Scientific & Clinical News

Dr. Brian G.M. Durie, co-founder and chairman of the IMF, offers his comments on the myeloma-related American Society of Hematology (ASH) presentations. From the relevant oral sessions and poster presentations, Dr. Durie highlights information of key interest to myeloma patients and caregivers. These ASH presentations consolidated the information of previously reported studies with longer-term follow-up, confirming many prior observations. Dr. Durie also focuses on important targeted agents, follow-up of some of exciting new anti-myeloma therapies, and new multi-drug combination regimens that offer effective treatment with a better schedule and lower toxicity for some patients. PAGE 5

Prof. Roman Hajek, a member of the IMF Scientific Advisory Board and a myeloma specialist in his native Czech Republic, is Professor of Oncology at Brno University and a physician in the Department of Hemato-Oncology at University Hospital Brno. Dr. Hajek also serves as Research Director at Faculty Hospital, Director of the University Research Centre for the Czech Myeloma Group, and Chairman of Czech Myeloma Group. In an interview with Myeloma Today, he shares information about the field of myeloma in the Czech Republic, as well as his experiences with international cooperation and being part of the IMF. Prof. Hajek also discusses the two posters he presented at the 50th annual meeting and exposition of the American Society of Hematology (ASH). PAGE 4

The XII International Myeloma Workshop, the premier biennial scientific myeloma meeting, took place from February 26th through March 1st in Washington DC. Members of the IMF Nurse Leadership Board (NLB) Beth Faiman and Elizabeth Bilotti attended the meeting and blogged daily to share information of interest with nurses and other healthcare professionals, as well as with the members of the myeloma the patient community. Myeloma Today presents a summary of their coverage of this landmark workshop and its in-depth discussions from the leading experts in the world working in myeloma. PAGE 12

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Dear Reader,

I’m going to take some editorial liberty and use this column to “crow” a little bit about my husband. At the recent XII International Myeloma Workshop, Dr. Brian G.M. Durie (yes, for those of you who didn’t know we’ll have been married 15 years come April 24th) received the Waldenström’s Award. This award is presented to a doctor/researcher in recognition of his or her contribution to the field of multiple myeloma. To receive this award you have to have done a lot, and it needs to be important.

Past recipients of this prestigious award are Drs. Bergsagel, Kyle, Salmon, Potter, Alexanian, Barlogie, Mellstedt, Anderson, Harousseau, and San Miguel. And now, Dr. Durie has been added to the list.

The award is presented at the opening ceremony of the International Myeloma Workshop, and on “his” night, I was beside myself, excited, proud, anxious and thrilled that he was being recognized. I can tell you he was too. He was anxious, thrilled, nervous and really excited. The recipient stands before his colleagues and as is customary, gives the Waldenström’s Lecture – it’s a big deal.

He gave a very elegant lecture. Not only did he talk about his body of work, he also provided the history of how myeloma research and treatment has progressed over the years. His lecture was brilliant – if I do say so.

After his lecture so many people commented that they didn’t realize how much Dr. Durie had done, and how important it was. So I thought I would take this opportunity and tell you some of the milestones he achieved. Dr. Durie has published hundreds of papers over the years and just as he didn’t have time to touch on them all, I don’t either, so I’ll follow his lead and just focus on some high points.

He published his first paper in 1975, “A Clinical Staging System for Multiple Myeloma.” It took two years to develop and it became known as the Durie/Salmon Staging System, which is still in use today. Also in 1975, he published a paper in Science on Plasma Cell Labeling, in which he commented that it was a great test but not widely feasible, which proved to be the case although it was a very rapid technique which he developed and later patented.

Dr. Durie became interested in what happens when the myeloma cell is not growing. Working with Diane Russell, they published a paper highlighting the point that myeloma is not always actively growing. Their paper, Reappraisal of Plateau Phase in Myeloma, was published in Lancet 1980.

Starting in 1981 at the University of Arizona he turned his attention to serum beta (β) 2 microglobulin and continued working on it with the South West Oncology Group (SWOG). Results demonstrated that serum beta 2 microglobulin and serum albumin reflect myeloma biology. In 1990 Dr. Durie, along with fellow authors Donna Stock-Novak, Sydney Salmon, Paul Finley, Jean Beckford, John Crowley, and Charles Coltman, published a paper in Blood, entitled Prognostic Value of Pretreatment Serum β2 Microglobulin in Myeloma. This important blood protein, along with serum albumin, is the backbone of the new International Staging System.

Dr. Greg Mundy and Dr. Durie began working together and looked at the relation between osteoclast activity and bone disease. The important lesson learned was that myeloma-derived factors trigger bone disease. Their findings, Relation of Osteoclast Activating Factor Production to Extend of Bone Disease in Multiple Myeloma, was published in the British Journal of Hematology in 1981.


In the late 1990s, working with Howard Urnovitz, he became interested in the role of viruses in myeloma. Their research led to the publication of Cell and Molecular Biology of Simian Virus 40: Implications for Human Infections and Disease, in the Journal of the National Cancer Institute, 1999. And suffice it to say – for a period of time, monkeys entered our life.

Continuing their work, their next paper, Circulating RNA in Microvesicles in Myeloma, was published in Acta Oncologica in 2000. This led to a whole new area of interest for Dr. Durie, and “voyager RNA” replaced monkeys in our household.

Dr. Durie became very interested in the role of FDG PET, and his paper Whole Body FDG PET Identifies High-Risk Myeloma was published in the Journal of Nuclear Medicine, 2002 and was cited at Best Nuclear Medicine Paper of 2002!

These days I think the work he is most proud of is the collaborative effort of the International Myeloma Working Group, which has published 11 papers to date and has many more in the hopper. Their work has dramatically changed the way myeloma patients are treated today. Myeloma Management Guidelines, International Uniform Response Criteria, Criteria for the Classification of Monoclonal Gammopathies, Multiple Myeloma, and Related Disorders (lead author Dr. Robert Kyle), and International Staging System, are just a few of the publications of this esteemed group.

What’s he interested in today? It’s “Voyager DNA” and the prognostic value of ALU retro elements and transmissible elements (TTEs), so stay tuned.

I have to say that when I learned that Dr. Durie would be the recipient of the Waldenström’s Award, I cried. Then I bought a very good bottle of champagne. We drank the whole bottle.

Susie Novis
MYELOMA TODAY IN CONVERSATION WITH PROF. ROMAN HAJEK

Please tell us a little about your medical background.

I graduated from Brno University and received my specialization in oncology and internal medicine. From 1995 through 1997 I worked in the US, including a total of six months as research investigator in Dr. Bart Barlogie’s myeloma program at Little Rock, AR. I am currently Professor of Oncology at Brno University, and work as a physician in the Department of Hemato-Oncology at University Hospital Brno. I also serve as Research Director at Faculty Hospital, Director of the University Research Centre for the Czech Myeloma Group, and Chairman of Czech Myeloma Group.

When was the Czech Myeloma Group formed?

The Czech Myeloma Group was formed in 1996 with the aims of sharing data among myeloma specialists in the Czech Republic and advancing the education of other medical professionals about this disease. We started small but our group has come a long way since its inception. In 2001, we formed The Czech Myeloma Group Foundation, which focuses on patient education and issues important to the myeloma patient community. In 2006, a new group called the Multiple Myeloma Patients Club came into being. We think of the three groups as a triangle of support for all members of the myeloma community in the Czech Republic. The three groups have very strong bonds with one another, and enjoy very good communication. Moreover, the University Research Centre of the Czech Myeloma Group was established in 2006 to accelerate the research in the field of monoclonal gammopathy in Central and Eastern Europe. The Czech Myeloma Group now has more than 150 physician and researcher members, and The Czech Myeloma Group Foundation and the Multiple Myeloma Patients Club serve between 2,500 and 3,000 myeloma patients in our country.

How many people are diagnosed with myeloma in the Czech Republic annually? And does the therapy they receive differ from what is available in the US and elsewhere?

