial responses). 47/70 pts had no response and progressed. 35 pts are alive (27-autologous; 8-allogeneic), of which 17 pts relapsed. 35 patients are dead: progressive disease, 23; sepsis/infection, 5; secondary malignancy, 2; pulmonary embolism, 1; and other causes, 4. Median OS was 3.5 yrs (95% CI 2.4 to 4.6) with no significant difference between auto and allo (median not reached) pts (P = 0.78). Median progression free survival (PFS) was 3.5 yrs (95% CI 0.6 to 6.3), and was not different for auto or allo (median not reached) HSCT (P = 0.8). 25/70 (36%) patients underwent HSCT (auto-24, allo-1) in CR1. OS of these patients was superior compared to pts transplanted later in their disease course (not reached vs. 2.5 yrs, P = 0.023).

Conclusion: Patients transplanted in CR1 have a better overall survival compared to being transplanted later in the disease course. Pts not achieving CR1 or presenting with recurrence of disease should be considered for early transplant. The optimal type of transplant in these patients needs to be further validated.