MYELOMA TODAY

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A PUBLICATION OF THE INTERNATIONAL MYELOMA FOUNDATION

Dedicated to improving the quality of life of myeloma patients while working towards prevention and a cure.

Highlights

Pieter Sonneveld, MD, PhD

William H. Matsui, MD

Carol Ann Huff, MD

IMF Launches Bank On A Cure®

WORLD'S FIRST DNA DATABASE FOR MYELOMA PATIENTS

The IMF's cutting-edge Bank On A Cure research initiative is running at full-steam and processing DNA samples. To date, thousands of samples have been collected from our "swish and rinse" kits, clinical trials in the United States and Europe, and from interested researchers around the world. However, we need more data. As was announced at the official launch of Bank On A Cure in New York City on May 9th, thousands more "swish and rinse" samples are needed in order to do the studies required to accurately predict patient response to treatment.

Dr. Brian G.M. Durie, Geraldine Ferraro, and Susie Novis at the Bank On A Cure launch event

Participating at the launch were the Honorable Geraldine Ferraro, myeloma patient, Dr. Brian Durie, IMF Chairman of the Board, Susie Novis, IMF President, and Professor Brian Van Ness, co-chair of the Bank On A Cure program. Ms. Ferraro voiced her support for this effort and provided a sample of her own DNA as proof of her commitment to this effort. To watch a video of the launch, and to learn more about Bank On A Cure, please visit www.myeloma.org.

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LOOKING FOR A LOCAL MYELOMA SUPPORT GROUP?

If you are interested in joining an existing group or starting a new group in your area, please contact Andy Lebkuecher, Director of Support Groups at imfsupport@charter.net or call him at 404-353-7127

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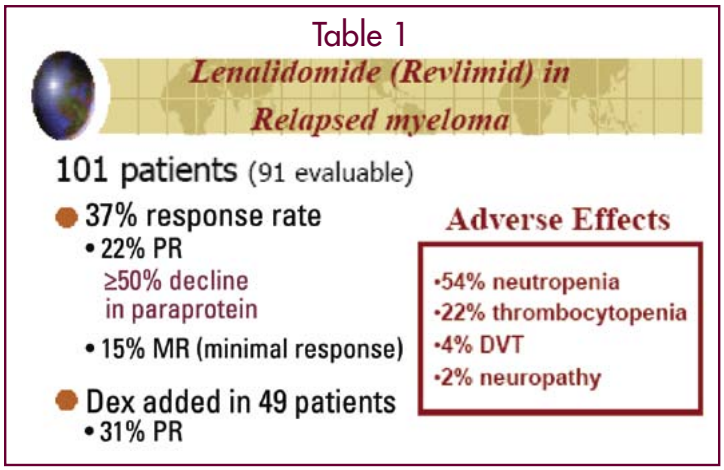
REVLIMID® (LENALINOMIDE): WHERE DO WE STAND?

By Brian G.M. Durie, MD

Revlimid is the immunomodulatory drug CC-5013, which is a thalidomide (Thalomid®) analog. Revlimid has been in the news for 3 to 4 years. It appears to have anti-myeloma activity that is similar to that of thalidomide, but with a different toxicity profile. On the one hand, Revlimid rarely causes the neuropathy that has been of such concern with chronic thalidomide use. On the other hand, it does cause reduction in blood count values, especially the white blood count and platelet levels.

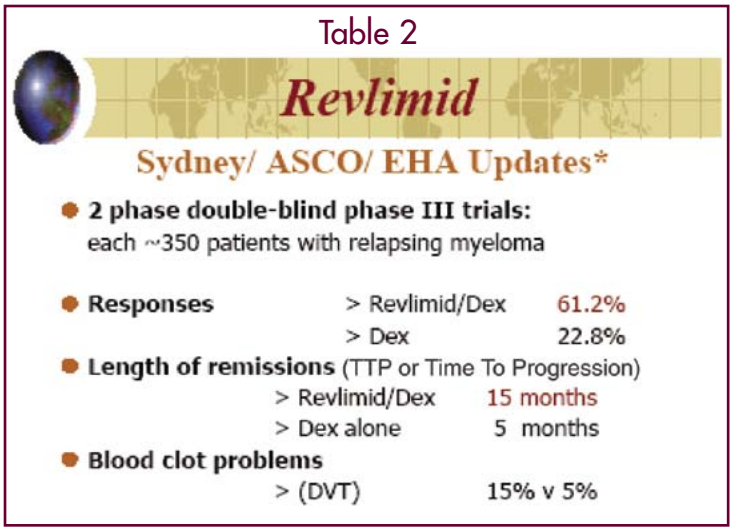
In 2001 and 2002, phase I-II trials from the Dana-Farber Cancer Institute in Boston, MA, and the University of Arkansas in Little Rock, AR, indicated responses in patients refractory to (failing on) prior therapies, sometimes including thalidomide. As summarized in Table 1, 22% of patients had at least a 50% reduction in myeloma protein levels (partial response [PR]), and 31% of patients reached PR when dexamethasone was combined with the Revlimid. The various side effects are noted.

Table 1



These promising results led to two large phase III double-blind trials, one in North America and the other in Europe, to compare Revlimid plus dexamethasone versus dexamethasone alone (with placebo instead of Revlimid). Results of these trials were presented earlier this year at the International Myeloma Workshop in Australia, at the ASCO meeting in Florida, and at the EHA meeting in Sweden. The data from the North American trial are summarized in Table 2.

Table 2



Both the response rate of 61.2% and the length of response of 15 months were significantly larger for Revlimid plus dexamethasone versus dexamethasone alone. Side effects with DVTs (deep vein thromboses) were higher with the combination (15% versus 5%). Daily baby aspirin use is now recommended along with Revlimid.

It is these very encouraging results, combined with the almost exactly duplicated study results from Europe, which have led to the expectation of approval of Revlimid for myeloma by the FDA, in some fashion. However, there are two very important nuances concerning the anticipated availability of Revlimid:

1. Revlimid FDA Approval Anticipated

- Data supporting the use of Revlimid in another blood cancer called MDS (Myelodysplastic Syndrome), a type of preleukemia, which sometimes has a 5q- chromosome abnormality, were submitted to the FDA earlier this year. This submission will receive expedited review, which means that a decision will be received from the FDA within 6 months, by Fall of 2005 at the latest.
- If there is approval for Revlimid use in MDS, this means that Revlimid will become commercially available. Myeloma would then become an "off-label" indica-

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IMF Calendar

July 22 - 23	Patient & Family Seminar	Toronto, CANADA
August 19-20	Patient & Family Seminar	Baltimore, MD
September 20	Clinical Meeting	St. Petersburg, RUSSIA
September 24	Patient & Family Seminar	Istanbul, TURKEY
September 27	Robert A. Kyle Award Dinner	Boston, MA
September 28 - October 2	Southwest Oncology Group (SWOG) Meeting	New Orleans, LA
October 7	Patient & Family Seminar	Madrid, SPAIN
October 10	Patient & Family Seminar	Rome or Torino, ITALY
October 22	Patient & Family Seminar	Heidelberg, GERMANY
October 28	Patient & Family Seminar	Paris, FRANCE
November 12	Ribbon of Hope Gala	Los Angeles, CA
November 19 - 21	Eastern Cooperative Oncology Group (ECOG) Meeting	Tampa, FL
December 3-6	American Society of Hematology (ASH) Meeting	New Orleans, LA

For more information, please visit www.myeloma.org or call 800-452-CURE (2873).
IMF(Japan) and IMF(UK) events are not included above.

BORTEZOMIB AS TREATMENT OF MM: ANALYSIS OF EFFICACY AND TOXICITY

By Pieter Sonneveld, MD, PhD

Multiple myeloma accounts for approximately 1% of all malignancies and 10% of hematological cancers. Although conventional and high-dose chemotherapy with autologous stem cell support can prolong remission and survival, myeloma remains an incurable disease with a median survival of 3 to 4 years. Recent advances in molecular genetics have provided the means to identify specific molecular mechanisms that regulate myeloma cell growth and survival. The developments of new drugs that block a critical survival mechanism within the myeloma cell or the bone marrow will provide new opportunities for therapeutic intervention.

VELCADE® (bortezomib) for injection, a novel molecule that contains a boronic acid, is a selective inhibitor of the proteasome. The proteasome is an enzyme found in all eukaryotic cells, thus also in humans. It also plays a central role in the degradation of proteins that control the survival of myeloma cells. Therefore, it was tested in several tumor testing systems that revealed that hematologic malignancies were sensitive to its effects. In a phase I study in patients with advanced hematologic malignancies, bortezomib showed activity in patients with multiple myeloma. The safety and efficacy of bortezomib has been assessed in two phase II studies of patients with relapsed or refractory multiple myeloma. In both studies, bortezomib induced clinically significant responses, with manageable toxic effects. A Phase II study (SUMMIT) in 202 myeloma patients treated with 1.3 mg/m^2 bortezomib intravenously for 2 weeks, followed by 1 week without treatment, for up to eight cycles, demonstrated an overall response rate of 35%. The median overall survival was 16 months, with a median duration of response of 12 months. A small randomized study (CREST) in 54 patients comparing 1.0 or 1.3 mg/m^2 bortezomib according to the same schedule confirmed the activity of bortezomib. In both studies some additional response occurred after addition of dexamethasone in patients with no or suboptimal response to bortezomib alone. Recently, the international prospective randomized study of bortezomib as compared with dexamethasone (APEX trial) was concluded in >600 refractory and/or relapsed myeloma patients. This trial showed a superior effect of bortezomib as regards response rate, complete response rate, time to progression, progression-free survival and overall survival. In addition it was shown that the response rate was better in patients who had received only one prior line of therapy as compared with those who received bortezomib at a later relapse. The toxicity profile of bortezomib was characterized by peripheral neuropathy, transient thrombocytopenia and fatigue, which were in general predictable and could be managed with appropriate precautions. The results clearly indicate that bortezomib has earned a place in the treatment of multiple myeloma at relapse and in patients who have failed prior treatment.

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Today, there are data that point towards the use of bortezomib at an early stage of the disease because of its greater efficacy in that situation. Ongoing trials will focus on that situation and these will elucidate the role of bortezomib in the upfront treatment situation.

However, there is limited clinical data of the efficacy and toxicity of bortezomib as a treatment for myeloma patients outside the context of a controlled clinical trial. Are the results as good as they look in the international journals or in the company publications? In order to get an idea of the everyday use of bortezomib, we performed a retrospective analysis in the Netherlands on the efficacy and toxicity of bortezomib in patients with relapsed or refractory multiple myeloma, who were not eligible for participation in a clinical trial and who received bortezomib in a named patient program or as part of their regular treatment (See Wu et al, Haematologica, 2005).

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BORTEZOMIB — continued

Table 1
Patient characteristics in Dutch surveillance trial

Number of patients	50
Median age in years (range)	58 (37–87)
Male/female	37/13
M-protein - IgA	10
- IgG	33
- Light chains	6
- Non-secretory	1
Cytogenetic abnormalities: n /total n	30/50 (60%)
Deletion of chromosome 13	14 (28%)
Number of prior treatments	
1	5 (10%)
2	13 (26%)
3	20 (40%)
≥ 4	12 (24%)
Prior thalidomide treatment	40 (80%)
Autologous stem cell transplantation	29 (58%)
Allogeneic stem cell transplantation	8 (16%)

These 50 patients with relapsed or refractory multiple myeloma were treated with bortezomib at nine medical centers in the Netherlands. All patients had received one or more prior treatments with chemotherapy. The median number of previous treatments was 3 (range 1-5). Twenty-nine patients had been treated with high-dose melphalan with autologous stem cell support and 8 patients had received allogeneic stem cell transplantation.

Thirty-four patients (68%) completed at least 4 treatment cycles of bortezomib and 19 patients (38%) received 8 cycles. Early discontinuation occurred in 15 of the 50 patients (30%) because of progressive disease, and in 12 patients (24%) because of toxicity.

A clinical response was observed in 23 patients (46%), including complete response in 2 patients, partial response in 15 and minimal response in 6 patients. The median time to response was 6 weeks. Blood counts generally improved when disease response was achieved. The median duration of response was 7 months and the median overall survival was 11 months. Response to bortezomib occurred in 5 of the 15 patients with deletion of chromosome 13, which usually predicts a poor outcome with conventional and high-dose chemotherapy. One patient had an additional minimal response when dexamethasone was added. This patient was previously refractory to corticosteroid treatment.

During treatment with bortezomib alone, the observed side effects were similar to those previously reported. The most common toxicities were diarrhea, anorexia, nausea, vomiting, thrombocytopenia, neutropenia, fatigue, and peripheral neuropathy. The majority of the gastrointestinal complaints were mild and manageable with routine support. Six patients had shingles (12%) and 3 patients (6%) developed a skin rash. Other toxicities were peripheral neuropathy such as numbness or pain (20%), low platelets (18%), diarrhea (6%), and neutropenia (6%). Dose reduction had to be performed in 18 patients (36%), and bortezomib was discontinued in 12 patients (24%) because of the side effects. A remarkable observation in our series was the high incidence of herpes zoster (shingles). Five patients developed shingles during treatment with bortezomib alone and 1 patient in combination with dexamethasone. We think that prophylactic antiviral antibiotics should therefore be considered in predisposed patients who receive bortezomib.

These data support those of the published prospective trials which have reported response rate with bortezomib alone of 35-50%.

Table 2
Response of patients to bortezomib in Dutch surveillance trial

Type of response	Number of patients (%)
Complete response	2 (4%)
Partial response	15 (34%)
Minimal response	6 (12%)
No response	27 (54%)

Bortezomib is now moving forward from studies in patients with refractory or relapse myeloma to its use in previously untreated patients. Small studies in USA and the UK have shown that this is feasible and may result in high response rates. However, in patients who were not previously exposed to chemotherapy, we have to re-establish the clinical efficacy as well as the side effects of

bortezomib, before we can confirm the value of the drug in that setting. Also, we have to confirm whether combinations with other drugs such as dexamethasone, thalidomide, and others are beneficial for patients to improve their immediate clinical situation and for long-term outcome. In France and the Netherlands, in cooperation with Germany, two large, unique randomized trials have been designed to investigate these important clinical issues, and these trials will also address the role of other novel agents such as thalidomide during induction or maintenance treatment. In addition, numerous smaller trials will investigate the use of bortezomib with other drugs or in specific groups of patients. MT

Relevant References

1. Attal M, Harousseau JL, Stoppa AM et al. A prospective, randomized trial of autologous bone marrow transplantation and chemotherapy in multiple myeloma. Intergroupe Francais du Myelome. N Engl J Med 1996; 335(2):91-97.