Each year, approximately 400 new patients are diagnosed with myeloma in the Czech Republic. The availability of myeloma therapies in the Czech Republic doesn’t really differ from what is available elsewhere, including in the United States. It is true that the drug approval process in the Czech Republic might lag slightly at times, but we currently have all the novel anti-myeloma agents, including Revlimid® (lenalidomide), available to both the newly diagnosed (thalidomide, bortezomib only) and the relapsed/refractory myeloma patients. Also, these drugs are covered by insurance, which is very important for the patients. And we practice good myeloma diagnostic and treatment guidelines.

Do you use the International Myeloma Working Group (IMWG) Uniform Response Criteria in Multiple Myeloma?

Most definitely. The work of the IMF-sponsored IMWG has been very important to the field of myeloma. These criteria were integrated into new guidelines which are valid for both Czech Republic and Slovak Republic.

What is your relationship with the IMF?

I am very happy to be a part of the IMF – it is an excellent example of international cooperation. I have been involved with the Foundation for many years and am now pleased to be a member of its Scientific Advisory Board. The IMF has provided a wonderful example of service to both the medical professionals and the patient communities, and we have made full use of this example in structuring the Czech Myeloma Group. The Czech Myeloma Group Foundation, and the Multiple Myeloma Patients Club. The Czech Myeloma Group became an IMF affiliate in 2007, and our relationship is very strong and positive. The IMF has done a lot for the myeloma community in the Czech Republic.

What is the status of myeloma research in the Czech Republic?

While the process of myeloma diagnosis and the key approaches to treatment are pretty much the same in the Czech Republic as in the US, it would be accurate to say that we are running fewer myeloma clinical trials. I would approximate the budget available for research here at about seven million Euros, equivalent to about nine million US dollars as of mid-March 2009. Our center, the University Research Centre (Czech Myeloma Group), has more than 40 highly qualified researchers on staff, and we are very actively involved in myeloma research.

You presented two posters at the December 2008 meeting of the American Society of Hematology (ASH)?

One of the posters I presented at ASH focused on optimization of the CVD (cyclophosphamide, bortezomib, dexamethasone) combination regimen for elderly patients and those with relapsed poor performance status who usually do not tolerate the full dose of Velcade® (bortezomib). As a consequence, such patients cannot fully benefit from the strong anti-myeloma potential of this agent. In our trial, we have evaluated the potential of reduced intensity CVD (50% reduction) in the CVD senior group, and the results were compared with the CVD regimen outcome in the CVD junior group (patients aged <65 years with good status performance). Both groups’ regimens were received at the same time in 28-day intervals for at least 4 cycles, unless the treatment was stopped because of disease progression. Duration of treatment and number of cycles were similar in both regimens, and there was no difference in overall response, but the higher total dose of bortezomib achieved by patients in each group resulted in a better response in both groups. In conclusion, we found that the CVD senior regimen is better tolerated than CVD junior, and that the reduced-intensity CVD regimen seems to be a good option with a well balanced efficacy/toxicity ratio especially for patients with poor status performance.

The second poster presented focused on autologous stem cell transplantation (ASCT) in multiple myeloma and the benefits from the newer drugs used in the relapse setting. In this report, we describe the long-term CONTINUES ON PAGE 8
Continuing Advances in Treatment

“ASH 2008 presentations consolidated the information of previously reported studies with longer-term follow-up.”

– Brian G.M. Durie, MD

The 50th Annual Meeting of the American Society for Hematology (ASH) was held December 5 through 9, 2008 in San Francisco, CA. There were eight simultaneous oral sessions that included talks about studies related to multiple myeloma, and over eight poster groupings concerning myeloma, not including posters on transplantation. In addition, the IMF sponsored a Satellite Symposium on December 5, Finding Your Way Through the Treatment Maze – Selecting the Best Treatment in the Era of Novel Agents. There was also an Education Program on Plasma Cell Disorders, as well as a session from the newly formed Ad Hoc Scientific Committee on Plasma Cell Biology: High-Risk Myeloma.

Myeloma treatment continues to advance as more research results from clinical studies of conventional, novel, and new therapies are becoming available. Additional longer-term follow-up results are now available from phase III clinical studies of combination therapies that include the novel agents bortezomib, lenalidomide, and thalidomide. Preliminary results are promising for some even newer agents that have entered phase I/II clinical studies. Additional agents are being developed, and some of these have entered early stage studies in animal models of myeloma and early clinical studies in patients.

This write-up summarizes key presentations at the 2008 ASH Annual Meeting. Key issues discussed during the meeting include those that have been of interest for some time. Newer issues were also discussed, and these include the following:

• What is the role of autologous stem cell transplant (ASCT) now that the novel therapies are available?
• Should the goal of treatment be cure of myeloma or management of myeloma as a chronic disease?
• How should risk factors be determined and how should information about risk factors be used?

Genetics and Risk

“The big problem with myeloma is that there is genomic chaos, with many chromosomal abnormalities. There is no single chromosomal abnormality that identifies standard or high risk myeloma.” There are multiple combinations of changes, and this makes it difficult to interpret correlations.”

High-Risk Myeloma

The High-Risk Multiple Myeloma Ad Hoc Scientific Committee is a new group that will report to the ASH Annual Meeting for three years on a probationary basis. This scientific committee was created in part because at the previous ASH Annual Meeting in 2007 myeloma was the single most frequently discussed disease and was the subject of a large number of simultaneous sessions. The Ad Hoc Scientific Committee Session on Plasma Cell Biology: High-Risk Myeloma was chaired by Dr. Raymond Powles (Parkside Oncology Clinic, Wimbledon, UK).

Dr. Powles said there are many unanswered questions related to high-risk myeloma, which include the following:

• Does early diagnosis alter risk?
• Which patients are most likely to develop bone disease, kidney disease, amyloid, bone marrow failure, and/or failure of their immune response?
• Which individual patients respond best to which drugs?
• Is early response to treatment an independent risk factor?
• Which patients are “cured” and do these include 10-year survivors?

How New Therapies May Redefine High-Risk Myeloma

Dr. William Dalton (Moffitt Cancer Center and Research Institute, Tampa, FL) observed that a high-risk population can be defined by response to therapy, progression to relapse, genetic factors, and epigenetic factors, which are changes to genes that are not inherited, and may be due to factors like diet or the environment. One really important question that still needs to be answered is how myeloma cells interact with other types of cells within the bone marrow (the bone marrow microenvironment). These interactions may be influenced by different types of growth factors and other molecules produced within the bone marrow.

Phase III Trials in Newly Diagnosed Myeloma

“Further follow-up on some of the new frontline therapies is worth highlighting. Of the studies presented, Dr. Cavo’s clinical trial shows that getting a better response before transplant can lead to a better outcome after transplant including overall survival.”

Dr. Michele Cavo (Istituto Seragnoli, Bologna, Italy) presented preliminary results of a phase III randomized study of three 21-day cycles of induction therapy with VTD (bortezomib, thalidomide, dexamethasone) compared with TD (thalidomide, dexamethasone) followed by stem cell collection, cyclophosphamide, HD melphalan, and consolidation. This analysis included 460 newly diagnosed myeloma. Results so far indicate that VTD is superior, at least for the nCR rate, across subgroups including patients with factors associated with poor outcome, such as missing parts (deletions) of chromosome 13 and/or 17 and translocation 4;14. VTD gave better response rates than TD after the first and second ASCT and consolidation.
Serious side effects that were higher with VTD included PN and skin rash; otherwise serious side effects were similar with both treatments. Of patients with serious PN while on VTD as induction therapy, 95% remained on therapy with no effect on response rate compared with patients with less severe or no PN. Discontinuations of induction therapy were higher for patients on TD than VTD, mostly due to disease progression. The estimated 2-year progression-free survival is longer for VTD, but there is no difference in overall survival between treatments. However, the follow-up period is very short, and fewer than half the patients have received their second ASCT.

First analysis of HOVON-65/GMMG-HD4 randomized phase III trial comparing bzt, adriamycin, dex (PAD) vs. VAD as induction treatment prior to HD mel in patients with newly diagnosed myeloma (abstract #653)

“The results with PAD were better than the results with VAD, but still not as good as with VTD. As we search for the best combination treatment, VTD seems to be one of the most promising options. Beyond that, VRD is also quite promising, see Dr. Richardson’s results below.”

