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.

Scientific & Clinical News

Dr. Brian G.M. Durie, co-founder and chairman of the IMF, was honored for a lifetime of achievement in multiple myeloma with the prestigious 2009 Waldenström's Award. In this issue of Myeloma Today, Dr. Durie shares some highlights of the traditional Waldenström's Award Lecture, a talk he gave during the XIIth International Myeloma Workshop in Washington, DC. Learn about some of Dr. Durie's contributions to key developments in the field of myeloma over the past 40 years. ***PAGE 5***

The XII International Myeloma Workshop, the premier biennial scientific myeloma meeting that took place from February 26th through March 1st in Washington DC, brought together 1000 specialists working in the field. Topics presented included molecular and signaling pathways, immune and antibody targets, the bone marrow microenvironment, clinical trials, pathogenesis, risk stratification and prognostics, new therapeutic agents, and transplantation in myeloma. Read excerpts of some of the issues discussed during the Workshop. ***PAGE 7***

Dr. Sergio Giralt, Professor and Deputy Chair of Stem Cell Transplantation and Cellular Therapy at the University of Texas M.D. Anderson Cancer Center in Houston, shares an overview of autologous stem cell transplantation (ASCT) in myeloma and its current place in treatment of the disease. Myeloma is the most common indication for high-dose chemotherapy with ASCT in North America today. Read about ASCT, and stem cell mobilization and collection. ***PAGE 8***

Dr. Sundar Jagannath, the principal investigator of a phase II clinical trial of carfilzomib in patients with relapsed and refractory myeloma, discusses the final results of his study of this novel proteasome inhibitor of the epoxyketone class. He shares the responses that patients achieved with the new compound, as well as information about the next phase of investigation. Learn more about carfilzomib and the study that has been expanded to enroll an additional 250 myeloma patients. ***PAGE 9***

Dr. Shaji Kumar, Associate Professor of Medicine at the Mayo Clinic in Minnesota, discusses the 1999 Mayo Clinic study of relapsed myeloma patients, as well as the study follow-up and his current research on behalf of the International Myeloma Working Group (IMWG). The IMWG project aims to find out what happens to patients who have exhausted their treatment options and to attempt to accelerate the process of approval for novel anti-myeloma agents currently in the research pipeline. ***PAGE 11***

LOOKING FOR A LOCAL MYELOMA SUPPORT GROUP?

If you are interested in joining a support group, please visit our website at **www.myeloma.org** or call the IMF at **800-452-CURE** (2873).

Special Event

Prof. Jean-Luc Harousseau, Professor of Hematology and Director of the Cancer Center René Gauducheau at Nantes, France, as well as one of the pioneers of high-dose therapy in myeloma and a co-founder of the Intergroupe Francophone du Myélome (IFM), is honored by the IMF with the seventh annual Robert A. Kyle Lifetime Achievement Award. To read about this important award, its distinguished recipient, and the ceremony that took place on May 15 in Monte Carlo, Monaco, please see the centerfold story. ***PAGE 12-13***

Profiles in the News

Charles Newman joined the IMF Board of Directors eight years ago, determined to give back to the IMF by contributing to the Foundation's governance. He became a member of the myeloma community in 1996 when his wife was diagnosed with the disease. Only weeks after Sharon's diagnosis, Charles was in attendance at an IMF Patient & Family Seminar. He found the experience so valuable that he became a regular at IMF meetings, even those designed for doctors. ***PAGE 4***

David Brown was diagnosed with myeloma in 1978, when he was 40 years old. More than 30 years later, he shares the story of coping with his diagnosis, undergoing treatment, and facing disease relapse. After initially choosing not to pursue myeloma education, David and his wife Prudy have since become regular participants in IMF Patient & Family Seminars when they come to their area, both to further educate themselves and to meet other myeloma patients and caregivers. ***PAGE 21***

Also in this issue...