2. Orlowski RZ, Stinchcombe TE, Mitchell BS et al. Phase I trial of the proteasome inhibitor PS-341 in patients with refractory hematologic malignancies. J Clin Oncol 2002; 20(22):4420-4427.

3. Jagannath S, Barlogie B, Berenson J et al. A phase 2 study of two doses of bortezomib in relapsed or refractory myeloma. Br J Haematol 2004; 127(2):165-172.

4. Richardson PG, Barlogie B, Berenson J et al. A phase 2 study of bortezomib in relapsed, refractory myeloma. N Engl J Med 2003; 348:2609-2617.

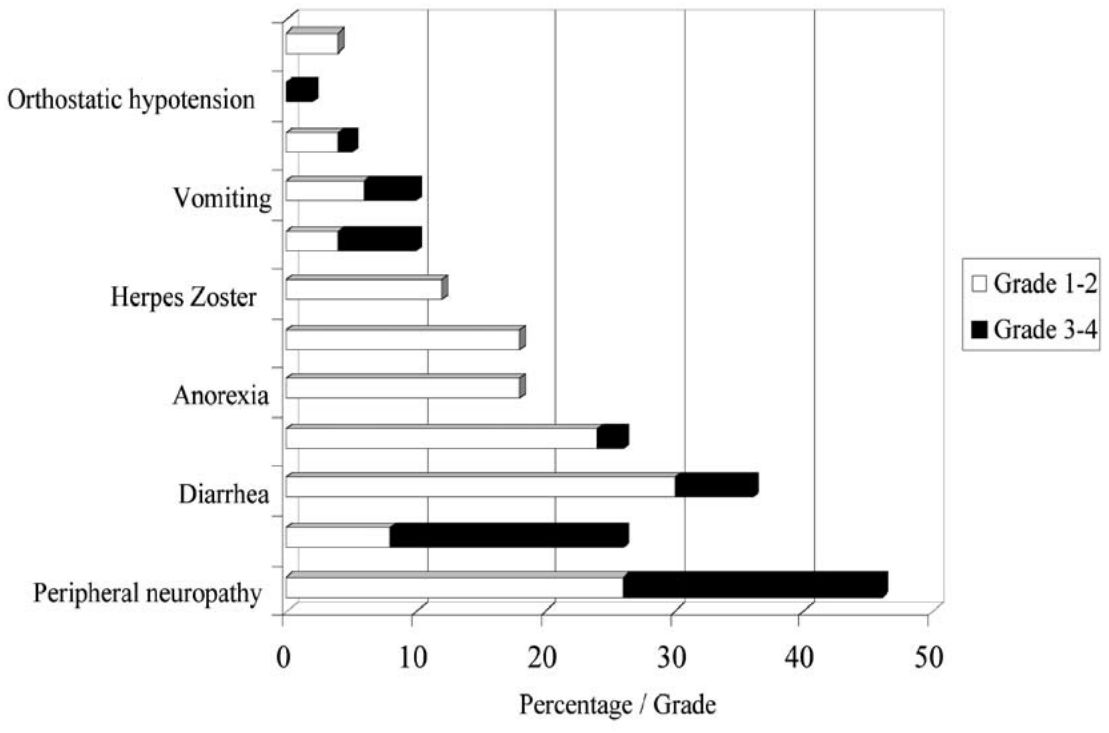
5. Oakervee HE, Popat R, Curry N et al. PAD combination therapy (PS-341/bortezomib, doxorubicin and dexamethasone) for previously untreated patients with multiple myeloma. Br J Haematol; 2005; 129; 755-762.

6. Wu KL, van Wieringen W, Vellenga E et al Analysis of the efficacy and toxicity of bortezomib for treatment of relapsed or refractory multiple myeloma: practice and experience outside the context of a clinical trial. Haematologica, 2005; 90; 996-997.

7. Richardson PG, Sonneveld P, M.W. Schuster et al. Bortezomib or high-dose dexamethasone for relapsed multiple myeloma. N Engl J Med; 2005; 352;2487-2498.

Note: For more information on VELCADE® (bortezomib) for injection, please visit www.myeloma.org or www.mlnm.com.

Figure 2
Observed toxicity of bortezomib in Dutch surveillance trial



UPDATE ON VELCADE® (BORTEZOMIB) FOR INJECTION

VELCADE may have a role in treating patients with frontline multiple myeloma

The British Journal of Haematology has published two phase II studies that showed strong single agent and high combination response rates in frontline myeloma. Overall response rates ranged from 88% to 95%, with complete and near complete responses ranging from 25% to 29%. The use of VELCADE in the frontline setting allowed for successful stem cell transplants for these patients. A complete response and near complete response rate of 57% was reported following single stem cell transplant preceded by induction with VELCADE, doxorubicin, and dexamethasone (PAD). This response rate was similar to the complete response and very good partial response rates previously published for tandem transplants. These data indicate that earlier use of VELCADE may improve overall response outcomes for myeloma patients. The phase III development program includes two trials with a third expected to be initiated shortly.

VELCADE, the first of a new class of medicines called proteasome inhibitors, is the first treatment in more than a decade to be approved for patients with myeloma and is currently used for the treatment of patients who have received at least one prior therapy. More than 12,000 patients have been treated with VELCADE in the U.S. to date.

VELCADE alone and in combination with dexamethasone

The multicenter phase II study assessed the efficacy and safety of VELCADE as a single agent and in combination with standard therapy dexamethasone in patients with previously untreated, symptomatic myeloma. Patients were treated for up to six cycles. Dexamethasone was administered the day of and the day after VELCADE if less than a partial response (PR) after cycle two or less than a complete response (CR) after cycle four was achieved. Response was assessed according to the European Group for Blood and Marrow Transplantation (EBMT) criteria. Results from 32 evaluable patients included:

- Overall response rate (CR+PR) for VELCADE alone or in combination with dexamethasone was 88%, with a complete and near complete response rate of 25%;
- After two cycles of therapy, single agent VELCADE achieved a response rate of 40%;
- Six of eight patients who achieved complete or near complete responses did so on VELCADE alone;
- Survival at one year was 87% with a median follow-up of 5.5 months;
- Improved response after the addition of dexamethasone was observed in 68% of patients who received dexamethasone.

Stem cell harvesting and engraftment was successful for all transplant patients in this study. Adverse events were reported to be manageable and included gastrointestinal events, neuropathy, myalgia, fatigue, and hematologic toxicities.

PAD Induction Therapy Prior to Stem Cell Transplant

The multicenter phase I/II study assessed PAD as induction therapy prior to stem cell transplant in previously untreated myeloma patients. Four cycles of PAD therapy were administered. Thereafter, patients underwent stem cell mobilization, and the ability to adequately harvest peripheral blood stem cells was evaluated. High-dose melphalan was administered, peripheral blood stem cells were infused, and the rate of hematologic recovery was assessed. Response, based on EBMT criteria, was measured after each cycle of PAD and three months after transplantation. Results from the 21 patients included:

- Overall response rate (CR+PR) was 95% with a complete and near complete response rate of 29%;
- Stem cell collection was adequate in 20 of 21 patients;
- Eighteen of 20 patients were successfully transplanted as two patients declined transplant;
- Post-transplantation, the overall response rate at three months was 95%, with a 57% complete and near complete response rate;
- No dose limiting toxicities occurred and adverse events included infections, hyperglycemia, peripheral neuropathy, postural hypotension, gastrointestinal events and atrial fibrillation.

The phase III program will further evaluate the clinical benefit of VELCADE in frontline myeloma. The first

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MYELOMA STEM CELLS: ATTACKING THE DISEASE AT ITS SOURCE

By William H. Matsui, MD and Carol Ann Huff, MD

The accumulation of abnormal plasma cells within the bone marrow is the hallmark of multiple myeloma. Although these cells are cancerous, they resemble normal plasma cells in several ways. For example, both normal and myeloma plasma cells are capable of producing immunoglobulins or antibodies. In addition, normal plasma cells are fully mature (or "terminally differentiated"), meaning that they have lost the ability to divide and form new cells. Myeloma plasma cells also appear to be incapable of replicating; thus, it has been unclear how they are formed. Our research focuses on studying the originating cell in myeloma (the myeloma stem cell) and developing treatments that target this cell and inhibit the production of new tumor cells.

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Cancer Stem Cells

Most cells in the body, such as those that make up the outermost layer of the skin, red cells, and neutrophils in the blood, and the neurons within the brain are terminally differentiated like normal plasma cells. As these cells are lost or used up they need to be replaced by new cells, but terminally differentiated cells cannot normally divide. Instead, they are formed by less mature cells known as stem cells. Stem cells are distinct from differentiated cells because they are capable of dividing many times. When a stem cell divides, two new cells are formed. One of the daughter cells goes on to produce differentiated cells by dividing a specific number of times, and with each division the resulting cells gradually mature and expand in number. Importantly, these maturing cells also lose their ability to divide an unlimited number of times. The other cell remains an exact copy of the original stem cell. This process is known as self-renewal, and it ensures that an adequate number of stem cells will be available to form new differentiated cells as needed. Thus, the vast majority of cells that make up most tissues and organs in the body are terminally differentiated and cannot replicate long-term. In contrast, stem cells are rare but have the capacity to divide an unlimited number of times.

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Like normal tissues, human cancers also appear to consist of both differentiated cells and stem cells. Several groups have examined the growth of human cancers, either in the laboratory or in animals, and have found that the majority of cells within an individual tumor lack the ability to form new cancer cells. These results may be explained by two possibilities.[1] The first is that all the cancer cells have an equal ability to form new tumors, but only a minority is able to do so at any point in time. The second is that the cells are not identical, and the ability to divide and grow is limited to only a few specialized cells (i.e., cancer stem cells). For many years, there was speculation that cancer stem cells existed, but they were not identified until the early 1990s when they were isolated in chronic myeloid leukemia and acute myeloid leukemia.[2-3] Because of the rarity of stem cells, they were not found in any other cancer until just a few years ago when they were identified in breast cancer and brain tumors.[4-6]

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MYELOMA STEM CELLS — continued

Studies examining cancer stem cells in a variety of unrelated tumor types have provided several important generalities regarding their behavior. First, the methods used to study normal stem cells that form blood cells (hematopoietic stem cells) and nerve cells (neural stem cells) can also be used to isolate myeloid leukemia and brain cancer stem cells. Thus, cancer stem cells highly resemble their normal counterparts. Furthermore, when cancer stem cells are propagated in the laboratory or injected into mice, they form cancers consisting of mature cells that are identical to the original tumor. These findings suggest that cancer stem cells can also undergo some degree of differentiation in addition to self-renewal. Therefore, cancer stem cells appear to be very similar to normal stem cells.

Multiple Myeloma Stem Cells

In multiple myeloma, the accumulation of abnormal plasma cells within the bone marrow is responsible for the main symptoms associated with the disease, namely bone disease, kidney failure, anemia, and a susceptibility to infections. Although the myeloma plasma cells are abnormal, several studies have suggested that they are terminally differentiated like normal plasma cells and rarely divide. One study found that the majority of the plasma cells located within the bone marrow of myeloma patients did not undergo cell division.[7] Likewise, several other studies examining the growth of myeloma patient samples in the laboratory demonstrated that only 1 in 1,000 to 1 in 100,000 were able to form new plasma cells.[8-9] It is well known that plasma cells are normally produced by B cells which play an important role in the immune system. Therefore, several studies examined whether B cells related to the myeloma plasma cells could be found within patients. In these studies, B cells with the same DNA sequences used to produce the abnormal immunoglobulin by myeloma plasma cells were found within the blood and bone marrow of myeloma patients.[10-12] Furthermore, mice injected with B cells from a patient with myeloma developed the disease.[13] Taken together, these studies suggest that myeloma plasma cells may be formed by B cells rather than plasma cells.

We studied whether plasma cells or B cells represent the cancer stem cell in myeloma, and initially developed a special assay based on previous work that allowed us to grow patient myeloma samples in the laboratory.[14-15] In this assay, bone marrow cells are collected from myeloma patients, and then placed in a specialized culture medium. This medium is very viscous so that cells cannot move freely, and as cells divide they form clusters, termed colonies, that can be easily identified and counted with a microsope. In order to determine whether myeloma plasma cells were able to form colonies, we specifically isolated plasma cells using a specific antibody which recognizes a protein called syndecan-1, or CD138, that is expressed only by plasma cells in the normal immune system. Plasma cells that expressed CD138 ($CD138^+$) did not form colonies, whereas cells that lacked CD138 ($CD138^{neg}$) could form myeloma colonies in our assay. We also injected $CD138^+$ or $CD138^{neg}$ cells into mice and found that only the mice receiving $CD138^{neg}$ cells developed myeloma. Taken together, these results suggested that $CD138^+$ myeloma plasma cells lack the ability to divide and form new cells, but that the stem cell was $CD138^{neg}$. Since cancer stem cells resemble their normal counterparts in myeloid leukemias and normal plasma cells come from B cells, we next examined whether the cells able to form colonies in our assay resembled B cells. We took $CD138^{neg}$ bone marrow cells, removed B cells using specific antibodies against B cell proteins (CD45, CD19, CD20, and CD22), then evaluated colony formation in our laboratory assay. The removal of cells expressing any of these proteins from the starting pool of $CD138^{neg}$ cells markedly decreased colony growth, indicating that myeloma stem cells were likely B cells.