Dr. Pieter Sonneveld, University Hospital Rotterdam, Rotterdam, Netherlands, presented early results for the first 300 patients of an expected 825 patients randomly assigned to either VAD or 3 cycles of PAD, followed by CAD, stem cell collection, and HDM with autologous peripheral blood SCT. Patients then received either thalidomide or bortezomib maintenance therapy for 2 years. Those patients who had a brother or sister with a matching white blood cell type could receive stem cells from their sibling instead of their own stem cells. In this study, patients from the Netherlands received one SCT, whereas patients from Germany received two transplants.

In this study, the CR/nCR for PAD was lower than expected, although response rates for PAD were higher than those for VAD. The only significant side effect for PAD was peripheral neuropathy, which was 16%, vs. 6% for VAD. Patients receiving bortezomib maintenance therapy continue to have improved responses.

Prospective, randomized phase III study of bzt, mel, pred, and thal (VMPT) vs. bzt mel pred (VMP) in elderly newly diagnosed myeloma patients (abstract #652)

“For the elderly patients who are ineligible for transplantation and can get either the MPT or the VMP combination, there was an excellent abstract from Prof. Palumbo with very promising results of the GIMEMA trial of VMPT, a four-drug combination. This is very important. Millennium’s VISTA trial demonstrated that VMP is clearly better than MP. So the reduced dose of bortezomib used in the GIMEMA VMPT regimen offers lower toxicity that is easier for elderly patients to tolerate than VMP.”

Dr. Antonio Palumbo presented the results of this GIMEMA trial in 395 patients over age 65 years who were not eligible for transplant and who received either VMP with no maintenance, or VMPT and maintenance with bortezomib and thalidomide. Although the study began with the standard bortezomib schedule, it was changed to weekly bortezomib. VMPT, that is, the combination that included both bortezomib and thalidomide, resulted in better responses. The time to PR for the majority of patients occurred in 1 to 2 cycles of treatment, but CR rates increased slowly over time, suggesting that a lower intensity but longer treatment might result in more CR. There was no difference in overall survival estimated at 3 years between the two treatments (VMPT vs. VMP).

Side effects involving the blood were similar between the two treatments. VMPT is associated with a higher rate of sensory neuropathy and infections. The switch from twice weekly to once weekly bortezomib did not result in a lower CR rate, but did reduce the rate of peripheral neuropathy for patients receiving VMPT. For patients receiving VMP, the less frequent dosing of bortezomib decreased the rate of peripheral neuropathy, but also decreased the CR rate slightly.

Dr. Palumbo concluded that VMPT doubles the response rate of VMP, and increases time to next therapy, but not overall survival. He said that a longer follow-up beyond the current 14 months is needed to measure the progression-free survival and overall survival. Because of the need for further investigation, VMPT shouldn’t be incorporated into the standard of care at this time.

Early Clinical Studies in Newly Diagnosed Myeloma

“Among early clinical trials testing new combinations of drugs in the frontline setting, the most exciting results were the very high response rate achieved in the lenalidomide, bortezomib, and dexamethasone study, which was presented by Dr. Paul Richardson. Aptium Oncology presented a study of lenalidomide, cyclophosphamide, and dexamethasone, which also demonstrated very high response rates upfront. But it is still too early to tell which of the new combinations currently in early clinical studies will yield the better treatment.”

Dr. Sundar Jagannath, St. Vincent’s Comprehensive Cancer Center, New York, and Dr. Antonio Palumbo moderated a session in which early phase clinical studies of therapy of newly diagnosed patients were discussed. The studies that appear promising, and are being expanded or are leading to further studies include the following:

- RCd: lenalidomide with cyclophosphamide and low-dose dexamethasone
- Lenalidomide, bortezomib, dexamethasone (the dexamethasone was reduced during study based on results of a study of lenalidomide with either high or reduced-dose dexamethasone)
- Bortezomib, dexamethasone, cyclophosphamide, lenalidomide (VDCR)
- Bortezomib and high dose melphalan before ASCT

IMF Satellite Symposium

“There were several presentations at ASH 2008 of potentially important targeted agents that are showing promise in clinical studies:

1. Pomalidomide (thalidomide analog CC4047) is the new IMiD® compound, a member of a group of novel immunomodulatory...
2009 IMF RESEARCH GRANT RECIPIENTS ANNOUNCED
The recipients of the 2009 IMF Research Grant awards were announced at the gathering of the Foundation’s Scientific Advisors, held at the 50th annual meeting of the American Society of Hematology.

Since 1995, the IMF’s research program has been funding the most promising clinical investigators from all countries in order to further research into better treatment, management, prevention and, ultimately, a cure for multiple myeloma. The 2009 IMF grant award presentations took place during the 50th annual meeting and exposition of the American Society of Hematology (ASH). Susie Novis (president and co-founder of the IMF) and Dr. Brian G.M. Durie (chairman and co-founder of the IMF) were on hand to present the awards.

The IMF grants are funded by donations from private individuals. Junior investigators receive funding in the amount of $50,000. Senior investigators are funded at $80,000. While IMF research grants traditionally support single-year projects, one of this year’s recipients is receiving continued funding based on the results of the investigator’s work in 2008. Over the years, the IMF research grant program has produced significant results that have both increased the overall understanding of the disease and have benefited myeloma patients by improving treatment options. We are certain that the work of the recipients of the 2009 IMF research grants will continue to contribute significantly to the field of myeloma.

2009 Brian D. Novis Senior Research Grants
“Conversion of antiapoptotic MCL1 to death-inducing forms in multiple myeloma”*

Ruth W. Craig, PhD
Dartmouth Medical School
Hanover, NH

The viability-promoting gene MCL1 is abundantly expressed in multiple myeloma and is associated with poor prognosis and drug resistance. Dr. Craig and colleagues are developing reagents that convert MCL1 to short variants, which promote cell death rather than survival. They will optimize these reagents for the induction of multiple myeloma cell death and develop methods for identifying patients likely to benefit from such reagents (i.e., with tumors abundantly expressing full-length but not short forms of MCL1). The goal is to convert a gene that is overexpressed in multiple myeloma to a form that renders these cells more vulnerable.

“Study of alterations of bone microenvironment cells in multiple myeloma patients in relationship with osteolytic bone lesions: identification of potential new therapeutic targets”

Nicola Giuliani, MD, PhD
University of Parma
Parma, ITALY

The aim of this project is to clarify the biological mechanisms involved in multiple myeloma induced bone disease, to identify new potential therapeutic targets, and to develop new approaches in the therapy of myeloma bone disease. Using both the analysis of bone cells obtained from myeloma patients and in vitro experimental models, Dr. Giuliani and colleagues aim to advance the knowledge of the pathophysiology and the therapy of myeloma bone disease.

2009 Brian D. Novis Junior Research Grants
“Promoting osteoblastogenesis with a novel clinical grade Dkk-1 neutralizing antibody in the treatment of multiple myeloma related bone disease”**

Samantha Pozzi, MD
Dana Farber Cancer Institute
Boston, MA

Bone disease occurs in the majority of patients with multiple myeloma. Ninety percent of patients affected by myeloma manifest osteolytic bone lesions that may result in bone pain, hypercalcemia, pathologic fractures, or spinal cord compression. Bisphosphonates are the only currently available treatment for myeloma-related bone disease, resulting in inhibition of bone resorption, without impact on bone healing. Recently increased expression of the Dickkopf-1 protein (Dkk-1) has been reported in a subset of myeloma patients with osteolytic bone lesions. The aim of this study is to test the effect of a Dkk-1 neutralizing antibody in the context of myeloma bone disease. Preliminary results of the antibody in vitro show enhanced osteoblast differentiation and function and reduction in osteoclast number and function, providing a novel therapeutic target in the prevention and treatment of bone disease.