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A Message from the President

Dear Reader,

In 1998 we went to Washington, DC, to participate in "The March," the first big grassroots cancer event to take place on Capitol Hill. More than 100,000 advocates representing every cancer joined together on the Mall – with about 400 representing the IMF and the myeloma community. We spent a very hot afternoon, under a blazing sun, listening to speeches by Cokie Roberts, Queen Noor of Jordan, Sam Donaldson, and Al Gore, to name a few. It was a seminal moment for me personally and the cancer community at large. That was the spark that led to the five-year doubling of the budget of the National Institutes of Health (NIH). It was also the birth of the IMF's advocacy program.

Greg Brozeit led our team as IMF Advocacy Director. We soon joined a broad range of groups representing the interests of the cancer community in Washington. This included One Voice Against Cancer (OVAC), the Cancer Leadership Council, the National Coalition of Cancer Research, and C-Change (formerly the National Dialogue on Cancer). We worked hard to ensure that the myeloma community was represented in the health debates taking place in Washington.

In 2002, the IMF, along with 40 other cancer organizations, all of whom belonged to OVAC, came together as a unified force to convey one important message to Congress: "Give the war on cancer the funding it needs." I had been asked to represent OVAC and testify on behalf of the entire cancer community before a major Senate hearing. Testifying along with me were Dr. Huerta, Dr. Heberman, brain cancer patient Mike Bruene, and Steve Case, Chairman and CEO of AOL Time Warner.

It was a humbling experience knowing that I was representing not only the IMF, not only the cancer community, but everyone who suffers from any disease. My role on the panel was to request funding for the NIH, the National Cancer Institute's (NCI) Bypass Budget, and the Centers for Disease Control and Prevention (CDC) cancer programs.

Since then, the IMF has continued to represent the concerns of the myeloma community to policy makers. We have fought for such issues as Medicare coverage of drugs with off-label indications (like thalidomide), as well as Medicare coverage of PET scans. Both of these important initiatives came to a successful conclusion.

IMF advocacy now takes on a new significance. The Obama administration has made health care reform its highest priority. Regardless of our political leanings, our community must be represented in this debate. As always we are here for you, to listen to you, and to advocate our community's concerns to all our political and governmental leaders and representatives.

Most importantly we need you! This is about your future and the future of all the patients yet to be diagnosed.

Be informed and get involved! The IMF's Cancer Patient Statement of Principles *(see page 18)* will guide us through this process. On our website, you'll soon find a new section devoted to advocacy.

This is a rare time in American political history. We intend to ensure that our voice is heard and acted upon, that the myeloma community is represented when policies have an impact on us. We intend to do this work with you and for you.

Susie Novis

Letters to the IMF

IMF Publications

I wanted to thank you for your extremely clear and informative brochure publication, Understanding Serum Free Light Chain Assays, which I have re-read once a year for the last three years when it's time for my MGUS re-screening. I really appreciate its sophistication, accompanied as it is by clarity of explanation that makes this information accessible, I think, to lots of people. I will continue to pay close attention to IMF and its resources; thank you all so much.

Priscilla M. Jensen

IMF Patient & Family Seminars

I just returned from the IMF Patient & Family Seminar in San Diego. My thought is… "Why did I wait all these years to go?" It was a great seminar, and everyone was helpful and friendly. It was so informative. Thanks to all who encouraged me to attend this meeting.

Martha Z. Hess

IMF Hotline

I called you in April 2008. It was my first call to the Hotline and it turned out to be the best call I ever made. Any information I can absorb on my own before my oncologist appointment is a tremendous help when the doctor begins to go over my treatment. In so many ways this is what the IMF has given me. Thank you for helping us understand and accept what we have and yet live each day with hope!

Yvonne Zuchowski

It is a bright sunny morning here in Illinois that has warmed up and melted most of our snow cover. The weather is definitely looking better and I am doing okay. It has been six and a half years since my myeloma diagnosis and four and a half years since my transplant, and very little change in my blood labs. I am writing because last night I met a lady at church who has had myeloma for about four months and she was not aware of your organization. I immediately told her about the IMF and your packets of educational information about the disease. I received one when I first got sick and it was a big help, as was the wise counsel and advice of the IMF Hotline coordinators, which it is always given in a caring, loving, positive, and cheerful manner. You are great and the service you provide is priceless.