Because of the difficulties obtaining repeated bone marrow samples, we also examined a number of myeloma cell lines. These were originally derived from myeloma patients, but unlike most patient samples, these cell lines can be easily and indefinitely propagated in the laboratory. Similar to myeloma patient samples, we found that the majority of cells within these cell lines were $CD138^+$ plasma cells. However, a small population of $CD138^{neg}$ cells that expressed B cell, rather than plasma cell, markers could be reliably found. We also found that these $CD138^{neg}$ cells had much greater potential to form colonies than the corresponding $CD138^+$ cells. These studies suggested that we could use these cell lines in addition to patient samples to study myeloma stem cells.

Strategies to Inhibit Multiple Myeloma Stem Cells

Our studies demonstrating that myeloma stem cells are B cells suggested that therapies that directly target B cells could inhibit their ability to form new cells. In addition to myeloma, B cells are the origin of several other cancers, such as certain lymphomas and leukemias.[16] Since a number of therapies specifically designed to inhibit cancerous B cells are currently used to treat patients with lymphoma, we examined whether one such drug, rituximab, could affect the growth of myeloma stem cells. Rituximab is a monoclonal antibody against CD20, a protein expressed on the surface of B cells and present on myeloma stem cells. We treated $CD138^{neg}$ cells from patient samples with rituximab, then evaluated them for colony formation. We found that after only 24 hours, rituximab was able to inhibit the growth of myeloma colonies in our assay by 65%.[15]

Testing This Approach in a Clinical Trial

If myeloma were analogous to a dandelion, the visible part of the weed would represent the plasma cells, whereas the root would symbolize the stem cells. Many available therapies significantly decrease the burden of plasma cells and improve symptoms in patients with myeloma, but relapse following treatment suggests that they are inactive against myeloma stem cells. This might be similar to cutting a dandelion off at ground level and eliminating the visible portion of the weed, but leaving the root untouched would allow it to grow back. Conversely, treatments like rituximab that selectively attack myeloma stem cells would not appear to work immediately since the plasma cells are not targeted. However, the inhibition of myeloma stem cells may lead to long-term remissions. An ideal strategy may be to combine therapies that target both myeloma plasma cells and stem cells. This would allow rapid improvement in symptoms caused by the plasma cells as well prevent the growth of new tumor cells.

Based on our laboratory studies, we have begun a phase II clinical trial to study the activity of rituximab against cancer stem cells in patients with myeloma. One of the challenges in studying agents that are designed to target cancer stem cells, like rituximab, is determining how best to measure the effectiveness of the treatment. Cancer stem cells represent a very small percentage of the tumor cells that are present in patients with cancer. Since standard response criteria measure changes in tumor bulk, they are not likely to reflect changes in the stem cell population, even if they are significant. That is, serum and urine protein electrophoreses and bone marrow aspirates which are standard measures to assess response in myeloma are likely not helpful in measuring the effectiveness of rituximab against myeloma stem cells.

If these are the sole criteria used, an approach that is effective against stem cells might be discarded prematurely because it appeared to be ineffective. This may explain why a prior trial of rituximab in myeloma concluded that it was not effective in treating myeloma.[17] In this trial, 19 patients with myeloma were treated with rituximab for 4 weeks, and responses, using standard response criteria, were measured at 3 months. Six of the 19 patients had responses (one partial remission and five with stable disease) with at least one patient with a response extending beyond two years. Thus, if the myeloma stem cells could be measured directly, it is possible that response rates might be higher. An alternative approach is to measure survival, and in particular progression-free survival, in looking at the effectiveness of treatment directed at rare populations of cells, as this may be a better reflection of efficacy.

Rituximab is being used to treat the myeloma stem cells. Although rituximab is active in vitro against the myeloma stem cell, it does not appear to have much activity against the mature plasma cells that make up the bulk of the tumor.[15] Thus, patients in this trial are being treated with a combination of cyclophosphamide, a drug with known activity against plasma cells, and rituximab in an effort to target the myeloma stem cell.

Cyclophosphamide is a chemotherapeutic agent that works by crosslinking DNA and interfering with cell division. It is a drug with known activity against plasma cells. Thus, it is being given in high doses to reduce the number of plasma cells in patients with myeloma and facilitate rituximab's ability to reach the myeloma stem cells. Cyclophosphamide has a unique pharmacology. It is a prodrug and must be metabolized in the body before it

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is active. Further, it does not kill all cells that are growing and dividing. Cells with high concentrations of the enzyme aldehyde dehydrogenase are resistant to cyclophosphamide. One population of cells that are not affected by cyclophosphamide are normal hematopoeitic progenitors, as they have a high concentration of this enzyme. Thus, even though high doses are given, the normal hematopoietic progenitors are unaffected by this and thus, following a relatively limited duration of low blood counts, all patients recover their normal hemoglobin, neutrophils, and platelets without the need for a stem cell transplant.

The primary objective of the trial is to measure progression-free survival one year after treatment. While standard responses will also be measured, we believe that assessing survival will be a better reflection of activity against the myeloma stem cell than the determination of partial and complete remissions. Equally important in this trial are the secondary objectives of using our laboratory assay to measure myeloma stem cells throughout the course of treatment and follow-up. At specified points in the treatment schema, clonogenic assays will be done to measure the effects of treatment on the myeloma stem cells.

We will then use statistical models to correlate the results of the laboratory assays with the clinical outcomes and in so doing, hope to develop a model for measuring disease response with in vitro assays prior to the determination of a survival benefit. If this can be done, it will enable us to speed the process of developing new therapies and develop more efficient ways to assess the efficacy of novel treatments.

As curing myeloma is the ultimate goal of everyone's efforts to understand and treat myeloma, we believe that novel approaches such as this offer the potential to better target the myeloma stem cell, giving us insight into better treatments for this disease.

Who Is Eligible?

Patients are eligible to participate if they have high-risk myeloma in first remission, either partial or complete. High-risk disease in this trial is defined as chromosome 13 deletion by FISH or cytogenetics, or beta-2 microglobulin > 5 mg/dL. Patients are also eligible: a) if they have relapsed myeloma that is responding to treatment, or b) immediately after their initial therapy if the treatment led to less than a partial remission.

Treatment Schema

Patients will undergo all screening tests to ensure that they meet the eligibility requirements and have adequate cardiac and pulmonary function to proceed. Once confirmed, patients will receive two doses of rituximab four days apart, followed by four daily doses of cyclophosphamide the following week. Approximately three weeks after completion of the cyclophosphamide, when blood counts have recovered, patients will be given rituximab once a week for four weeks. Rituximab will also be given on a maintenance schedule every 3 months beginning with month 3 from the start of treatment.

Safety, Tolerability, and Monitoring

Both rituximab and cyclophosphamide have been given to thousands of patients with hemtologic malignancies and their safety and tolerability are well known. Rituximab has been used predominantly in the treatment of lymphomas, either alone or in combination with chemotherapy, including cyclophosphamide. Cyclophosphamide is an active agent in the treatment of myeloma both in combination with corticosteroids and as a part of the chemotherapeutic preparative regimens used in bone marrow transplantation.

Patients will be monitored closely with serial assessments both of tolerance and of disease status by means of serum and urine protein electrophoresis and through bone marrow analyses. Secondary studies will be done in the laboratory to measure the effectiveness of treatment using measurements of myeloma colony formation and assessments of the mechanism of rituximab's action.

Future Directions

The results of this trial and our laboratory studies will allow us to examine the efficacy of combining agents with activity against both myeloma stem cells and mature plasma cells. We expect that the results of both these endeavors will allow us to design and develop future

clinical trials with the ultimate goal of producing long-term remissions. MT

References

1. Reya T, Morrison SJ, Clarke MF and Weissman IL. 2001. Stem cells, cancer, and cancer stem cells. Nature. 414: 105-111.

2. Bedi A, Zehnbauer BA, Collector MI, Barber JP, Zicha MS, Sharkis SJ and Jones RJ. 1993. BCR-ABL gene rearrangement and expression of primitive hematopoietic progenitors in chronic myeloid leukemia. Blood. 81: 2898-2902.

3. Lapidot T, Sirard C, Vormoor J, Murdoch B, Hoang TC-CJ, Minden M, Paterson B, Caligiuri MA and Dick JE. 1994. A cell initiating human acute myeloid leukaemia after transplantation into SCID mice. Nature. 367: 645-648.

4. Al Hajj M, Wicha MS, Benito-Hernandez A, Morrison SJ and Clarke MF. 2003. Prospective identification of tumorigenic breast cancer cells. Proc Natl Acad Sci U S A. 100: 3983-3988.

5. Hemmati HD, Nakano I, Lazareff JA, Masterman-Smith M, Geschwind DH, Bronner-Fraser M and Kornblum HI. 2003. Cancerous stem cells can arise from pediatric brain tumors. PNAS. 100: 15178-15183.

6. Singh SK, Hawkins C, Clarke ID, Squire JA, Bayani J, Hide T, Henkelman RM, Cusimano MD and Dirks PB. 2004. Identification of human brain tumour initiating cells. Nature. 432: 396-401.

7. Drewinko B, Alexanian R, Boyer H, Barlogie B and Rubinow SI. 1981. The growth fraction of human myeloma cells. Blood. 57: 333-338.

8. Hamburger A and Salmon SE. 1977. Primary bioassay of human myeloma stem cells. J Clin Invest. 60: 846-854.

9. Takahashi T, Lim B, Jamal N, Tritchler D, Lockwood G, McKinney S, Bergsagel DE and Messner HA. 1985. Colony growth and self renewal of plasma cell precursors in multiple myeloma. J Clin Oncol. 3: 1613-1623.

10. Bakkus MH, Van R, I, Van Camp B and Thielemans K. 1994. Evidence that the clonogenic cell in multiple myeloma originates from a pre-switched but somatically mutated B cell. Br J Haematol. 87: 68-74.

11. Billadeau D, Ahmann G, Greipp P and Van Ness B. 1993. The bone marrow of multiple myeloma patients contains B cell populations at different stages of differentiation that are clonally related to the malignant plasma cell. J Exp Med. 178: 1023-1031.

12. Jensen GS, Mant MJ and Pilarski LM. 1992. Sequential maturation stages of monoclonal B lineage cells from blood, spleen, lymph node, and bone marrow from a terminal myeloma patient. Am J Hematol. 41: 199-208.

13. Pilarski LM, Seeberger K, Coupland RW, Eshpeter A, Keats JJ, Taylor BJ and Belch AR. 2002. Leukemic B cells clonally identical to myeloma plasma cells are myelomagenic in NOD/SCID mice. Exp Hematol. 30: 221-228.

14. Matsui W, Huff CA, Vala M, Barber J, Smith BD and Jones RJ. 2003. Anti-tumour activity of interferon-alpha in multiple myeloma: role of interleukin 6 and tumor cell differentiation. Br J Haematol. 121: 251-258.

15. Matsui W, Huff CA, Wang Q, Malehorn MT, Barber J, Tanhehco Y, Smith BD, Civin CI and Jones RJ. 2004. Characterization of clonogenic multiple myeloma cells. Blood. 103: 2332-2336.

16. Kuppers R, Klein U, Hansmann ML and Rajewsky K. 1999. Cellular origin of human B-cell lymphomas. N Engl J Med. 341: 1520-1529.

17. Treon SP, Pilarski LM, Belch AR, Kelliher A, Preffer FI, Shima Y, Mitsiades CS, Mitsiades NS, Szczepek AJ, Ellman L, Harmon D, Grossbard ML and Anderson KC. 2002. CD20-directed serotherapy in patients with multiple myeloma: biologic considerations and therapeutic applications. J Immunother. 25: 72-81.

NOTE: This clinical trial is open at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins and is actively accruing patients. If you would like more information or are interested in participating, please contact either Carol Ann Huff, MD, at 443-287-7104 or Kathryn Rogers, RN, at 410-614-1766.

BANK ON A CURE — continued

The Honorable Geraldine Ferraro prepares to "swish and rinse"

Many members have contacted the IMF with questions about Bank On A Cure. In order to help everyone understand the means and mission of this important research initiative, we would like to provide the following:

Bank On A Cure ("The Bank")

- Is the first international cooperative DNA bank for genetic analysis that will allow physicians to develop customized, effective therapies for individual patients with myeloma.
- Identifies genetic results that will provide predictions of an individual's drug response or adverse effects of therapies.
- Assesses genetic results that will help identify risk factors for developing myeloma and identify genetic factors that serve as predictors of disease progression.
- Serves to contribute to more effective therapy choices, while improving the quality of life of myeloma patients.
- Serves as a model for other disease that would benefit from DNA banking and genetic analyses.
- Has recruited experts from around the world in basic research, clinical practice and public health to serve as an international team dedicated to understand and applying genetic information to treatment choices for individual patients.
- Already has over 3000 DNA samples in its bank, developed state-of-the-art technologies for testing large numbers of genes; and developed commitments for 4000 more samples, including sample donations from individual patients with the BOAC Kit.
- Has, in preliminary studies, already identified genetic traits that appear to alter the effective dose of some drugs received by patients.
- Has preliminary results that have identified genetic factors that may be associated with adverse side effects, such as blood clotting.
- Has identified genetic variations that may put some ethnic groups at higher risk for developing myeloma.

In order to assure that we have a sufficient number of samples to perform the studies necessary to accurately predict patient response, we need the assistance of all myeloma patients. We need more samples! (At the present time, we have a sufficient number of "control" samples from friends and caregivers of patients, and we thank you!) Therefore, we are enlisting your help to make sure that we reach our goal of making tens of thousands of samples available to our researchers. We urge you to organize a "swish and rinse" event in your local support group! Plan a "swish and rinse" at your home! Investigate opportunities at your local hospital! For more information about providing samples or to receive a sample kit, please contact me at the IMF at 800-452-CURE (2873) or e-mail David Smith at dsmith@myeloma.org. MT

Geraldine Ferraro and Professor Brian Van Ness

IMF HONORS KENNETH C. ANDERSON, MD

By Robert A. Kyle, MD

Kenneth C. Anderson, MD, of the Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, will receive the 2005 *Robert A. Kyle Lifetime Achievement Award* on September 27th.