“Preclinical evaluation of a novel small molecule multi-cyclin dependent kinase inhibitor AT7519 in multiple myeloma”

Loredana Santo, MD
Dana Farber Cancer Institute
Boston, MA

In multiple myeloma, the abnormal activation of Cyclin Dependent Kinases (CDKs) mediate uncontrolled cell cycle progression. Therefore, CDKs represent promising therapeutic targets for myeloma. The overall goal of this project is to evaluate a novel small molecule multi CDK inhibitor, AT7519 (Astex Therapeutics), in myeloma. Preliminary data demonstrate the efficacy of AT7519 in myeloma both in vitro, in myeloma cell lines, in patient-derived myeloma cells, and in vivo, in a xenograft mouse model of human myeloma. Ongoing studies are focused on AT7519’s mechanism of action. These studies will provide the rationale for clinical trials with AT7519 for the treatment of myeloma.

“Potential therapeutic role of nanobodies in multiple myeloma: study in the 5TMM model”***

Karin Vanderkerken, PhD
Vrije Universiteit Brussel
Brussels, Belgium

This project aims at targeting the myeloma cells by nanobodies, small single-domain antigen binding entities (raised in camels or llama) approximately four times smaller than a classical antibody fragment and very stable. As result of their small size, these...
nanobodies are not immunogenic and are able to penetrate the cancer cell. In the current project, the idioype secreted and expressed by the myeloma cells will be used as antigen for the generation of nanobodies. In the first year of this study, nanobodies were developed and the biodistribution of the nanobodies in tumor-inoculated mice is being investigated. In the second year of this study, Vanderkerken and colleagues will couple the nanobodies to siRNA in order to obtain a specific targeting to the myeloma cells in the bone marrow. This study will provide evidence of the usefulness of these antibodies in targeting myeloma cells. If proven useful, further research will include the search of a common antigen (for different myeloma patients).

2009 IMF Aki Horinouchi Research Grant
“Development of a novel therapy for multiple myeloma by using newly synthesized curcumin analogs” ***

Dr. Hiroyuki Shibata
Tohoku University
Sendai, JAPAN

Curcumin is a dietary compound having tumor suppressive potential with low toxicity. Curcumin regulates dozens of molecules that give a malignant phenotype to cancer cells, including myeloma cells. Clinical investigation of curcumin in myeloma has already been initiated. While molecular targeted therapy is theoretical, a single target therapy is ineffective in almost all cases as each cancer cell has >500 malignant molecules. In spite of its multi-targeted nature, curcumin is so difficult to dissolve that we cannot use it for therapy. The aim of this study is to develop a new curcumin analog that has enhanced potential and utility in myeloma therapy.

*This grant was awarded in the names of Carol Klein and Nancy Moses.
**Second year funding of 2008 grant. The 2009 grant was awarded in the name of Chris Hollyer from the proceeds of Coach Rob’s Benefit Bash and Golf Tournament.
***This annual myeloma research grant was instituted in 2002 by IMF Japan in memory of its founder, Aki Horinouchi.

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PROF. ROMAN HAJEK — continued from page 4

outcome of 185 patients with newly diagnosed symptomatic myeloma treated with ASCT between 1996 and 2001 in the clinical trial of the Czech Myeloma Group. We specifically analyzed the benefit of the newer drugs used in the relapsed setting. The conditioning regimen in all patients was high-dose melphalan (200mg/m2). When symptomatic relapse after ASCT occurred, 34.6% (45/130) of patients were treated by conventional chemotherapy alone, 22.3% (29/130) by a thalidomide-based regimen, 10.7% (14/130) by a bortezomib-based regimen, 22.3% (29/130) underwent re-transplantation, and 10% (13/130) of patients received a combination of newer drugs and re-transplantation. In multivariate analysis thalidomide and/or bortezomib treatment in the relapse was the strongest factor for long-term survival. In conclusion, we found that accessibility of the thalidomide and bortezomib was independent of other prognostic factors. The use of the newer drugs in the relapsed setting significantly improved prognosis of patients.

Are you seeing a trend toward long-term survivorship of myeloma patients in the Czech Republic?

Yes, I can confirm this. And we have been having a lot of deep discussions in our myeloma group about how to best provide for our patients as they live longer and longer with their disease. As the number of long-term myeloma survivors increases, we must prepare to provide for their care in the future. In our center, the number of myeloma patients we are treating is increasing every year and, in part, this is due to prolonged survival. The use of novel agents is one reason we are seeing significantly improved prognosis of myeloma patients.

What is your outlook for the myeloma community in the Czech Republic?

We are continuing to improve early diagnosis of myeloma and, in cooperation with the IMF, have a six-year program already in place that aims to address all issues pertaining to this. By 2012, I hope that the myeloma patients being diagnosed in the Czech Republic will have a much improved quality of life due to earlier diagnosis of their disease. We are working on several unique programs for patients, such as Myeloma Spa and Psychological Network, as well as on our epidemiological tool, such as Register of Monoclonal Gammopathy.

I hope that we are moving in the direction of being able to achieve CR for most of our patients. Using combinations that include the one of three novel anti-myeloma agents we currently have in our arsenal, as well as the one or two new agents likely to become available in the relatively near future, more and more of our myeloma patients will be able to survive for longer periods without relapse.

Even while the debate about whether or not myeloma is a curable disease continues among members of the scientific community, our patients are benefiting from tangible gains that myeloma research has yielded and continues to yield. I suppose the best way I can summarize my personal hope for the future is that myeloma patients will be able to look forward to the same life expectancy as those who do not have the disease. Short of a cure, I do believe that this is our ultimate goal. MT
**KOREAN MULTIPLE MYELOMA WORKING PARTY COMES ABOARD IMWG**

By Jae Hoon Lee, MD

In Korea, we have been witnessing an unprecedented rise in the incidence of myeloma: a 30-fold increase over the past 25 years (Lee and Bang, *Korean J Hematol* 41:225, 2006). Rapid industrialization, which is associated with increased exposure to radiation and air pollution, as well as environmental pollution with chemical carcinogens such as dioxin and an aging society, are suspected key factors for this increase. The median life span in Korea has increased more than 16 years during the past 32 years and has reached 79 (M 77, F 81).

We are continuing to see increases in lifespan of 0.5 year annually. The median age of myeloma patients has also increased from the mid-50s in the 1980s to 66 in 2005. Korea is a prime example of a society in which disease patterns, especially cancer, are changing rapidly to correlate with Western patterns. However, the incidence of overall lymphoid malignancies, including multiple myeloma, is still lower than that in Caucasian populations.

Korea has 50 million people, and the incidence rate of myeloma is 1.5~2.0/100,000. We have 1,000 new myeloma patients diagnosed annually, and almost 5,000 patients are estimated to have this disease in Korea at present. Cytogenetic characteristics are not different from Western studies (Bang et al. *Cancer Gen Cytoget* 168:124, 2006). We have performed some genetic polymorphism studies in which we could define NQO1 (Kang et al, *Korean J Lab Med* 26:71, 2006) and CYPA1*2A (Kang et al, *Acta Hematologica* 119:60, 2008) polymorphisms as possible explanations of the relatively lower incidence of myeloma in this Asian population. Unfortunately, we do not yet have any statistics on MGUS incidence in Korea, although we are now working on this. My impression is that it is lower compared to published Caucasian data.

We have constructed the Korean Myeloma Registry, a very sophisticated web-based patient registration system, and 4,000 patients diagnosed after the year 2000 have already been registered. By using this registry, we can conduct very efficient retrospective studies. According to the registry, the median age of myeloma patients in Korea is 63 years, a bit lower than in the US and Japan, and the median survival is 70 months, implying the improved survival in the era of targeted agents. Smoldering myeloma is 8.7 % of all registered patients. Using this registry, we have been conducting large-scale retrospective studies efficiently; some of them have already been published. As of this year, we are participating in global projects of the IMWF. We have conducted more than 20 studies which showed both similarities and differences between “Eastern myeloma” and “Western myeloma,” especially in terms of drug toxicity.

Years ago, Drs. Robert Kyle and Brian Durie encouraged us to form the Korean Multiple Myeloma Working Party. Our group is now only 3 years old but it consists of 100 young and talented hematologists who are performing dozens of clinical and laboratory studies, including international new drug trials.

The Korean Multiple Myeloma Working Party is pleased to now be able to join groups from other countries and participate in ongoing and future projects of the International Myeloma Working Group (IMWG). We really appreciate the IMWG for inviting our Korean group aboard.