Bob Reeves

It has taken me far too long to express my gratitude for the information and assistance you have provided me. I am especially thankful for your referral to Diplomat Pharmacy and their relationship with the Chronic Disease Fund. As a result, I have received significant financial help (through the Medicare Part D donut hole, etc.) with the purchase of my Revlimid®.

Barry Kimmel

MYELOMA TODAY IN CONVERSATION WITH CHARLES NEWMAN

What events led to your involvement with the IMF?

My wife Sharon was diagnosed with multiple myeloma in 1996. She had complained about some symptoms that turned out to be unrelated to myeloma, but our physician was very thorough in the tests that he ordered, which led to further laboratory testing and, eventually, to the myeloma diagnosis. Like many others, we first thought the diagnosis to be melanoma, not myeloma. But within four or five weeks of the diagnosis, with much research behind me, I found myself at an IMF Patient & Family Seminar in Houston, TX. The experience was enormously valuable to my myeloma education, so I proceeded to attend the next five or six meetings in a row. In total, I have now attended about ten IMF Patient & Family Seminars around the country.

Some people might assume that once they've attended one IMF seminar to gain knowledge about myeloma, there is no point to attending subsequent meetings.

At every IMF Patient & Family Seminar I've attended, I either learned something new or I deepened my knowledge and understanding of issues I was already familiar with. And not only have I received valuable information from the formal sessions conducted by the medical faculty, I have also gained tremendous insight from the patients and caregivers I've met at the meetings. The physicians who make presentations at the IMF seminars might differ in their practical and philosophical approaches to myeloma, but the information they share is very useful. And the "informal" information shared by the attendees – about their experiences, specific physicians, various myeloma therapies, etc. – have helped Sharon and me when we've had to make choices over the years. Many of the patients and caregivers I know are extraordinarily knowledgeable about myeloma. One such patient is Michael Katz, who has been a member of the IMF Board of Directors since the early days of the Foundation and is a co-founder of the Multiple Myeloma ListServ, an online forum that has also been a terrific source of information for me. In my opinion, there is always more to learn about myeloma, so I continue to pursue all avenues that expand my knowledge.

Has your wife pursued myeloma education with equal dedication?

What has worked best for our family is to have a division of labor. Sharon's responsibility is to fight myeloma. My responsibility is to learn as much as possible about the most effective approaches for her in this fight. I research the options and alternatives and make recommendations as I lay out the information I've learned, then Sharon makes the decision. After all, she is the one undergoing the therapy. That's how we've always done it. In retrospect, given how bleak the myeloma survival statistics were thirteen years ago, it was good that Sharon didn't have to cope with processing that information. She had enough to deal with. So I have been the one immersed in learning about myeloma. Sharon rarely accompanies me to the various meetings and seminars.

Have you attended educational meetings other than the IMF Patient & Family Seminars?

Yes. After being introduced to the IMF Patient & Family Seminars, I subsequently started attending meetings for physicians and clinicians. I have gone to many annual meetings of the American Society of Hematology, and have attended several of the biannual International Myeloma Workshops. Both forums afforded me an opportunity to meet and speak with many of the researchers and clinicians working in myeloma and to learn the latest thinking in the field. As a result, I would say that Sharon's treatment has always been "ahead of the curve." I'd like to stress that many of the educational avenues I have pursued exist as a direct result of IMF initiatives – this includes both patient/caregiver and clinical/scientific forums.

Do you find the information shared at clinical and scientific meetings accessible to you as a non-medical professional?

In general, I tend to be rather analytical. In my professional life, I have been an entrepreneur, but I have a bit of a science background – with degrees in both theoretical and applied mathematics – so I have been taught the disciplines of thinking logically and rigorously. I can look at data and interpret statistical results. Actually, with myeloma information, once a person gets comfortable with the new vocabulary, the material is not difficult for any lay person to comprehend. As patients and caregivers, we don't need to understand the underlying biology of the disease, but we do need to understand the pros and cons of various treatment options. Knowledge is invaluable, and patients and caregivers should not abdicate myeloma education to their doctors.

What has been your wife's experience with myeloma?