Dr. Anderson has developed the world's most successful research and clinical program devoted to multiple myeloma. He has attracted many talented young investigators and has led them in making important contributions to the understanding of multiple myeloma and ultimately to successful therapy of this devastating disease. His group consists of young research fellows as well as seasoned researchers, molecular biologists, immunologists, transplant biologists, and clinicians who effectively work together. He and his group developed monoclonal antibodies that are used to characterize the B-cell malignancies. These antibodies have been utilized to purge tumor cells from the collected hematopoietic stem cells. They have pointed out that adhesion molecules on myeloma cells play an important role in localizing tumor cells within the bone marrow and also, in regulating tumor cell growth and survival. They have clarified the mechanisms of regulating autocrine and paracrine cell growth at both the cellular and molecular levels. They have developed a model of human myeloma using SCID mice which allows the study of the mechanisms of plasma cell growth *in vivo*. Dr. Anderson and his colleagues have also demonstrated multiple abnormalities in the cell cycle regulatory proteins which result in abnormal growth, control, and survival. Signaling cascades mediating cell growth, survival, and drug resistance have also been delineated. They have shown that apoptotic pathways in myeloma cells are important. Furthermore, mechanisms of resistance to apoptosis have been studied in an effort to develop new therapies for myeloma. They have emphasized the role of the microenvironment in regulating growth and survival of myeloma tumor cells. Most importantly, these studies have identified multiple agents targeting the tumor cell-tumor host interaction.

Drs. Robert A. Kyle and Kenneth C. Anderson

These laboratory investigations have resulted in important new therapies for the treatment of multiple myeloma at the bedside. Dr. Anderson and his group have developed novel immune-based therapeutic approaches for multiple myeloma. These include the development of anti-tumor vaccines as well as *ex vivo* expansion of allogeneic and autologous antigen specific T cells, for allografting and autografting respectively. His laboratory has identified new treatment targets of the tumor cell and its bone marrow microenvironment. They have designed and lead multiple clinic protocols to demonstrate the efficacy of these agents. Most importantly, Dr. Anderson's group played a major role in the development of the proteasome inhibitor, bortezomib. His identification and validation of targets to improve patient outcome in myeloma shows great promise.

Born in Worcester, Massachusetts, Kenneth Anderson graduated from Boston University, and received his MD from Johns Hopkins University School of Medicine in Baltimore, Maryland. Following internship and medical residency at Johns Hopkins, he became a fellow in medical oncology

PLEASE SEE DR. KENNETH C. ANDERSON NEXT PAGE

DR. KENNETH C. ANDERSON — continued

at Dana-Farber Cancer Institute. He was also a clinical fellow in medicine at Brigham and Women's Hospital. He advanced from Instructor in Medicine to Professor of Medicine, and is currently the Kraft Family Professor of Medicine, Harvard Medical School. He is currently Chief, Division of Hematologic Neoplasia, Dana-Farber, and Director of the Jerome Lipper Multiple Multiple Myeloma Center.

Dr. Anderson has received many honors, including the *Waldenström Award for Myeloma Research* as well as the *Doris Duke Clinical Research Clinical Scientist Award*. He has served as visiting professor at many prestigious institutions, including Yale University, University of Pennsylvania, and University of Chicago. Dr. Anderson has also given many lectureships including the University of Utah, University of Puerto Rico and Mayo Clinic. He has also served on the editorial boards of *BLOOD, Journal of Clinical Oncology, Transfusion,* and *American Journal of Hematology*. Dr. Anderson is Associate Editor of the *European Journal of Haematology* and Section Editor of Myeloma for *Leukemia*. His bibliography is impressive from both a qualitative and quantitative standpoint and consists of more than 400 peer-reviewed papers, book chapters, and books.

Dr. Anderson is Chair of the National Comprehensive Cancer Network (NCCN), Multiple Myeloma Clinical Practice Guidelines Committee, and is a Cancer and Leukemia Group B principal investigator. He serves on the Scientific Advisory Board of the International Myeloma Foundation. He is also on the Board of Directors and Chair of the Scientific Advisory Board of the Multiple Myeloma Research Foundation, as well as on the Board of Directors and Chair of the Leadership Committee of the Multiple Myeloma Research Consortium. Dr. Anderson has served on the National Cancer Institute Scientific Review Group D and was cochairman of the National Cancer Institute Progress Review Group on Leukemia, Lymphoma and Myeloma. He also serves on external Advisory Committees at the University of Indiana Cancer Center, MD Anderson Cancer Center, and the Amyloid Center at Boston University.

It is evident from his many activities that Ken is never too busy to help others. Dr. Anderson has done more for the field of multiple myeloma and related disorders than anyone else. He is most deserving of this Lifetime Achievement Award. MT

The IMF Welcomes David Siegel, MD, PhD

The IMF is pleased to announce that Dr. David Siegel has joined its Scientific Advisory Board.
Dr. Siegel is Division Chief, Myeloma and Lymphoma, at the Cancer Center of the Hackensack University Medical Center in Hackensack, New Jersey.
He was Director, Myeloma and Stem Cell Transplantation, Atlantic Health Systems (1998-2002); Assistant Professor of Medicine, Myeloma and Transplant Research Center, Arkansas Cancer Research Center (1995 -1998).
Dr. Siegel received his MD from New York University School of Medicine (1986), and his PhD from the Sackler Institute of Basic Medical Sciences (1985).

NUTRITION WITH CANCER: INCREASING CALORIES AND PROTEIN

By Heather-Ann Younker RD, CNSD, and Angela Langner RD

Good nutrition is important during cancer and its treatments. Trying to maintain adequate calorie and protein intake during cancer treatments can be very challenging for the patient. Cancer treatments may cause nausea, vomiting, dry mouth, loss of appetite, and other side effects, resulting in suboptimal nutritional intake. Your Registered Dietitian will provide you with specific nutritional guidance based on your needs. Below are a few suggestions to help increase calorie and protein intakes.

Heather-Ann Younker RD, CNSD
Outpatient Transplant Dietitian
Hackensack University Medical Center
Hackensack, New Jersey

- Eat 5 to 6 small meals per day, rather than 3 large ones.
- Eat your favorite foods at any time of day. For example, if you find breakfast foods most appealing, eat them for dinner.
- Take advantage of the times of day when you feel hungry. For example, if you are hungriest in the morning, make breakfast your biggest meal.
- Exercise lightly or take a walk before meals to increase your appetite. (Be sure to consult with your physician before undertaking any exercise program.)
- Drink nutritious drinks, such as milkshakes and commercial liquid supplements. Cold drinks are usually tolerated best.
- Drink fluids *between* meals instead of *with* meals. Fluids with meals can make you feel too full, thereby reducing your food intake.

Angela Langner RD
Inpatient Transplant Dietitian
Hackensack University Medical Center
Hackensack, New Jersey

- Keep a variety of nutritious snacks available such as nuts, granola bars, pudding, and cheeses.
- To increase caloric content, add butter, cheese, cream cheese, gravy, peanut butter, mayonnaise, whipped cream, salad dressing, jam, and honey to appropriate foods.
- To increase your protein intake, increase your consumption of eggs, cottage cheese, hard or semi-soft cheeses, ice-cream, yogurt, nuts, seeds, wheat germ, peanut butter, fish, beans, tofu, and legumes. MT

Creamy Macaroni and Cheese Casserole

Makes 6 servings.

1-1/2 cups uncooked macaroni
1/2 cup mayonnaise
1 can cream of mushroom soup
2 cups cheddar cheese, grated
1/2 cup evaporated milk
1/2 cup onion, chopped (if desired)

Preheat the oven to 325°F Cook the macaroni and drain. Combine all the ingredients in a 2-quart casserole, sprinkling some of the cheese on top. Bake in the oven for 30-35 minutes.

Weight Gain Milkshake

Makes 2 servings.

1/2 cup whole milk
2 cups ice-cream of choice
1 teaspoon vanilla

In a blender, combine all the ingredients and blend until smooth.
To vary the flavor, try adding chocolate syrup or fruits.
To increase protein content, add protein powder.
Pour and enjoy!

IMF HOTLINE COORDINATORS ANSWER YOUR QUESTIONS

The IMF Hotline 800-452-CURE (2873) is staffed by Nancy Baxter, Debbie Birns, and Paul Hewitt.
The phone lines are open Monday through Friday, 8am to 4pm (Pacific Time).
To submit your question online, please email TheIMF@myeloma.org.

Question: My father-in-law has myeloma and may be a candidate for a stem cell transplant. I am pregnant. Can my baby's umbilical cord blood be used for his transplant?

Answer: First, let us provide some background information, and then you will better understand the answer to your question. The standard type of transplant used for myeloma patients involves harvesting and then reinfusing the patient's own stem cells after high-dose chemotherapy. This is called an autologous transplant , with "auto" referring to "self," the source of the stem cells. This procedure is generally well tolerated by myeloma patients and, on average, provides a remission of 18 to 36 months duration.

Nancy Baxter

Transplantation of stem cells from a matched donor is called an allogeneic transplant, and its use in myeloma patients is still considered experimental. Because they are more fragile in the transplant setting than patients with other hematologic cancers, myeloma patients almost never undergo full allogeneic transplant with high-dose chemotherapy because the risk of death is considered too high. Instead, researchers have developed the "mini-allo," a procedure in which lowered doses of chemotherapy are given to a patient prior to an infusion of stem cells from a matched sibling donor. The mini-allo is best performed on a patient with a low tumor burden, so it generally follows within 3 to 6 months after an autologous stem cell transplant. The desired result is to produce just enough graft versus host disease (GVHD) to allow the donor stem cells to fight the myeloma. Too much GVHD can kill the host, or leave the host debilitated. That is why in most cases, only the blood of a perfectly matched brother or sister can be used. Even then, clinical trials of mini-allo have reported treatment-related mortality (death) as a result of GVHD to have occurred in 12-17% of patients involved in the studies. There is little long-term data on the patients who have had a mini-allo because it is still a relatively new procedure, and one that should be performed in the context of a clinical trial.

The use of umbilical cord blood in the allogeneic transplant setting is still experimental. There are two problems:
1. The number of stem cells in an umbilical cord is too low to supply what is needed for an adult patient. Umbilical cord blood has been largely confined to use in pediatrics.
2. It is highly doubtful that a grandchild would be an HLA match (a system of genetically matching blood) for a grandparent. If the HLA match is not exact, then the risk of GVHD is increased, and the risk of death is increased.

One group of researchers recently reported results from a program in which umbilical cord blood was collected and used for transplantation in a *sibling* that has a disease and would benefit from a stem cell transplant. Data from 21 patients has been collected. The average age of the recipient of umbilical cord blood was 6 years. One-quarter of recipients had acute lymphoblastic leukemia (ALL). The rest of the recipients had other cancers or non-cancerous conditions that are treatable with stem cell transplants. None had myeloma.

Another group of researchers analyzed data from studies including umbilical cord blood transplants in 171 adults who were primarily diagnosed with leukemia. These patients did not have acceptable donors for allogeneic stem cell transplants and underwent transplants with umbilical cord blood. Following the cord blood transplant, acute GVHD occurred in approximately 32% of patients, and at 2 years, the incidence of chronic GVHD was 36%. Death related to the transplant procedure was 51%.

If you still wish to store the cord blood "just in case" for the future, there are private firms that provide this service. You may also wish to donate the cord to the Red Cross. MT

THE INTERNATIONAL MYELOMA FOUNDATION'S CDC INITIATIVE

By David Smith

The Centers for Disease Control and Prevention (CDC), in a three-year initiative, is funding programs that target specific populations on the importance of education and awareness regarding hematologic malignancies. The IMF is thrilled to have received a grant from the CDC to help in these efforts. Our educational grant is focused on communities that:

- Have high incidence rates of multiple myeloma, compared to the general population;
- Are underserved by other educational efforts;
- Are located in inner-city areas of major metropolitan centers;
- Could benefit from the IMF's expertise in patient education.

Our Goals

- Conduct outreach directed at African-Americans, the elderly, the underserved, the uninsured, and the under-insured;
- Utilize an educational video, brochures, and response methods to educate and gauge the message reception and comprehension;
- Encourage important steps in the patient's medical decision-making that can lead to an earlier diagnosis and improved education about treatment options;
- Improve (and when necessary, redesign) those educational materials that address the specific needs and concerns of the targeted communities.

Our Cities of Focus

The work plan approved by the CDC focuses on specific areas based upon myeloma incidence rates and the location of medical facilities available to address patients' needs. At the present time, our efforts are concentrated in:

Atlanta, GA
Baltimore, MD
Birmingham, AL
Chicago, IL
Cleveland, OH
Detroit, MI
Jackson, MS
Los Angeles, CA
Newark, NJ
Oakland, CA
Philadelphia, PA
San Diego, CA
San Jose, CA
St. Louis, MO

Starting in September 2005, we will expand our efforts to also include:

Boston, MA
Charleston, SC
Houston, TX
Kansas City, MO
Miami, FL
Montgomery, AL
Raleigh/Durham, NC
New Orleans, LA
New York, NY
Pittsburgh, PA

Why African-Americans

The CDC has data that identifies African-Americans as not only more likely to develop myeloma than other populations, but also as being a particularly underserved community that often experiences a later-stage diagnosis than other populations.

How We Will Know That This Initiative Is Working

- Growth in Support Groups, particularly the establishment of new groups in these targeted inner-city areas;
- Increased hotline calls from previously undiagnosed or underserved patients, as well as their families, friends, and caregivers;
- Higher web traffic to the areas of the IMF website that are focused on this program.

Where To Reach Out

The gateways to our targeted communities include:

- Doctors (not limited to Hematologists and Oncologists, but any doctors treating this population);
- Nurses at hospitals and clinics that serve the needs of these communities;
- Social Workers at hospitals and clinics that serve the needs of these communities;
- Any health care professionals who treat these communities;
- Community groups in these metropolitan areas;
- Church groups in these metropolitan areas;

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CDC INITIATIVE — continued

- Veterans Administration facilities that treat the populations of these areas.