**IMF Myeloma Manager “webinar” program a huge success**

IMF’s Mike Katz recently conducted a series of well-attended and well-received “webinars” (web seminars) about the Myeloma Manager Personal Care Assistant, the IMF’s exciting new software to help manage patient laboratory results and other aspects of myeloma care. The webinars covered the features of this exciting new tool, and participants had the opportunity to ask questions and provide feedback about the tool, as well as suggestions for new features. The webinar was attended by participants using a web browser; no special equipment was required. The Myeloma Manager Personal Care Assistant software is being distributed free of charge. For more information, please email ThetIMF@myeloma.org or call 800-452-CURE (2873).
On Saturday, November 15, 2008 more than 1,100 guests congregated at Los Angeles’ historic and elegant Wilshire Ebell Theatre & Club for the IMF’s 2nd Annual Comedy Celebration benefiting the Peter Boyle Memorial Fund. The event raised over $630,000 in support of the IMF’s cutting-edge research programs.

The evening began on the red carpet where reporters camped out to speak with the celebration’s star-studded performers. Entertainment Tonight and Extra cameras rolled as Ray Romano, the night’s host, spoke fondly of Peter Boyle, his co-star from Everybody Loves Raymond.

At the cocktail party before the show, guests mingled while bidding on the items in the silent auction, including a custom alligator-covered guitar autographed by Keith Richards of the Rolling Stones.

At the close of the auction, the guests filed into the theater for the main event, a comedy show hosted by Ray Romano and featuring appearances by Jeff Garlin, Patricia Heaton, Kevin James, Robert Klein, and Doris Roberts, with a special musical performance by Dan Aykroyd and Jim Belushi as The Blues Brothers with The Sacred Hearts.

Leslie Moonves, President & CEO of the CBS Corporation, introduced the evening by professing his own affection for Peter Boyle, then passing the microphone to Susie Novis, IMF President, and Dr. Brian Durie, Chairman of the Board. Susie and Dr. Durie also introduced a short video that updated the audience on the progress being made with Bank On A Cure® and other research programs, with the support of the Peter Boyle Memorial Fund.

Ted Danson, noted actor and conservationist, spoke eloquently about the connection between environmental pollutants, the effects on sea life, and myeloma as he introduced a video by Hardy Jones. “To celebrate the life of Peter Boyle to raise money and awareness tonight is a great joy to me,” Danson told the audience.

And then, the heart of the show: Ray Romano made the audience laugh throughout, sharing stories about his family, the price of fame, and the pitfalls of having a very distinctive voice. Jeff Garlin and Kevin James both
Event

BENEFITING THE PETER BOYLE MEMORIAL FUND

$630,000 for myeloma research

brought the house down with hilarious sets while Patricia Heaton and Doris Roberts shared their favorite memories of Peter. And after a series of funny political observations, Robert Klein declared, “I knew Peter for 38 years. He was a joyful guy. I spent a lot of time with him at the end of his life, and it would be nice to know what the hell got him, so it doesn’t get others.” He concluded his time on stage by playing an impressive version of Ode To Joy on his harmonica.

But the harmonica playing didn’t end there. As The Blues Brothers, Dan Aykroyd and Jim Belushi tore up the stage with The Sacred Hearts, treating the audience to a set of rousing blues standards. By the time they were done, the sold-out theater was on its feet.

Loraine Alterman Boyle, Peter’s wife, with her daughters Lucy and Amy, closed the performances by graciously thanking the audience for joining them in celebrating Peter by supporting the IMF research.

A VIP champagne and dessert reception served as the evening’s perfect coda to a great celebration of a well-lived life.
February 26, 2009

The opening remarks to the workshop referred to President Obama having addressed the effort to cure cancer, and alluded to the role that the myeloma community will play in achieving that goal.

The scientific sessions started with myeloma experts discussing what dose of cyclophosphamide they would use given a particular patient case. New information on prognosis and cytogenetics opens the door for many opportunities. Current knowledge regarding risk stratification based on the prognostic value of chromosomal abnormalities is growing, with mention of the old players \((t(14;14), t(14;16)\) and \(17p\) deletion\) as well as some new kids on the block \((1p, 1q, +5 and 12p deletion)\). How this will all play out we don’t know, but it appears as though it may provide a means by which we can tailor therapy to suit a patient’s genetic profile for best response and least toxicity.

The next generation of novel agents is currently being explored in both the lab and the clinic. Of note, there are over 20 monoclonal antibodies \((e.g., CD56, CD138, CD40)\) under investigation with the basic science laying the groundwork to establish appropriate targets. Another class of agents under exploration targets kinases specific to myeloma cells.

Looking at the current understanding of pathogenesis, from plasma cells to MGUS to myeloma to aggressive myeloma, provides an opportunity to try and block a pathway in an effort to stall the disease in a particular phase. This may be one way to establish control once a diagnosis has been made, or even a way to employ primary or secondary prevention.

The day ended with an intense panel discussion on “control vs. cure.” One issue addressed was the importance of depth of response. There is a subset of patients in whom a complete remission \((CR)\) is not a realistic goal, but the best response they achieve is enough to sustain a durable remission. Distinguishing this subset of patients may enable us to provide quantity of life with corresponding quality of life. Other questions that must still be resolved are: When designing clinical trials, what is the most important endpoint \((CR, overall survival, quality of life)\)? What variables should be considered when determining the best overall outcome \((age, patient preference, risk stratification)\)? Should the answer be specific to each individual?

February 27, 2009

The day began with experts discussing the current approaches to supportive care in myeloma. The possible causative factors, evaluation, and interventions for peripheral neuropathy were highlighted. The remainder of the morning focused on the results of Phase III clinical trials in France, Canada, Italy, and Spain. Phase III clinical trials are studies that have been conducted to compare a standard-of-care therapy with an experimental treatment. Intergroup studies involve many different hospitals and institutions that accrue patients to the trials.

There was a common theme presented among several of the intergroup trials as they most commonly included the use of five key drugs: lenalidomide, bortezomib, thalidomide, cyclophosphamide, and melphalan. These drugs were used alone and in combination in various stages of myeloma treatment in attempting to identify the best myeloma treatment regimens for newly diagnosed patients and for those who have been previously treated, before or after autologous bone marrow transplantation.

An overriding theme to current trial design in the newly diagnosed setting appears to include “maintenance.” It would seem as though any amount of residual disease being addressed with a therapeutic agent might be considered “treatment” of the remaining detectable myeloma protein rather than maintenance, when additional therapy is given after much of the paraprotein has disappeared. Many of the study designs also appear to follow a general framework of induction, transplant, and consolidation, followed by maintenance with novel agents scattered throughout the schema. Numerous intergroup studies are also focusing on the asymptomatic (smoldering) phase of myeloma in an effort to halt or delay the transformation to symptomatic disease as evidenced by end organ dysfunction. One such study will address the...
The data presented evidenced the large number of studies being conducted. What was concluded after review of all these studies by the last decade? Hundreds of clinical trials have demonstrated that patients may achieve a remission for months to many years. In most cases, side effects are manageable, and research is ongoing to determine the best drugs to manage myeloma.

The afternoon sessions included new clinical agents and current trends in myeloma. Various combination therapies were discussed. Promising preliminary results of trials with new drugs, such as elotuzumab (HuLuc 63) in combination with bortezomib, panobinostat (LBH589) with bortezomib, and carfilzomib (PR-171) were reported. There are many different combination therapies currently available, as well as new agents in the pipeline. While we do not yet have the “gold standard” regimen for everyone, we have successfully transitioned into an era of newer therapies that give hope both to patients and practitioners.

February 28, 2009

Over 1,000 participants gathered to hear the consensus statements from the International Myeloma Working Group (IMWG). The morning sessions focused on clarifying many different criteria by which patients should be evaluated at diagnosis and relapse; when to resume treatment; and certain prognostic factors. Clarification of these details is critically important to the future of patients as it will provide uniformity in clinical trials reporting and ensure that all patients receive the same standardized evaluation of their disease at diagnosis and throughout treatment. The consensus statements were driven by the science behind the results of clinical trials and agreed upon by an international panel of experts.