How To Reach Out

The IMF is proud to present an educational video entitled "I have myeloma... What's next?" funded by our CDC grant. This video was created to address the needs of African-American and other underserved communities. The video is hosted by sports broadcaster James Brown.

How Our CDC Grant Helps You

Remember, the IMF is here to help. If you live in one of the areas targeted by our initiative, this outreach is an opportunity to expand your myeloma community and welcome new people into your local support group. But no matter where you live, this educational outreach is vital. Increasing the number of people who are aware of myeloma increases not only the visibility of the disease, but also increases the number of people fighting to find a cure. MT

Note: Please contact the Principal Investigator, David Smith, with any questions you may have. David can be reached at dsmith@myeloma.org or 800-452-CURE (2873). The IMF Hotline Coordinators are also important resources for information and can be reached at the above number. The IMF Director of Support Groups, Andy Lebkuecher, is available to assist you as well — he can be reached at 404-353-7127 or imfsupport@charter.net.

BE AN EFFECTIVE ADVOCATE FOR THE MYELOMA COMMUNITY!

Your commitment is needed to help shape public policies to benefit the myeloma and cancer communities. For more information about how to become an effective advocate, please check regular updates in the IMF email newsletter, The Myeloma Minute (register at www.myeloma.org) and see the Advocacy section for updates and tips including:

- Timely updates on congressional action impacting cancer issues;
- Sample letters to contact your members of Congress and the administration;
- Assistance to set up meetings with your members of Congress at home and in Washington;
- Suggestions to contact your local media to highlight cancer issues.

For more information, please contact IMF Director of Public Advocacy Greg Brozeit at greg.brozeit@sbcglobal.net or 330-865-0046.

CANCER, CIVIL RIGHTS, AND POLITICAL PLACEBOS

"[There] is a very frequent attitude that can be observed even in the political sphere...
People would sooner put up with false, impure, untruthful, and evil things than cause or have problems.
There is a willingness to purchase well-being, success, public regard,
and approval from reigning opinion by dispensing with the truth."

From "Salt of the Earth": An interview with Joseph Cardinal Ratzinger (Pope Benedict XVI)

By Greg Brozeit

When truth meets politics to collaborate for change, great things can happen for future generations. I would argue that in the latter half of the 20th century, the best example of this nexus in American history was the civil rights movement. There can be no arguing the fact, despite the insidious racism that still exists in some parts of our culture, that the civil rights movement changed our national character fundamentally for the better. Today, only the most hardened racists would dispute this.

Our nation changed because people who seemingly had no stake in the issues of racial segregation and discrimination decided it was their business. When Andrew Goodman and Michael Schwerner journeyed from New York to Mississippi to join James Chaney to register voters, they were part of a national movement that declared it was time for fundamental change. They were representative of citizens from all backgrounds who fought for change and ultimately paid with their lives. Their deaths helped provide the final impetus for passage of the landmark Civil Rights Act of 1964, the law that changed the face of our nation.

Thanks in large part to its passage, public policies that preserved the Jim Crow system are today intolerable. Today's children can hardly comprehend that a world with, for example, segregated public facilities even existed.

I cite this example because I have become convinced that the civil rights movement must be the model for the cancer advocacy community. I am often asked what would it take for Congress and the president to agree to make cancer research among the highest national priorities—as high as the war on terrorism, as high as education or as high as building roads and bridges.

Cancer issues will only become a high national priority when a critical mass of those who don't feel they will be touched by cancer decide it should become one, just as happened in the civil rights movement. First, there has to be better public education so that Americans understand that one of three females and one of two males will be diagnosed with cancer in their lifetimes. Second, when Americans understand that it may be possible to make all cancers chronic conditions, change may be possible. Once they appreciate the realistic opportunity in cancer research, and that our federal government is the largest single entity in the world capable of supporting cancer research, they will demand that it be vigorously supported.

Unfortunately, cancer advocacy is a tricky business. First, there has to be recognition that patient advocates and public policy advocates are not the same thing. Patient advocacy is about how one negotiates the terrain of medical care and bureaucracy to treat a disease—how to maneuver through the medical system, how to interpret what your doctor is telling you, how to access the best the treatments, therapies and drugs, and so on. A patient advocate may or may not be an effective cancer public policy advocate. Regrettably, the issues some advocate for may not coincide with the mission they seek to support.

For example, I met a gentleman whose wife recently died of breast cancer. He has two young daughters. When he learned of my work with the IMF, we discussed cancer advocacy. During the time his wife was fighting her cancer, he was most interested in treatment issues. Now that he has two daughters to care for, he said he was less concerned about treatment and mostly interested in prevention. I tried to explain to him that this was a false choice.

As Dr. Bill Nelson, a prostate cancer clinician and researcher from Johns Hopkins recently stated at the opening session of this year's Scientist<—>Survivor Program® of the American Association of Cancer Research

PLEASE SEE ADVOCACY NEXT PAGE

ADVOCACY — continued

meeting, "There has not been a single drug discovered and developed for the purpose of cancer prevention. Each of the drugs tested for ability to prevent cancer… were already marketed, and generating substantial revenue, for other indications." The moral: if you're interested in cancer prevention, support the broad spectrum of cancer research.

A more difficult problem is defining what the cancer constituency is. This is important because the most basic concept in American politics is constituency. In other words, whose interests are being represented and acted upon? This is not as simple as it first appears to be.

The IMF Advocacy Program seeks to represent three overlapping myeloma constituencies that comprise the myeloma community. First and most obvious are patients and caregivers. Another is those who have suffered the loss of a loved one to myeloma. The last is the most overlooked: future patients and families. As IMF Board Member Michael Katz frequently reminds me, those of us in the myeloma community have a duty and obligation to reach out for those coming after us. They do not yet understand what will face them—positive or negative.

Within these myeloma constituencies there are also subgroups. In the patient community, for example, one with smoldering myeloma may be most interested in supporting immunology research (i.e., strengthening the immune system to prevent the onset of active myeloma). Those goals may be different for a patient with severe bone issues. Complicating the picture is the tendency of some cancer advocates (the same happens with all disease types) to separate *their* perceived constituency from the broader cancer advocacy community.

And this highlights the ultimate conundrum for advocates for myeloma research and every other specific tumor type. As regular readers of my articles know, when Congress funds the National Institutes of Health, it does not allocate funding by disease type. So asking Congress to spend more on myeloma research is not realistic or productive. Our motto should be, "It's the cancer, stupid." This is particularly true now, as the NIH budget increases far less than the level of inflation, which actually results in a decrease of research activity from year to year.

In times of plenty, it was easy for Congress to make the right decisions. This was the case when the NIH budget was doubled over the period from 1998-2003. But now, in times of fiscal restraint, some in Congress and the administration are seeking to minimize medical research funding. They can do so because the cancer advocacy community has fragmented goals which dilute the overall strength of their constituency.

The source of this misguided advocacy can be traced to the incredible success of breast cancer advocates in early 1990s to establish a research program at the Department of Defense. The model they established—literally shaming Congress into action to devote more resources to breast cancer research—worked when they were virtually the only ones making the case for their disease. Congress has realized since then that allocating funding for specific disease programs has the effect of politicizing the priority-making process for cancer research. And their actions over the past eight years have reflected this. The breast cancer advocacy model of the early 1990s is obsolete today for all the other disease groups who seek to expand "their" piece of the pie. Today, Congress wants NIH to focus on scientific opportunity rather than political pressure.

Consider the issue of low clinical trial participation among eligible patients. Many patients are wary of clinical trials because they fear the possibility of being given a placebo. They want to know the truth and the realistic odds for good outcomes. Yet, too many advocates willingly accept and advocate for political placebos. Using as an analogy the observations of Pope Benedict XVI, advocates for disease-specific funding may feel that they are doing the Lord's work, but ultimately their advocacy does not recognize two important facts:

1. Determining and treating the genetic causes of cancer may have less to do with specific disease types than past research indicated; and

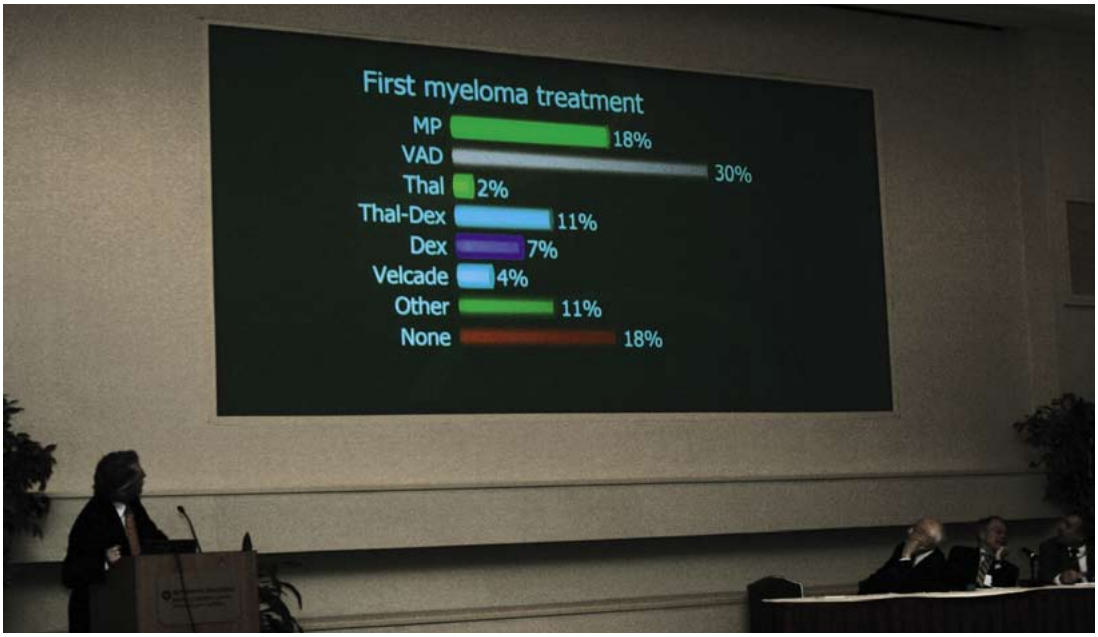
2. Taking into account the dwindling resources of the NIH, it is unwise for advocates to make political arguments that *their* cancer deserves increased funding at the expense of other research priorities. Such decisions must be made by researchers, not politicians or advocates.

Please see ADVOCACY page 24

ATLANTA IMF PATIENT & FAMILY SEMINAR

By Charlotte Pueschel

If you have ever attended an IMF Patient & Family Interactive Seminar, you already know what a special experience it is—talking to excellent doctors, as well as fellow patients and caregivers. Of course, there is also great food, making new friends and connecting with old ones, and learning about support groups. (If there is not one in your area, why don't you start one?) Or, you can become a buddy for a newly diagnosed patient by calling the IMF Hotline at 800-452-CURE (2873).



I knew that I would learn a lot at this, my first seminar on myeloma, but my experience far exceeded my expectations. I felt like these people were part of my family! My name is Charlotte Pueschel from Charlotte, North Carolina, and I was diagnosed with IgA multiple myeloma in January of 2004. I underwent an autologous stem cell transplant at Duke University Medical Center in June of 2004, and was in remission until February of 2005. Now it's back to the Decadron/thalidomide treatment. I know that many of you can relate!

The Wyndham Peachtree Hotel in Peachtree City, Georgia was the site of the IMF seminar on March 18th and 19th. (Peachtree City is about an hour southwest of downtown Atlanta). The presenters at the seminar were Dr. Brian Durie of the Cedars-Sinai Cancer Center in Los Angeles, Dr. Tom Hefner of Emory University in Atlanta, Dr. Robert Kyle of the Mayo Clinic in Minnesota, Dr. Frits van Rhee from the University of Arkansas for Medical Sciences in Little Rock, and Dr. David Vesole from the Medical College of Wisconsin.

Dr. Hefner gave us a complete overview of the disease called "Multiple Myeloma 101." The first described case was in 1844, in a patient named Sarah Newbury. We learned that J. von Rustizky coined the name "multiple myeloma" in 1873. In 1958, melphalan was discovered to be the first effective treatment for myeloma. Dr. Hefner defined terms that so many of us are familiar with, such as MGUS, SMM (smoldering multiple myeloma), M-spike, paraprotein, Bence-Jones protein, microenvironment, plasma cell, and plasmacytoma. He also talked about the minimum and maximum criteria for diagnosis and lytic bone lesions. Dr. Hefner also provided an in-depth explaination of SMM (where there are neither lytic bone lesions, anemia, renal insufficiency, nor hypercalcemia).

Dr. Kyle also discussed SMM, and the indications for therapy, which include an increased M-protein in the urine, decreased hemoglobin, elevated calcium or creatinine, lytic bone lesions, or extramedullary plasmacytoma. As therapy for hypercalcemia, Dr. Kyle recommends:

1. Hydration,
2. Prednisone,
3. Diuretics, and
4. Bisphosphonates (such as Zometa® or Aredia®).

For treatment and prevention of infections as a result of lowered immunity, Dr. Kyle recommends the pneumonia vaccine, antibiotics for the first two months after diagnosis,

PLEASE SEE ATLANTA NEXT PAGE

ATLANTA — continued

prophylactic penicillin, and gammaglobulin IV injections, if available.

Dr. Durie discussed myeloma as a bone disease and showed us, in explicit detail on x-ray, how the bones and spine are affected by myeloma. Bone lesions cause pain, fractures, pressure on the nerves and spine, and an increased calcium level. If you have been diagnosed with bone lesions, you need to be sure to have a full skeletal x-ray survey, a CT scan or MRI with gadolinium, a bone density test, and/or a full-body FDG/PET (Positron Emission Tomography) scan. Dr. Durie also discussed Aredia and Zometa, both of which stop bone destruction and are the primary therapies for myeloma bone disease. Dr. Durie reported that either of these bisphosphonates should be prescribed as an ongoing therapy, unless otherwise discussed with your doctor.

Osteonecrosis of the jaw, as discussed by Dr. Durie, is exposed bone in the maxilla or mandible, caused by the effects of bisphosphonates on bone resorption. Poor healing and secondary infection can lead to loss of teeth and segments of jaw bones.