Many aspects of the published consensus guidelines were clarified, with two key changes: (1) Patients who do not secrete a monoclonal protein in the blood or urine should be allowed to participate in clinical trials on the basis of serum free light chain analysis; and (2) Patients who are being evaluated for disease relapse should fit the CRAB (elevated Calcium, Renal failure, Anemia, Bone lesions) criteria for organ damage that also accompany a rapid rise in M-protein of 50% in two measurements within two months.

Discussions of transplantation included the issues of changing the preparative regimen to improve overall survival with decreased symptoms and the approval of a new drug (plerixafor) that may increase the yield of stem cells collected and make stem cell transplantation a viable option for more patients. Questions exist that still need clarification: Is achieving CR necessary? If a CR has been achieved, does the duration matter? Is there a difference in the response achieved from novel agents versus chemotherapy and transplant, and which is better? Does transplant need to be done in first remission? Should multiple agents be administered upfront or should combinations be reserved for relapse?

The day concluded with more discussion regarding newer therapies and clinical trial results for newly diagnosed and relapsed myeloma.

March 1, 2009

The morning started with heated debates. Controversial topics included sequential vs. “kitchen sink” (multi-drug combination chemotherapy) approaches to treatment, and support for/against a risk stratification approach. Does one want to be “conservative” or “innovative” when caring for patients? Should goals of therapy consider stratification by age, striving for a cure in individuals less than 65 years, disease control for the 65-80 age group, and quality of life in patients older than 80 years? Of note, some studies seem to suggest that bortezomib may change the biology of myeloma, which is especially important in high-risk patients.

One debate focused on allogeneic transplantation. One doctor argued that, especially in younger patients, cure can be achieved. Another doctor argued that the degree of mortality and decreased quality of life is not worth the risk. High-risk patients with poor cytogenetics may not benefit from allografting, and younger patients may develop graft vs. host complications that may impair quality of life, long-term. Both doctors agreed that we need to minimize toxicities, improve efficacy, and introduce newer agents into the regimen through further clinical trials.

Following the debates were several presentations. Many new drugs have been approved for myeloma in the last 10 years, and there are several drugs under investigation that seem quite promising. The combination of vorinostat and bortezomib has been shown to be effective in relapsed myeloma. The combination of panobinostat and bortezomib has shown activity in very advanced myeloma. Perifosine in combination with lenalidomide and dexamethasone in patients with relapsed myeloma has shown good tolerability in early-phase trials. Novel combinations can lead to encouraging results, high response rates, and manageable toxicities.

The next session raised a new series of questions: Given the efficacy of novel agents, should we use two-, three-, or four-drug combinations? What is the best drug combination? Will more drugs upfront improve overall survival or treatment-free intervals? Is the added toxicity worth the risk earlier on in the disease course? Should transplant be performed early in the disease or later on in therapy?

While these and other questions remain unanswered, there are several conclusions that can be made from this conference. There are many effective therapies to treat myeloma both in newly diagnosed and in previously treated patients. A large number of pre-clinical drugs are in development. Existing classes of drugs, such as immunomodulatory agents (lenalidomide and thalidomide) and proteasome inhibitors (bortezomib), are being expanded by the addition of new agents. And additional non-chemotherapy drugs (elotuzumab, panobinostat, vorinostat, and carfilzomib) offer hope for future synergy and improved outcomes.

Continued collaboration among members of the myeloma community is sure to improve patient outcomes and be the most effective way to either “cure” or “control” myeloma. The meeting adjourned with high hopes for achieving the goals set out for the future.
Education & Awareness

SPOTLIGHT ON ADVOCACY

Health Care Reform a Top Issue in 2009

By Christine Murphy, MA

With a new Administration and Congress, the health care reform debate is rapidly moving through the legislative process. The health care reform debate will largely focus on four specific areas: coverage, delivery system reform, prevention and wellness, as well as financing. Shortly before the New Year, key players in the healthcare reform debate put together principles on what healthcare reform entails. Senate Finance Committee Chairman Max Baucus (D-MT) released a white paper with objectives to achieve universal coverage, reduce health care costs, and improve the quality of care our system provides. Baucus’ plan achieves these objectives through individual responsibility to hold health insurance – once high quality, affordable care is accessible to all. His plan seeks to reach that point through measures to shore up the employer-based system, through a one-stop insurance marketplace for individuals and businesses, and through limited expansions of public programs. The plan also includes a number of insurance reforms to make the market work better for American healthcare consumers, and delivery system reforms that emphasize better quality, primary care for more patients, and a stronger focus on preventive care. Baucus also suggests potential savings and efficiencies that can be found in a remade healthcare system to reduce the cost of reform.

Senator Ted Kennedy (D-MA), Chairman of the Health, Education, Labor, and Pensions (HELP) Committee, announced a group of committee lieutenants to help him craft a healthcare overhaul bill in the 111th Congress. Senator Kennedy, a long-time leader on healthcare issues, will be one of the key players in the healthcare reform debate. Senator Tom Harkin (D-IA) will chair the prevention and public health group and Senator Barbara Mikulski (D-MD) will head the group on improving quality of care. The relevant Committees in both the House of Representatives and the Senate with jurisdiction over the health care reform debate have held a series of hearings since the beginning of the year on various issues to be considered in this important debate including access to care, ensuring affordable health coverage, and health workforce shortages.

Congress will be moving very quickly on health care reform with the first bills expected to be introduced and moving through the legislative process during the Spring and Summer months. The International Myeloma Foundation will be following the healthcare reform debate closely in 2009. For more information on IMF’s advocacy activities, please visit www.myeloma.org.

Support Groups

PEOPLE HELPING PEOPLE

You are never alone in your battle against myeloma.

West Bend, Wisconsin – Sue and Rob Enright have been involved with the IMF since shortly after Rob’s diagnosis. In 2007, they assisted with the Myeloma Mobile visit to Wisconsin by organizing a picnic for the four myeloma support groups who attend while the Tuohy Family made a stop during their cross-country education and awareness tour. Sue has also been an active participant in the IMF Cell Phone Recycling Program.

Sue and Rob have been members of the Racine and the Madison myeloma support groups in Wisconsin, and they helped with the Racine group. In 2008, Sue and Rob took part in the IMF Support Group Leaders Retreat because they wanted to continue to reach out to patients and decided to start up a new myeloma support group after relocating. Once Sue and Rob settled into their new home in the West Bend Area of Wisconsin, they contacted IMF’s Robin Tuohy and asked for assistance with starting a myeloma group in their new area.

IMF’s David Gerard obtained some grant money to get the group off the ground and Mike Katz helped Sue create a template for the group’s website. When it came to finding a location for the new group’s meetings, Sue was a dynamo in seeking out a space on the premises of St. Joseph’s Hospital. The hospital was so impressed with the knowledge and skills Sue acquired at the IMF Support Group Leaders Retreat that they decided she was qualified to facilitate the new group on her own. When the hospital sponsored a community health fair, Sue and Rob secured permission to distribute the IMF Patient Handbooks along with information about their support group.

The local West Bend newspaper wrote an article about Rob and Sue and their efforts, which helped further spread the word about the new support group.

Sue and Rod invite you to join them at their meetings. The West Bend Area Multiple Myeloma Group meets on the second Thursday of each month from 7 to 8:30PM in the lower level Conference Room “A” of St. Joseph’s Hospital in West Bend. For more information, please contact the Enrights via myelomawisconsin@yahoo.com or at 262-674-1474.

www.myeloma.org
San Diego IMF Patient & Family Seminar

I really have to congratulate all of you at the IMF for organizing and pulling off yet another wonderful event. All of your hard work paid off, but now I hope you get some time to rest up a little! When you have time, I’d really like to get a copy of the photos you took of us silver-donor folks getting our plaque and pin from Susie and then the one you took of the four of us City of Hope patients (Val, Carol, Tom and Gwen). We all underwent the same treatment there as part of a clinical trial. It’s called TMI for Total Marrow Irradiation — Carol Ramnarine was the first person in the world to have this done in 2005; I was #10 in 2006, Tom was #11 in 2006, and Gwen was #28 just 3 weeks ago. I attached a photo of me in front of the machine right before my first treatment. Thanks again for everything you do for all of us myeloma patients. All of you folks there are so fantastic and I truly appreciate all of your hard work.

Valerie Stevenson

letters to the IMF

ASH REPORT — continued from page 6

Drugs that includes thalidomide and lenalidomide. The study presented at ASH of 60 patients with relapsed myeloma treated with pomalidomide plus low-dose dexamethasone showed very encouraging responses in patients who had failed both thalidomide and lenalidomide. This appears to be promising as a back-up therapy.

2. Carfilzomib (proteasome inhibitor PR-171) seems promising with anti-myeloma activity similar to bortezomib, but with lesser neuropathy. Further studies are planned and ongoing.

All of the new agents in myeloma have been tested as single agents. Now there are planned or ongoing clinical trials of new agents in combination with bortezomib, investigating the new agents’ ability to enhance the activity of bortezomib. This includes a randomized phase III study of perifosine (KRX-0401, alkylphospholipid oral AKT inhibitor) + bortezomib+dexamethasone vs. bortezomib+dexamethasone in relapsed/refractory myeloma. Two ASH presentations of the bortezomib plus vorinostat combination showed very promising results, even in patients who were refractory to bortezomib alone. This has led to two new large international randomized trials of bortezomib plus vorinostat. Because vorinostat is already approved by the FDA for the treatment of cutaneous T-cell lymphoma (CTCL), there is hope that the myeloma trials will expand this drug’s application.”

Finding Your Way Through the Treatment Maze — Selecting the Best Treatment in the Era of Novel Agents

New therapies in development to target different points in pathways thought to be important in the development of myeloma include monoclonal antibodies targeting receptors on the surface of myeloma cells and agents affecting intracellular signaling pathways such as:

- new proteasome inhibitors
- histone deacetylase inhibitors (HDAC)
- heat shock protein (HSP) 90 inhibitors
- new immunomodulatory drugs

Maintenance therapy was discussed in the question and answer period. Dr. Moreau felt that maintenance with thalidomide was beneficial mainly for patients who had a response of less than VGPR. Dr. San Miguel noted that thalidomide was not approved for this purpose. Dr. Palumbo said that maintenance is not currently a routine recommendation, but adding a third drug for consolidation after a sub-optimal response was appropriate. Ongoing trials may clarify the role of maintenance therapy.

New Treatments in Early Stage Development

As the natural history of myeloma is better understood, new therapies are being developed to target specific pathways involved in the development of myeloma. Targets include the interaction of myeloma cells with the bone marrow microenvironment, proteins and receptors on myeloma and bone marrow cells, and molecules within cells involved in the development of myeloma.

Progress is being made in developing therapies targeted to specific growth factors and other molecules essential for the development and progression of myeloma. Because many of these therapies have limited activity as single agents, they will likely be used in combinations, particularly with the novel therapies bortezomib, lenalidomide, and thalidomide. Combining agents with different mechanisms of action may increase their activity while reducing the likelihood of side effects.

Future Directions

New therapies that are targeted to specific pathways in myeloma development continue to enter clinical trials. The novel therapies bortezomib and thalidomide have moved from the relapsed, refractory setting to the frontline setting, and lenalidomide may be expected to do the same. The trend of combining these therapies with conventional chemotherapy, each other, and/or and targeted therapies is continuing, expanding the treatment options for patients with multiple myeloma. Multiple myeloma is becoming more like a chronic, long-term disease as new treatment options continue to become available. 

Editor’s Note: Lynne Lederman, PhD, is a medical writer based in Mamaroneck, NY. To read the full text of her report, please visit the IMF website at www.myeloma.org.
IMFERS RAISE FUNDS TO BENEFIT MYELOMA COMMUNITY

By Suzanne Battaglia

Mistletoe for Myeloma

For the past two years, Thomas (now 11) and Julia (now 7) have been raising funds for the IMF. They decided to do this after their grandfather, Rick Daniels, was diagnosed with myeloma. Rick has always been very involved in their lives, picking them up from school, taking Tom to his basketball games and Julia to gymnastics, and spending hours playing with them.

This past holiday season, the kids sold mistletoe in front of their local grocery store in order to raise money for the IMF. “The whole family participated in cutting down the mistletoe, bringing it home, and tying bundles of it with ribbons,” says Staci Pastis, the children’s mother. “It was a wonderful way for our family to spend a winter evening together, and we all enjoyed it immensely. When it came time to sell the mistletoe, it wasn’t easy for the kids to approach strangers, but they made it clear that all of the money they make goes to cancer research. It made them feel like they were doing something to help their grandfather, and the entire process has taught them that they can make a difference in the lives of others with myeloma.”

You Are Invited to “Afternoon Tea”

In both 2007 and 2008, Carol Klein and Nancy Moses, two volunteers in Washington, DC, organized very successful events. Carol and Nancy’s husbands both have multiple myeloma, and Carol’s husband, Benson, is a member of the IMF Board of Directors. Carol and Nancy developed an event they called “Afternoon Tea.” Held at the Four Seasons Hotel in Washington, DC, the 2007 and 2008 events garnered a total of $150,000 with very low overhead.

This method of community fundraising has proven to be a very simple but effective way to raise money for research, raise public awareness of myeloma, and to do both while having fun. The IMF would like to invite you to host a similar event in your area. We will work with you every step of the way, and will even provide support.

The IMF is the lifeline of research, education, advocacy, and support for over 180,000 patients, caregivers, medical professionals, and researchers battling multiple myeloma. The spirit of our organization is “people helping people.” The IMF’s goal is to fund the best research and to provide the most up-to-date information to patients and caregivers, thereby improving patient quality of life, until we find a cure. If you have any questions, please do not hesitate to contact me. Thank you in advance for considering hosting this worthwhile event in your community.

Veterans Against Myeloma

Veterans Against Myeloma (VAM) is a growing team of veterans battling multiple myeloma. Servicemen and women dedicate their lives to preparing for and fighting the enemy as an effective team. Veterans diagnosed with myeloma face a challenging new threat, and their new goal is to win the battle against myeloma by helping to find a cure. VAM team spirit is strong as the veterans are joining forces to support increased funding for myeloma education and research. If you are a veteran with myeloma and want to participate, please contact me (see my contact info below). Hopefully one day together we can say, “Mission Accomplished!”

Your Old Cell Phone = Dollars for a Cure

Time Magazine reported that Americans change their cell phones every 18 months. It is estimated that there are 200 million used cell phones lying idle in America’s drawers and closets. So why not put them to good use? The IMF has partnered with Donate A Phone, a project of ReCellular Inc., and receives a donation for every cell phone you turn in. ReCellular accepts all handheld portable wireless phones capable of operating on either cellular or PCS networks, whether they are working or not. Newer phones are refurbished and marketed throughout the world as economical alternatives to brand-new phones. Damaged phones can supply parts to repair other phones that can then be returned to services as refurbished used phones. Badly damaged phones and obsolete models have no monetary value to us or to you, but ReCellular will absorb the expense of recycling these phones in an environmentally friendly manner. Models under two years of age are most in demand and can yield more than $20, while older phones typically generate $1–$10. Donate A Phone provides all donors with a tax receipt, but it is up to donors and their tax accountants to determine the value of the phones for tax purposes. If you’d like to donate one or more phones, please contact Kemo Lee at klee@myeloma.org or 800-452-CURE (2873) and request our self-mailers.

Join Us

We are grateful to all IMFers who contribute their time, imagination, and hard work to benefit the myeloma community. Our FUNdraising program provides you with the tools, assistance, and expertise to make your event a success. Choose an established event model or create your own — no idea is too large or too small. Join us in working together toward our common goal... a CURE. Please contact me, Suzanne Battaglia, at sbattaglia@myeloma.org or 800-452-CURE (2873).