As for beginning bisphosphonate therapy, your doctor should be the one to tell you when to start, but the baseline evaluation before the therapy is instituted should include checking for renal disease, dental problems, and documented bone disease.

Dr. Vesole, whose topic was "Novel Therapies," discussed autologous, allogeneic, and non-ablative allogeneic stem-cell transplants. Those of us who have gone though a transplant are all too familiar with the chemotherapy, the side effects, and the lowered immunity complications that can arise afterwards. Dr. Vesole gave a thorough description of single vs. tandem transplants. Post-transplant maintenance therapy can include thalidomide, pamidromate, or thalidomide with prednisone. He also discussed the newly approved drug VELCADE® and the soon-to-be-approved drug Revlimid® as new and effective therapies for myeloma.

Dr. van Rhee discussed autologous and allogeneic transplants. He is of the opinion that skeletal x-rays should be obsolete since PET scans show clearer pictures of the affected bones. If you are considering a clinical trial, Dr. van Rhee suggests that you check the track record of the drug, find out about any toxicities, and ask what the side effects are.

From my perspective, these seminars are an invaluable tool for gathering information about myeloma and provide great opportunities for networking and community/personal support. If you have never attended an IMF seminar, please consider attending one near you. For those of you reading this article whom I met in Atlanta, thank you for touching my life in such a special way. Your strength, humor, humility, and wisdom lifted my spirits and motivated me to touch the lives of others who are going through this disease and its treatments. See you at the next seminar and keep on keeping on! MT

ADVOCACY — continued

Cancer is too big an issue to be dominated by narrowly defined interests. This includes the advocacy of encouraging Congress to fund research for specific diseases. Such activities come at the expense of building collaboration among advocates for all diseases—especially cancer—to provide comprehensive support for the NIH and its largest institute, the National Cancer Institute.

The real, broadly defined goal must be eliminating suffering and death due to cancer. To paraphrase Neil Armstrong's immortal words when he set foot on the moon, we in the myeloma and cancer communities tend to focus too much on small steps rather than build the foundation needed to take the many giant leaps needed to conquer all cancers.

What is needed is consensus among all Americans to end cancer and make it the civil rights issue of the early 21st century. This will lead to a day when cancer can be dumped into the dustbin of history along with public segregation and discrimination. That is the truth and the only way we will overcome this beast called myeloma. MT

CHICAGO IMF PATIENT & FAMILY SEMINAR

"The seminar inspired me so much that starting a myeloma support group in my area is now one of my top priorities. With newly found hope, education, and knowledge of the IMF's passion for finding a cure, we feel more in control of our situation. We would encourage all patients, caregivers, family members, and friends to attend at least one IMF seminar. They will be hooked!"

Kathy Cartwright

By Kathy Cartwright

Wow, what a weekend! My husband, Jeff, and I attended the IMF Patient & Family Seminar held June 10th and 11th in Chicago, Illinois. My family and I have been living with multiple myeloma for over 4 years. I was diagnosed at the age of 39 years. My husband and children, Mary Kate (now 16) and Chris (now 14) know all about dealing with myeloma.

The Chicago seminar was the first IMF educational meeting that we've experienced. I promise it won't be our last! Our weekend started on Friday when we attended the "Quality of Life" session. In the evening, we enjoyed cocktails and dinner hosted by the IMF, where we had the opportunity to meet other myeloma patients and caregivers. It was good to hear their stories, and learn about their personal challenges and triumphs in dealing with their disease.

The Windy City welcomed us with open arms at the IMF Patient & Family Seminars on June 10th & 11th.

Saturday was a day with a very full itinerary. After a great breakfast, we headed to the meeting room, where we listened to an excellent faculty of myeloma experts presenting the latest information on myeloma disease and treatment options. We took ample notes about a wide range of therapy options, bone disease, transplantation, and research. By the end of the seminar, we had learned a lot and had met more wonderful people. I believe that everyone walked away from the seminar with something. I know that we surely did. This whole experience left us truly excited and filled with hope!

Once home, we called my folks and shared our experience with them. My mother said that she would love to attend an IMF Patient & Family Seminar in the St. Charles/ St. Louis area, so we hope that the IMF comes to our area soon! I also spoke to other family members, some of my local "myeloma friends," and a friend in Ohio whom I met 3 years ago while we were both harvesting our stem cells. I wanted to share our experience and what we had learned.

On Tuesday following the seminar, I had an appointment with my doctor. With all the information we gathered at the IMF seminar still so fresh in our minds, we had a lot of questions. My doctor was pleased to hear that we had attended the IMF event and was happy to answer our questions and explain how the information we learned might pertain to my case.

The seminar inspired me so much that starting a myeloma support group in my area is now one of my top priorities. With newly found hope, education, and knowledge of the IMF's passion for finding a cure, we feel more in control of our situation. We would encourage all patients, caregivers, family members, and friends to attend at least one IMF seminar. They will be hooked! MT

To learn more about upcoming IMF Patient & Family Seminars, please see the calendar on page 4 of this newsletter, visit the IMF website at www.myeloma.org, or call 800-452-CURE (2873).

ALLAN WEINSTEIN JOINS THE IMF BOARD OF DIRECTORS

Myeloma Today: When were you diagnosed with myeloma?
Allan Weinstein: I was diagnosed around September of 2002. I had a symptom but it wasn't a typical myeloma symptom. I was treated for an infection, but the infection recurred, and my internist didn't like that. He discovered that I had an elevated protein level in my blood, so he looked further and ran some more tests. I had about 10% plasma cells, elevated IgG, and an isolated bone lesion in my sacrum, which was not painful.

Allan Weinstein

MT: Did you require treatment?
AW: Yes, but I did not start treatment immediately because I needed time to understand what my treatment options were. Then I received three rounds of VAD, followed by three rounds of thalidomide and dexamethasone. I had my stem cells collected and, in July of 2003, underwent an autologous stem cell transplant.

MT: How have you been feeling since the transplant?
AW: My bone marrow biopsy is clear. My IgG has been stable in the 1600 to 1700 range, slightly above normal, for more than two years. I feel fine.

MT: Please tell us about your professional background.
AW: I am retired. In my first career, I had been an academician—ultimately, a full professor of Bioengineering and Orthopaedic Surgery at Tulane University, where I ran a research department. I did all the normal things that an academic scientist would do. I have a PhD and my background is all in bone replacement materials and devices, so the bone part of myeloma is something that I understood very well. In my second career, after I left academics, I went into industry. For ten years, I ran a company in the orthopaedic area. We took the company public and I retired. I was talked out of retirement to run a company involved in spinal disc prostheses. But now I am back in retirement and I won't be talked out of it again, although I am still on the Board of another spinal company, and now I've joined the Board of the IMF.

MT: How did you come to be involved with the IMF?
AW: After I was diagnosed, I started seeking out information about myeloma online, and I found the IMF website. I attended the very first IMF Patient & Family Seminar that I could get to. I've been going to one IMF seminar a year ever since. That's how I met Susie Novis. We got to chatting and we've stayed in touch ever since. Because of my background, I was asked to join the management committee for the Bank On A Cure® project. Eventually, I was invited to join the Board, which I was very happy to do.

MT: What is your outlook for the future?
AW: I'd like to see the IMF keep growing. Obviously, I would like to see a cure found, and the work that the IMF is doing will certainly help that along. Bank On A Cure is a great project. It has tremendous potential for understanding more about the disease process and for tailoring individual treatments. The IMF Patient & Family Seminars are a fantastic program. I tell every new patient I meet through my support group here in Phoenix that they should attend at least one seminar. The educational value of these seminars is incomparable. Also, they are an opportunity to meet people who are long-term survivors. When you are first diagnosed and you start reading the myeloma literature, it can be very scary. "Myeloma is an incurable disease" are devastating words. And some people fixate on the life expectancy statistics in the literature. They become very discouraged about their future. But there is no statistic that applies to an individual patient. Every patient is different. To meet people who are 10- or 15-year survivors is very encouraging. And I've met many long-term survivors at the IMF seminars! These are not isolated cases. I am also encouraged by the impressive amount of research being done in the field of myeloma. And the IMF is playing a big part in that. My outlook is very positive. MT

A CONVERSATION WITH TIM & DONNA EAGAN

Donna: I have always led a very healthy lifestyle and have never had any major illnesses. My mother died at age 61 of a heart attack. My father's health was good and he lived until he was almost 90. Then one day in 1992, I started feeling like I had caught the flu. When I started vomiting, it was time to go see my general practitioner. One of the tests she ran showed that my creatine level was elevated, and she promptly referred me to a nephrologist. By that time, my creatine was measured at 17 mg/dL, very high when you consider that normal values for an adult female are generally in the range of 0.5-1.1 mg/dL. The nephrologist put me in the hospital and ran a bunch of tests. In November of 1992, a bone marrow biopsy revealed the M-protein. The diagnosis was multiple myeloma.

Tim & Donna Eagan

Tim: We were led to believe that Donna had six months or so left to live. The prognosis was not good.

Donna: They told me I was on my way out. At that time, I was asked if I would be willing to participate in a study by the Southwest Oncology Group (SWOG). I thought that I was dying anyway, and felt that this would be one way for me to help others with myeloma. The study was run by Dr. Sid Salmon out of Arizona. Dr. Brian Durie was working on that study as well.

Tim: A diagnosis of myeloma is a family affair. Being a hospital administrator by trade, I was somewhat familiar with myeloma, and I certainly used all the resources at my disposal to gather more information. But in 1992 the resources available to myeloma patients were limited. However, I found the IMF, and its Board of Directors and its consulting physicians were all very helpful. Brian Novis had just passed away from myeloma. Susie Novis was a great help and shared a lot of materials and information with me. I also combed through medical books on my own. We found a local oncologist and Donna started receiving both dialysis and chemotherapy at the same time. She was placed on the VAD (Vincristine, Adriamycin, and Dexamethasone) protocol.

Donna: I did nine sessions of VAD and although it certainly had its bad moments, I tolerated it reasonable well. My creatine level started to drop and, eventually, I was able to get off dialysis. Another bone marrow biopsy was performed in June of 1993. The great news was that my myeloma was in remission.

Tim: I believe that early diagnosis, as well as education and quick and effective treatment, are all vital to a good outcome.

Donna: In June of 1993, I was started on low-dose alpha interferon maintenance (0.3cc three times a week), which continues to this day at the same dosage and frequency. I am still part of the SWOG study. Most of the time I feel pretty well. When I don't, it's usually because I'm trying to do too much. For me, rest and relaxation is key to helping me cope, so I try to do things for myself that make me feel better.

Tim: Every six weeks, Donna has her blood work done. Every three months, she sees her oncologist. And every three to four months, she has the 24-hour urine test done.

Donna: I am now staring my thirteenth year in remission. I feel very lucky, and I would like to encourage newly diagnosed patients to try and keep a positive outlook. Don't give up. Stay strong. I am living proof that when they say it's over, it's not necessarily over. I will be 65 in August and I was 52 years old when I was diagnosed with multiple myeloma. I am seeing a time in my life that I never thought I'd see. MT

CANCER ETIQUETTE

What to Say, What to Do When Someone You Know or Love Has Cancer

By Rosanne Kalick

We've all made verbal mistakes. The goal is to lessen our chances for verbal blunders. The most likely time for error occurs when a family member, friend, or colleague tells of his diagnosis. Casual acquaintances usually find out after the dust has settled, but those closest to the situation, whether prepared or not, are likely to react viscerally. Even the period before the test results come in may be a volatile one. If, for example, you say to your friend who's awaiting biopsy results, "It's nothing," you're denying the very real anxiety felt by the person awaiting those results.

As one who was told by many, "It's nothing," and found out twice that "nothing" was really something, I recommend saying, "It's likely to be nothing serious," or "I hope it's nothing." This changes wishful thinking into a reality check. It may not be wise to say, "You'll be fine." "You'll probably be fine" is a better choice. The first statement makes you sound omnipotent. Of course, you want the patient to be fine. You can't deal with the possibility that she won't be fine any more than she can. Assuming everything will be all right, however, doesn't give the patient "wiggle room." How can he speak to you of his fears of treatment, of dying, of disfigurement, if you say everything will be fine? It shuts down the communication artery, which is exactly what you don't want to do. Changing one word can change the tone of the message.

Remember that waiting for test results gives new meaning to Einstein's theory of relativity. This is a particularly stressful time. The cancer clock is on for the patient.

There are no absolutes, just guidelines. One size does not fit all. One guideline may be that less is more. Pause before you speak. It's perfectly OK to say, "I don't know what to say." There is no single perfect response, no litany for proper speech. Everyone is in a state of shock when a diagnosis is made. The patient, too, may not know what to say. Your response could be as simple as "I'm sorry to hear that." If you're a close friend or member of the family, an expletive may communicate what you need to say. A hug may be just the right response.

A screaming toddler is told by his parents, "Use your words." We need to do the same. Although cancer is no longer the silent disease, it still, in many instances, strangles us verbally and emotionally. It should not be a disease of miscommunication as well as runaway cells.

How Are You?

I would be remiss if I did not include a reference here to the question most commonly asked of the patient, "How are you?" There is inherently nothing wrong with such a question. But is it the standard "How are you?" we routinely ask when we aren't really interested in the answer? Is it the mundane "How are you?" where the expected reply is the one word "fine," or "OK?" Or is the actual question, "How are you, really?" A variation could be "How are you today?" This permits focus on a cancer snapshot rather than the entire album. Recovery is measured in small steps. Just adding the word today may give your friend an opportunity to indicate progress in the last 24 hours. Conversely, if it's been a bad day, you both are speaking of only one day; the implication is that tomorrow might be a better day. In any case, if you ask the question, be prepared for the real answer. The question does connote caring and concern. It is often the way that communication starts. In general, if you're not prepared for the answer, don't ask the question.

It's critical that even the "How are you?" question be an open-ended one. As a patient, I needed to know there would be space for my truth, my words, whether they were upbeat or not. The "How are you?" question should give me the opportunity to speak of my fear, concerns, and even anger. We may all be in denial about cancer at times, but as a friend, caregiver, loved one, you need to let me know that I can have my moments of truth, painful as those moments might be. Good words can do that. MTO

REFLECTIONS ON MYELOMA

By Mark Patton

My name is Mark Patton and I'm a professional patient. OK, I'm not really a professional patient, but if there's ever an opening for one I'll apply. My adventures in cancerland started with my multiple myeloma diagnosis in February 1991. Over the past 14 years, I've had two bone marrow transplants (BMTs) and three peripheral blood stem cell transplants (PBSCTs). I've taken to calling myself *The World's Most Transplanted Person*. It has a nice ring to it, don't you think?

I was very fortunate to be diagnosed early (Stage IA). Back in October of 1990, I was playing golf with four of my brothers. While teeing off on the last hole, I heard a loud pop in my chest and felt a sharp pain. Wow! How do you hurt yourself playing golf? (I would find out later that breaking a rib while exercising is a fairly common occurrence for folks with myeloma.) The pain subsided in a couple of weeks and I went about my business.

Mark and Mary Grace

Then, in February 1991, I was talking to my brother on the phone. After the call, I stood up and it felt like an electric current shot up my spine. My legs gave out and down I went like a big bag of potatoes. My wife, Mary Grace, came running from the bedroom and helped me struggle to my feet. I had to assure her it wasn't the cocktails.

The next few weeks were a wild, emotional roller coaster. We tromped through an endless number of offices, exam rooms, procedure rooms, and hospital hallways. We were eventually summoned back to our orthopedic surgeon's office. Jim, who was a friend of ours, wanted me to do a CT scan. I noticed he was perspiring. I didn't take this to be a good sign because his office was cool.

Several days later, we convened one last time. The scan had revealed the lytic lesions in my spine, ribs, and skull. You can imagine my disappointment. Did I really have to invest all that time, energy, and money to be told my biggest problem was that I had holes in my head? Heck, I had known that my entire life.

Within weeks of being diagnosed, Mary Grace and I were sitting at the Arkansas Cancer Research Center in Little Rock (ACRC). Dr. Bart Barlogie laid out the Total Therapy protocol for us. Mary Grace took notes and asked good questions. I stared at my shoes and wished I could go home and hide under the bed.

Now you might think being diagnosed with multiple myeloma at the age of 41 is the worst thing that ever happened to me. But it wasn't. The worst was yet to come. During one of our next trips to ACRC, Mary Grace went in to be tested to see if she could donate platelets to me when I needed them. Dr. David Vesole, my primary transplant doctor in Little Rock, called our apartment later that day and said he wanted Mary Grace to come back in and do some tests. She said it was no big deal. I felt an instant, over-powering sense of dread.

We met with Dr. Vesole in short order. He told Mary Grace the tests revealed she had chronic lymphocytic leukemia (CLL). I was stunned. We seemed to be hurtling towards a black hole that was sucking up every ray of light and hope. I was at a loss as how to proceed.

One of the docs suggested she begin the Total Therapy protocol side-by-side with me. Without hesitation, she said, "No, first we will get Mark through his treatment and then we'll see about me."

It was, and will forever be, the most courageous thing I've ever seen anyone do. She put her life on hold, and in jeopardy, to help save mine. To me, she's a hero in the truest sense of the word.

Please see REFLECTIONS ON MYELOMA next page

Reflections on Myeloma — continued

We regrouped and soldiered on month by month through the strenuous chemotherapy regime of the clinical trial. I never went into complete remission, so I got to enjoy five sessions of total body irradiation, off-protocol, for good measure.

Over the next eight years (1992 to 2000), I was on a maintenance dose of dexamethasone (20mg every other day). My quality of life was outstanding. Life was good.

From time to time I would try new myeloma treatments as they became available. Two of these drugs were high dose vitamin A and Interferon. I waved the white flag on both due to the side effects.

My disease reared its ugly head again in early 2000 and I went on thalidomide for 18 months. The peripheral neuropathy in my hands and feet got to be pretty bad though, so I threw in the towel. I joined the VELCADE brigade for a while. It works wonders for some people. For me, it just made me sicker than a dog and I abandoned ship.

When my numbers began rising once again, Dr. Vesole informed me that I would be the guest of honor at another PBSCT. That transplant took place in February 2003.

As of this writing, I am 55 years old. In the past 14 years, I have seen babies born, friends pass on, siblings married, tikes turn into teens, and teens turn into adults with families. I thank God every day for my life and for Mary Grace.

It's kind of funny that I've turned out to be the person I wanted desperately to talk to when I was first diagnosed. Back then, I would have given anything to speak with a long-term survivor. Now I am one.

I got the Myeloma Institute for Research and Therapy's newsletter recently. There's a volunteer there who's also a 14-year survivor. Our ranks are steadily growing, thanks to the great strides made in treating our disease.

I don't know why I've been so blessed to survive for so long. Perhaps it's to help others. If you have questions or concerns, or need encouragement, take advantage of the services and resources offered by the IMF, the American Cancer Society, and the National Institutes of Health. Or, send me an email at mytransplant@sbcglobal.net.

I wish you best of luck. Keep your chin up, a song in your heart, and your hospital gown tied in the back. See you in remission. MT

I am thrilled to report that my wife, Mary Grace, has never had to undergo any treatment for her CLL.

Just for the record, I had a tandem transplant in October 1991 (BMT and PBSCT) and another tandem in March 1992. My last PBSCT was February 2003. So I've had 2 BMTs and 3 PBSCTs for a total of five transplants. My doctor, David Vesole, sees these as 3 transplants, but I'm sticking with my math.

A few tips from Mark Patton about Autologous Bone Marrow or Stem Cell Transplantation:

One of the very best places to chat with myeloma survivors is the Association of Cancer Online Resources (www.acor.org). You can seek out a myeloma community and a BMT Talk group.

Don't compare your treatment plan with other patients. You'll forever be wondering why that patient is doing something you're not, or why you're doing something they're not. Make your treatment decision and give it your best shot.

Back in the early 1980s, transplant patients were often kept in isolation for a month. Today, many autologous procedures are done on an outpatient basis. Check with your doctor to see if you might qualify for this approach.

There is nothing painful about doing a BMT or PBSCT. Any unpleasantness is the result of chemotherapy and/or radiation treatments.

J.C.'S SUPPORT FOR MYELOMA PATIENTS GROWS

By Greg Brozeit

You don't meet many myeloma patients at golf tournaments benefiting the IMF. So when a team captained by Dr. Steven Johnson—a myeloma patient—won the 6th annual "J.C." Golf Tournament at the Wapicada Golf Course in St. Cloud, Minnesota, on May 21, 2005, it became sort of a "man bites dog" kind of story.

That… and the weather. This was the second year in a row I participated. It was the second year in a row the weather broadcasters predicted continuous rain and occasional thunderstorms; the second year in a row that it rained right up to the beginning of the tournament; and the second year in a row that the promised rain held off for the entire round. For some reason, despite satellite pictures to the contrary, rain seems to stay away from the "J.C." Golf Tournament. I'll leave it to you to draw conclusions.

Dr. Steven Johnson and his winning team

Greg Brozeit joins the "J.C." Golf Tournament team

This year, 180 golfers and 50 volunteers and dinner guests celebrated the life of "J.C." Johnson. Taken together with this year's contribution, the "J.C." Golf Tournament donations to the IMF are now approaching $100,000. Next year's tournament promises to be just as successful—at least we know the weather will allow play.

Dr. Steven Johnson's (no relation to "J.C.") team score of 15 under par easily won this year's tournament. "Playing in the tournament gave me a confidence boost," said Steven, "I hadn't played for a while but I've played four times since the tournament, broken 90 twice and have gone back to work in my dental office. I'm not walking 18 holes—yet—and only working half days, but with the grace of God I'll continue to get my strength and endurance back."

Steven found out about the tournament after reading an announcement in *Myeloma Today*. But much more important than the win is the story of how he came to participate. Steven, a dentist for the Army Reserve, was called up to active duty in July 2003 and was found to be anemic following a routine blood donation. That, as many myeloma patients know too well, eventually led to diagnosis in December 2003.

Steven attended an IMF seminar in Minneapolis, joined a support group, and worked with his oncologist to decide on auto and allo transplants (with his sister as a donor). Now his future includes more golf, getting back in the office to treat patients, and defend-ing his team's championship at next year's "J.C." Tournament.

Coincidentally, Steven's sister-in-law has a father who was diagnosed with smoldering myeloma. He was treated by Dr. Robert Kyle at Mayo Clinic. That was more than 30 years ago and his smoldering myeloma still has not developed into active disease.

The organizers of the tournament and the IMF are grateful to everyone for contributing to our success, including Anton's Restaurant for providing more than 230 free prime rib dinners to the participants, Miller Auto Plaza for furnishing a car in the hole-in-one competition, and the legendary band "Canoise" for entertaining everyone late into the night. MT

The J.C. Golf Tournament is held annually in honor of Janet "J.C." Johnson, who lost her battle with myeloma in 1999. She fought myloma like a demon, even though she wasn't always the best patient. It was probably her selfless, friendly energy that inspired a gathering of her friends, about two months after her death, to come up with the idea for this tournament. It was as if everyone had the same thought at the same time. It had been J.C.'s wish that her friends and family help fight cancer by supporting research whenever possible. Maybe this tournament was her idea all along.

SECOND ANNUAL LEONA CRAVOTTA MEMORIAL GOLF TOURNAMENT

By Katelyn Marie Martin

Katelyn Marie Martin and golf pro Kevin Daughtrey

Last year, I organized the Leona Cravotta Memorial Golf Tournament in honor of my grandmother for my senior project at the Blue Ridge Virtual Governor's School. The tournament was so successful that my family and I decided to hold the tournament again this year. As last year, the tournament brought out many fellow supporters for the fight against multiple myeloma. It was gratifying to see that most of last year's participants were in attendance, but there were also quite a few new faces.

My family and friends worked as event volunteers. We were a little nervous about the weather because it rained the entire week before, but on Sunday afternoon, May 22, 2005, the sun was shining. It was a beautiful day for a round of golf! Fifteen teams, 19 hole sponsors, and 2 tournament sponsors gathered at Tanyard Country Club in Louisa, Virginia. Before the teams set out to play, I said a few words about multiple myeloma and thanked everyone for coming out to support the myeloma community.

After all the teams came in around 5:00pm, we were ready for a cookout and the awarding of event prizes. One of the tournament participants did something quite unexpected that really touched me and my family. He donated two Washington National tickets to be given away at our raffle. It was an extremely nice gesture and gave the tournament a little extra bit of fun. And, thanks to these tickets, we were able to raise even more money for the IMF!

The 2005 Leona Cravotta Memorial Golf Tournament turned out to be a success. My family and I are very glad to be able to contribute to the IMF once again this year. This is something my grandmother would have done herself, and she would be proud of us for doing it. We are already looking forward to holding next year's tournament. MT

Leona Cravotta Memorial Golf Tournament first-place team

VELCADE — continued

international, multicenter trial, named VISTA was initiated in January, 2005, to evaluate VELCADE in combination with melphalan and prednisone in non-transplant patients. The second large, multicenter, randomized phase III international trial, named HOVON, will assess PAD prior to stem cell transplant followed by maintenance therapy with VELCADE compared to vincristine, adriamycin, and dexamethasone (VAD) as induction therapy prior to transplant with thalidomide maintenance. This study is planning to enroll 800 patients and will compare progression-free survival, response rate, survival, and the overall safety and tolerability of the two regimens. MT

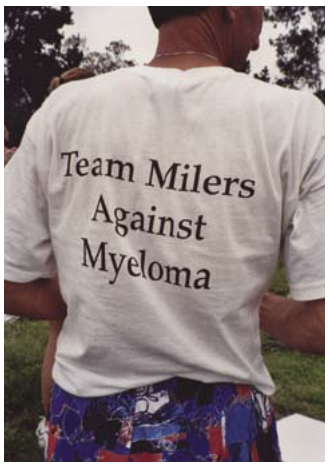
For more information about VELCADE clinical trials, patients and physicians can call 866-VELCADE (866-835-2233).

TEAM MILERS AGAINST MYELOMA

By Kendra Goffredo

Tony (58) and Kendra (25) Goffredo

My father and I always said that someday we would run a marathon together as father and daughter. This year, we signed up to run in Rock 'N Roll Marathon in San Diego, California. While I was readying myself for a 27-month commitment to the Peace Corps in Ecuador, my father, a multiple myeloma survivor, was living each day to the fullest. We set a goal to finish the marathon in under 4 hours, and then set out to raise myeloma awareness and funds for a cure. Together, we completed the 26.2-mile run in 3:35:40 finishing 1008 and 1010 out of a field of 20,000 other runners. More importantly, we raised almost $4,000 for the IMF, with money still coming in. I am happy in knowing that I am leaving for the Peace Corps having attained the goal of running my first marathon with my dad in record time, while raising myeloma awareness and money along the way, and with my dad's health in a "safe place." MT



RECYCLING FOR MYELOMA

Anthony and Kayla Tenboer

When Kayla and Anthony Tenboer began collecting bottles and cans to raise funds for myeloma research in honor of their grandpa, Wayne "Whitey" Tenboer, their family wasn't sure they'd make enough money to buy a test tube. But what began as a modest project for Kayla, 11, and Anthony, 8, has grown beyond anything anticipated by their parents, Kelvin and Sara Toenboer. Within just a couple of months, the kids had raised thousands of dollars! In addition, their efforts and dedication have attracted several donors who have contributed generously to the search for a cure for myeloma.

Whitey Tenboer worked hard as a farmer, while holding down other jobs to support his family. He also served as a youth group leader at his church. He remained active in his community and continued to work until only weeks before his death in December 2004. We are sure that Whitey would be very proud of his grandkids' efforts on behalf of the myeloma community. Thank you, Kayla and Anthony! MT

2005 "RIDE FOR THE CURE" BENEFIT POKER RUN

By Celeste Montalvo-Jackson

The second annual "Ride for the Cure" Benefit Poker Run was held on May 22, 2005, in Southern California. Once again, the myeloma awareness and fundraising event was held in honor of my dear friend, Darrell, who was diagnosed with multiple myeloma in 1999. Darrell underwent chemotherapy, an autologous stem cell transplant, and then an allogeneic transplant from a sibling in 2000. He was placed on thalidomide and had a positive response to this therapy, but the myeloma relapsed in 2003. Darrell had to stop taking thalidomide because he could no longer afford the high cost of the insurance co-pay for his medication.