UPCOMING MEMBER EVENTS

April 19, 2009 “A Song For Ireland” Musical Celebration – Philadelphia, PA – Contact Doug Farrell at 215-870-5189

April 20, 2009 “Marathon for Mom” as part of the Boston Marathon – Boston, MA – Donate online at www.marathonformom.myeloma.org

April 25, 2009 “Miles For Myeloma 5K” – Philadelphia, PA
Contact Karen Horan at karen.horan@verizon.net

April 25, 2009 4th Annual Music Against Myeloma – New York City, NY
Donate online or buy tickets at www.myeloma.org

May 16, 2009 10th Annual “JC” Golf Tournament – St. Cloud, MN
Contact Bob Zins at 320-291-2130

May 16, 2009 “Carrol’s Cause” Party – Scranton, PA
Contact Diane Lewis at 570-342-8291

May 31, 2009 3rd Annual “Afternoon Tea” – Washington, DC
Contact Carol Klein at carol@klein@verizon.net

June 6, 2009 2nd Annual Carolyn Czerkies Charity Golf Outing – Yorkville, IL – Contact Craig Czerkies at 630-724-9577

June 6, 2009 The Julie Smudz 5K Memorial Run – Delaware, OH
Donate online at www.myeloma.org

June 20, 2009 Schirinzi Golf Tournament Prato, ITALY
Contact Vittorio Schirinzi at vschirinzi@tin.it

July 12, 2009 8th Annual Multiple Musicians Against Multiple Myeloma – Long Island, NY – Contact Naomi Margolin at nmargolin@aol.com
International Affiliates

UPDATES FROM AROUND THE GLOBE

CELGENE Will Cover Long-Term Costs of the Revlimid® in the UK

The IMF praises an innovative proposal for reimbursement to give myeloma patients access to Revlimid® (lenalidomide) in the UK, an example of how a government agency can strike a balance between cost and value for cancer treatments that extend survival and lessen the overall burden on the healthcare system.

Revlimid is an oral drug that has been shown to lengthen life, often by years, and improve quality of life for patients with multiple myeloma, without the debilitating side effects that have typically been associated with chemotherapy. Under the preliminary plan announced by NICE, the National Institute for Health and Clinical Excellence, Revlimid (plus the steroid dexamethasone) would be approved in the UK for patients who have been treated with at least two previous drug regimens. However, the manufacturer CELGENE will cover the cost of the drug for remissions lasting more than about two years (26 cycles of treatment, 28 days each) after the start of Revlimid treatment. This approach covers long-term costs and eliminates budget uncertainties for the government.

“We support this plan because it builds on a positive approach to treatment, supporting the long-term value of Revlimid and its potential for success, not the risk of possible failures,” said Susie Novis, president and co-founder of the IMF. “This plan will allow the government to budget for reimbursement, while it continues to encourage innovation and research to discover and develop new drugs.”

The Revlimid approach builds on changes announced in the UK for the NHS (National Health Service) to pay more for drugs considered cost-effective based on increased survival and quality of life. Multiple clinical studies have demonstrated that Revlimid extends survival and, in 2008, a study reported at the British Society for Haematology Annual Meeting documented that Revlimid not only has the ability to add years to myeloma patients’ lives, but years that represent a good quality of life.

Other companies have proposed a variety of risk-sharing plans. Some bring their drugs in line with comparable treatments. In the case of Velcade® (bortezomib), another novel anti-myeloma treatment, the European distributor charges for the drug only when there is a positive outcome.

Dr. Brian G.M. Durie, chairman and co-founder of the IMF added: “We are pleased to see biopharmaceutical companies and government agencies working closely together to provide patients with access to important new drugs based on their value, not just their cost.”

Editor’s Note: The IMF continues to strive to find better ways to serve our community—wherever in the world it may be. If you have ideas to contribute to our continued growth and development, please feel free to contact us at TheIMF@myeloma.org or 800-452-CURE (2873).
Freelite™ Serum Free Light Chain Assays Aid in the Diagnosis and Monitoring of Multiple Myeloma

• “Elimination of the need for urine studies in the screening algorithms for monoclonal gammapathies by using serum immunofixation and free light chain assays.”¹

No more 24 hour urine collections.

• “Changes in serum free immunoglobulin light chains (FLC) are a more rapid indicator of treatment response than intact immunoglobulins due to their shorter half-life.”²

An additional aid in monitoring treatment.


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Persist despite the odds.
Give the gift of encouragement.
Lay the groundwork for a better tomorrow.
### 2009 IMF Calendar of Events

<table>
<thead>
<tr>
<th>Month</th>
<th>Event Description</th>
<th>Location</th>
<th>Date</th>
<th>Event Description</th>
<th>Location</th>
<th>Date</th>
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<tbody>
<tr>
<td>April</td>
<td>Oncology Nursing Society (ONS) – San Antonio, TX</td>
<td>San Antonio, TX</td>
<td>April 30-May 3</td>
<td>Myeloma Canada Patient &amp; Family Seminar – Calgary, CANADA</td>
<td>Calgary, CANADA</td>
<td>Sept 11-12</td>
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<tr>
<td>May</td>
<td>IMF Regional Community Workshop – St. Louis, MO</td>
<td>St. Louis, MO</td>
<td>May 9</td>
<td>IMF Physician Community Workshop – Valencia, SPAIN</td>
<td>Valencia, SPAIN</td>
<td>Oct 12</td>
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<td>May</td>
<td>Robert A. Kyle Lifetime Achievement Award – MONACO</td>
<td>MONACO</td>
<td>May 15</td>
<td>IMF Regional Community Workshop – Murcia, SPAIN</td>
<td>Murcia, SPAIN</td>
<td>Oct 13</td>
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<tr>
<td>May 29</td>
<td>American Society of Clinical Oncology (ASCO) – Orlando, FL</td>
<td>Orlando, FL</td>
<td>May 29</td>
<td>IMF Regional Community Workshop – Pamplona, SPAIN</td>
<td>Pamplona, SPAIN</td>
<td>Oct 15</td>
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<td>June 13</td>
<td>IMF Regional Community Workshop – Munster, GERMANY</td>
<td>Munster, GERMANY</td>
<td>June 13</td>
<td>IMF Physician Community Workshop – Stuttgart, GERMANY</td>
<td>Stuttgart, GERMANY</td>
<td>Oct 26</td>
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<tr>
<td>June 16</td>
<td>IMF Physician Community Workshop – Berlin, GERMANY</td>
<td>Berlin, GERMANY</td>
<td>June 16</td>
<td>3rd Annual Comedy Celebration – Los Angeles, CA</td>
<td>Los Angeles, CA</td>
<td>Nov 7</td>
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<tr>
<td>June 20</td>
<td>IMF Regional Community Workshop – Denver, CO</td>
<td>Denver, CO</td>
<td>June 20</td>
<td>IMF Regional Community Workshop – Florence, ITALY</td>
<td>Florence, ITALY</td>
<td>Nov 14</td>
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<tr>
<td>July</td>
<td>IMF Regional Community Workshop – Milwaukee, WI</td>
<td>Milwaukee, WI</td>
<td>July 25</td>
<td>IMF Regional Community Workshop – Bologna, ITALY</td>
<td>Bologna, ITALY</td>
<td>Nov 16</td>
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<tr>
<td>June 26</td>
<td>IMF Patient &amp; Family Seminar – Dallas, TX</td>
<td>Dallas, TX</td>
<td>June 26</td>
<td>IMF Physician Community Workshop – Pavia, ITALY</td>
<td>Pavia, ITALY</td>
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<tr>
<td>July 17</td>
<td>IMF Support Group Leaders’ Retreat – Dallas, TX</td>
<td>Dallas, TX</td>
<td>July 17-19</td>
<td>IMF Regional Community Workshop – Stuttgart, GERMANY</td>
<td>Stuttgart, GERMANY</td>
<td>Nov 19</td>
</tr>
</tbody>
</table>

Other events/meetings will be posted in later editions of Myeloma Today as dates are finalized. For more information, please visit www.myeloma.org or call 800-452-CURE (2873). IMF–Latin America, IMF–Japan and IMF–Israel events are not included above.

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### We speak your language

The IMF publishes a comprehensive library of informative myeloma resources. Used by patients, caregivers, healthcare professionals, and anyone needing a reliable source of up-to-date information regarding the disease, these publications are critical to a better understanding of myeloma.

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