Last year, when I took on the task of the "Ride for the Cure" event, I had never experienced a motorcycle poker run, let alone organized one. Unfortunately, Darrell had pneumonia and was too sick to join the 2004 ride. Some of the funds raised at last year's event went towards his medical expenses, the rest to the IMF.

Darrell

Darrell and I have known each other since junior high school, and I was moved to take action on his behalf. I began to act as Darrell's patient advocate because I strongly believe that all patients should receive the therapy that is deemed to be a medical necessity by their physicians. I am working to get such an assembly bill passed.

This year, I am happy to report that things are looking up. My buddy has qualified for the Working Disabled Medi-Cal Program and, because he has been feeling better, Darrell was able to celebrate in style by leading this year's ride. And it just so happened that the 2005 "Ride for the Cure" coincided with his birthday!

Darrell is widely known to be a motorcycle enthusiast, and many friends, fellow riders, and local businesses turned out to support their brother. Over 125 bikers lined up, ready to take part in the ride. It was overwhelming to see the miles of motorcycles—these big-hearted bikers really know how to show their loyalty!

For the Poker Run, each participant received one card at each of the five stops on the ride's route. The winner received a cash prize. The high card holder selflessly donated his winnings back to our cause.

I would like to thank all the riders for their participation and for helping make the 2005 "Ride for the Cure" Benefit Poker Run such a success. And very special thanks are due to the many event sponsors for their generous support of Darrell and the rest of the multiple myeloma community. MT

DONATE FOR DREW DAY

To know Drew Spaeth truly is to love him. Dedicated father of two, husband, baseball coach, mentor, surfer dude, and all-around incredible guy, Drew touches everyone he meets with positive energy, kindness, and generosity.

Drew Spaeth

Drew has myeloma. And that is why his family and friends have organized the Donate for Drew Day. This fundraising and awareness event will feature live music, auctions, food, and drinks. All proceeds go to the IMF. If you so choose, you can also be tested for the National Marrow Donor Program registry. For more information, please call Patrice Spaeth at 760-634-8019. You can also donate online at www.drew.myeloma.org. Come join the festivities! MT

MAIL FOR THE CURE

People often ask, "What can I do to help? I don't have a lot of time or money, but I'd love to help in some way." That's when we tell them about the Mail For The Cure fundraising campaign, a simple but powerful concept by which YOU can make a big difference to the myeloma community. Here's how it works:

All over the country, people just like you mail letters to their friends and relatives asking for their support of myeloma research and other important IMF programs. You will be surprised at the response you'll get when you give people a chance to help you fight the fight!

The IMF will provide you with a letter template for you to personalize, and specially-coded IMF donation envelopes to be included with each letter. These envelopes allow us to track how much was raised as a result of your efforts. The total of all monies received will be computed for the IMF Honor Roll, a year-end supplement to Myeloma Today.

For more information, please contact Suzanne Battaglia at sbattaglia@myeloma.org or 800-452-CURE (2873). Please join us in this exciting campaign! MT

Member Events Calendar

August 29, 2005
12TH Corporate Cup Challenge Golf Tournament
Naperville, IL
Contact: Brad Springer, brad@handheldpower.com

September 10, 2005
Donate for Drew Day! (Music, Food, Auction, NBMR Drive)
Encinitas, CA
Contact: Patrice Spaeth, 760-749-0909

September 24, 2005
Walk For the Cure
Rochester, MN
Contact: Eve Friedli, evefmail-curewalk@yahoo.com

October 15, 2005
Walk for Myeloma
Miami, FL
Contact: Denise Vidot, peaches2822@aol.com

November 14, 2005
1ST Annual Golf Tournament & Benefit for the IMF
Sponsored by the Phoenix and Tucson Support Groups and the Arizona Multiple Myeloma Institute
Phoenix, AZ
Contact: Barbara Kavanagh, bjkavan@aol.com

You know you want to do something for your community, and the IMF can help you. We are ready to provide you with the tools, assistance, and expertise you'll need to make your event a success. We have over 12 years of experience helping members around the world raise funds for research and education programs. FUNdraising is fun (get it?) and easy to do, and you'll have the satisfaction of knowing that you've made a difference! For information, contact Suzanne Battaglia at sbattaglia@myeloma.org or 800-452-CURE (2873).

Sharing the Hope

There came a time, there came a day
the doctor said, yes I heard him say
you have myeloma that is its name
then we went home, home we came.

What to do, where do we turn?
How can we know where can we learn
about this cancer with the weird name?
Yes, I remember myeloma is its name.

Then we discovered this group and took note
that their motto was "Sharing the Hope."
We found some folks just like us
there was really no problem, really no fuss.
Learning was easy, easy as can be
just like learning the ABCs.

Some were survivors of many years
it was a blessing to hear those voices of cheer.
Some were unfortunate, their cancer was bad
yet they were excited, they were so glad
to hear there is hope for others some day.
The future's exciting, soon we will say,
"A cure's been discovered," and we pray
that it will be quickly on the way.

The faces keep changing, there still is no cure
but we know, we know for sure
that coming soon, coming fast
a cure will be found, found at last!

So many have gone since we first started
for too many have already departed.
Though they are gone we continue to meet
knowing someday this cancer we'll beat.

This is the story of our new friends.
We hope that this story does not soon end.
No longer discouraged, we no longer mope
for with these friends we are "Sharing the Hope!"

Jerry Sawyer
North Texas Myeloma Support Group

IMF Hotline

Thank you so very much for the informative counseling and the email information on neuropathy pain. Words cannot express my appreciation for the IMF Hotline. Your friendly, cheerful, positive, and informative responsives to my many questions are outstanding. I always feel better just from talking with you.

Robert Reeves

Thank you so much for checking in with us—that is so thoughtful! Rog got a NOT multiple myeloma diagnosis from Mayo Clinic in Minnesota, then a third opinion that agreed that he does NOT have myeloma. Rog DOES still have MGUS, which has to be monitored and can become something serious, even myeloma, in later years... I hope that you know how very grateful we are for the comfort you brought to us at such a scary, emotional time. The calm, hopeful, controlled, and informed demeanor of the IMF staff taught us—in the few conversations we had— how to approach these health issues more successfully. Your service is invaluable. Thank you again for all you did for us, and all you have meant to us at such a dark and stressful period in our life. We pray that soon IMF will have wonderful new developments that will bring joy, hope, and a cure to all those that are dealing with multiple myeloma and other serious health issues.

Judy and Roger Jones

IMF Patient & Family Seminar

I just got back from the IMF seminar in Los Angeles. It was TERRIFIC. I can't stress enough how everyone should attend at least one. It was full of current information, presented quickly, and by experts. You fed us, taught us, and encouraged us! I went, I saw, I heard, I learned... What amazed me too were the different personalities of the doctors, from funny to serious, from suits to leather pants. It was also great to meet other patients. We drove 9 hours to get to the seminar. Even at nearly $3 a gallon it was worth it!

Geneva Tibbits

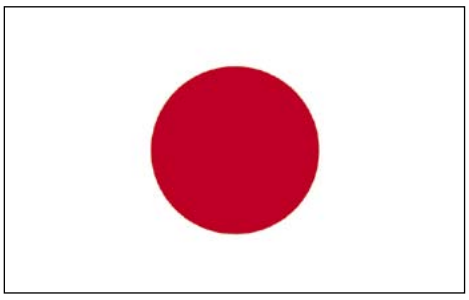
JAPAN

By Midori Horinouchi

The IMF's Tokyo branch, **IMF Japan** (a.k.a. The Myeloma Patients Association of Japan) was founded by Mr. Akira Horinouchi in October 1997. The branch started with just a few participants but, by May 2005, we had grown to include one thousand members. Currently, our medical support team consists of 63 doctors. The major activities of **IMF Japan** are:

- Operation and maintenance of our mailing list, utilized by IMF-Japan members to exchange vital information;
- Disseminating Japanese translations of the latest myeloma medical news via our website http://myeloma.gr.jp/;
- Assisting patients who wish to obtain a second opinion;
- Publication of the Japanese-language myeloma handbook, available free-of-charge;
- Hosting annual Myeloma Patient & Seminar;
- Holding annual General Meeting—the 2004 meeting was attended by about three hundred people;
- Annual award of a myeloma research grant, created in memory of Aki Horinouchi—this year's grant was awarded to Dr. Yutaka Hattori of the Keio University Hospital for his research on molecular targeting and gene-therapy of angiogenic growth factors for the treatment of refractory multiple myeloma; and
- Lobbying the Ministry of Health, Labor, and Welfare for early approval of myeloma treatment drugs such as thalidomide and bortezomib.

All **IMF Japan** activities are funded by donations and are made possible through the efforts of patients, family members, and other volunteers. Our slogans are: "Information can save your life! Have hope! And never give up!" It is an honor for us to be able to work with the IMF because, *Until There is a Cure... There is the IMF.* MT



LATIN AMERICA

By Christine Battistini

The newest branch of the International Myeloma Foundation is located in São Paulo, Brazil. **IMF Latin America** was founded in September 2004. The office currently serves all of Latin America.

I was motivated to reach out to the Latin multiple myeloma community by my experience as a caregiver. My mother, Maria Helena Telles, was diagnosed with myeloma in 1997. She fought a courageous and inspiring battle with her disease until her recent passing. From the time my mother's diagnosis was confirmed, the IMF was our source of information and support.

IMF Latin America is growing fast. Patients, caregivers, and physicians in all parts of Latin America are eager to have access to the latest information about myeloma. Our website www.myeloma.org.br provides a variety of educational materials in Portuguese and will soon be offering information in Spanish, too.

We are excited to be able to host a Latin American Clinical Conference and our first IMF Patient & Family Seminar in July, with both meetings being attended by IMF's Susie Novis and Dr. Brian G.M. Durie.

Our mission is to increase the awareness of multiple myeloma in Latin America, bring the medical community the information necessary to enable early diagnosis, and offer the many invaluable IMF programs and services to the Latin American myeloma community.

We are honored to be part of the truly **International** Myeloma Foundation family and we strongly believe in Brian Novis' words: *One person can make a difference. Two can make a miracle.* MT

tion. Revlimid most likely could be made available to myeloma patients at the discretion of the treating physician. The major concern would become how exactly reimbursement is handled.

- The combination of Revlimid plus dexamethasone, the successful treatment in the trials summarized in Table 2, will most likely also be submitted to the FDA for review. At this point, the earliest that any specific approval might be received for myeloma is sometime in 2006.

2. Expanded Access Program (EAP)

In the interim, the Celgene Corporation plans to activate an Expanded Access Program (EAP) for Revlimid in multiple myeloma. It is proposed that this be a multi-center, single-arm, open label trial for Revlimid plus dexamethasone (as used in the recent trials) for previously treated myeloma patients (at least 2 prior cycles of anti-myeloma therapy). Eligible patients will have relapsed or refractory myeloma. Prior use of thalidomide is allowed. Patients will continue on therapy unless myeloma progression occurs and/or Revlimid becomes commercially available. This, therefore, cycles back to item 1 above.

Thus, one way or another, it seems that the long wait for Revlimid may be nearing an end. Hopefully, very soon this drug will be in the hands of patients requiring treatment. The IMF will be tracking developments concerning activation of EAP and/or commercial availability of Revlimid. For further information, please visit our site at www.myeloma.org or call 800-452-CURE (2873). MT

This quarterly publication is available free of charge.
To subscribe, fill out the form below, visit www.myeloma.org, or call 800-452-CURE (2873).

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Dear Reader:

I have just returned from a very successful meeting in Stockholm, Sweden, where exciting updates on myeloma research and treatments were presented. The 10th Congress of the European Hematology Association was the most attended to date, with almost 5,000 participants from all over the world. Dr. Durie and I saw many of our old friends and colleagues, and met with new people who will clearly be important contributors to the myeloma community. Leaders in myeloma treatment and research from the United States and Canada, Europe, Asia, and South America attended and participated in discussions on the development of new drugs and ways to better utilize old ones. Opinions about myeloma treatment are modified on a constant basis. Without the dialogue and research, many of the new developments currently available would never have been brought to the public.

While in Stockholm, Dr. Durie and I met with Professor Gareth Morgan, co-chair of Bank On A Cure®. Together with our European colleagues, we discussed the IMF's mission to promote cutting-edge research in myeloma. These discussions were extremely positive and resulted in confirmed commitments to work together on Bank On A Cure, utilizing their expertise and pooling Europe's clinical data.

Collaborating together internationally fulfills our vision and mission. Over the past 15 years, the IMF has been working worldwide, resulting in offices in the UK, Japan, and Latin America. These offices function under the leadership and guidance of Executive Directors native to those countries, and funding support of these offices is made possible by donations from private individuals and industry within those regions.

With the expansion of the European Union and the growing impact that myeloma is having on its population, it is only natural that we extend our activities there. The IMF will officially open an office on the continent in early autumn. Under the leadership of the IMF's Executive Director of European Operations, the IMF Europe will focus on providing myriad services to patients, while working with the medical and scientific communities on projects promoting access to care, new drugs, clinical trials, and research projects.

Here's why this matters to you. Quite simply, working together with researchers and doctors around the world brings you advancements in treatment. Over the past five years research collaboration on an international level has brought concrete results, expanding and expediting clinical trials, making new drugs a part of mainstream treatment strategies in the United States.

I've been involved with myeloma since 1988. If you look at the history of myeloma, the progress made over the last five years is truly unprecedented, and our toolbox has never been better stocked. The broad spectrum of new drugs now accessible to myeloma patients would not be available without international collaboration. It's critical that the IMF continues to foster, support and promote global cooperation.

Susie Novis
President

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