Sharon's grandfather died of myeloma. When I reviewed his medical records and compared them to the level of care Sharon receives, I felt like I was reading something from the Middle Ages. And the patients who are being diagnosed today are light-years ahead of where Sharon was thirteen years ago. But we were very fortunate. Sharon had a stem cell transplant before they were common, and the approach turned out to be remarkably effective in her case. She was also one of the first myeloma patients to receive thalidomide as maintenance therapy. For the past eight or nine years, there has been no sign of the disease, and she has been free of treatments for six years. At the time Sharon was diagnosed, I remember her telling me that she hoped to live long enough to see the youngest of our four children through high school. If it wasn't for the IMF, I am not sure that we would have been this fortunate with Sharon's myeloma. The IMF has been at the forefront of education for both the patient and the medical communities, and has made a significant difference in our lives.

How did you become a member of the IMF Board of Directors?

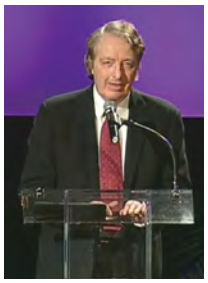
I was invited to join the IMF Board about eight years ago. The Foundation has been such a prized part of our family's life for so many years, that I was happy to have an opportunity to give back by contributing to the IMF's good governance. And I absolutely adore the people at the IMF. They are wonderful, giving, caring people. Every time I attend a Board meeting, it is like having the pleasure of seeing good friends. They are an extraordinary group, unlike any other group of people I've ever met.

Continues on Page 10

2009 WALDENSTRÖM'S AWARD

Dr. Brian G.M. Durie is Honored for a Lifetime of Achievement in Myeloma

Dr. Durie, congratulations on being the 2009 recipient of the prestigious Waldenström's Award for lifetime achievement. The award, named for Prof. Jan Waldenström, a pioneer in treating blood cancers, was bestowed at the opening of the XIIth International Myeloma Workshop in Washington, DC. As recipient, you presented the traditional Waldenström's Award Lecture, and we would like to ask you about what you discussed in your talk.



Brian G.M. Durie, MD
Aptium Oncology
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I was truly honored to receive the Waldenström Award, and very thankful to all those who made it possible. In my Waldenström Lecture, I touched upon some of the reasons that I might have been standing at that podium, and summarized the key developments in the field of myeloma from when I first started working on this disease through the present day. In addition, I assessed how I see things moving forward. I have been working on myeloma for 40 years and, in my lecture, I tried to convey some of the lessons I've learned along the way.

What have been some of those lessons?

When I studied at the University of Edinburgh, anatomy was a major part of the program. I am a clinician at heart, and understanding anatomy has served me well over the years when trying to identify what might be wrong with an individual patient.

When I worked at the Mayo Clinic in Minnesota, it was very clear that for all the research being performed at that institution, the patient always remained the number one priority. I have never lost sight of this in the years that have followed. That ethos is key to the Mayo Clinic, and it is reflected in Bob Kyle and his colleagues, as well as in all the doctors who have passed through the Mayo Clinic over the years and those who work there today.

At the University of Arizona, I was recruited by Sydney Salmon to work on the myeloma staging system. At that time, Syd was working on a method of measuring myeloma cells in the body. Myeloma was unique in that it was possible to calculate the number of cancer cells based upon the amount of monoclonal protein produced, and to correlate the total number of myeloma cells with the physical features that a patient manifested. In 1977, we established the first myeloma clinic there and, over the following years, I pursued a variety of projects at my myeloma laboratory.

After many years at the University of Arizona, I moved back to the UK to become head of the Haematology Department at the University of London. Three or four years later, I came back to the US and settled in Los Angeles. There, the International Myeloma Foundation, which was started while I was still in London, became a major commitment for me. The IMF mission of being dedicated to improving the quality of life of myeloma patients while working toward prevention and a cure has remained a focus for me for the last 20 years.

Much of your work in the field of myeloma over the decades is still important today. Your work on the Myeloma Staging System dates back more than 30 years!

The Myeloma Staging System took two years to develop and was published in *CANCER* in 1975. That was my first major published paper. I applied statistics to the analysis of myeloma outcomes. The lesson of that work was that applying new techniques to old problems can lead to progress. The correlations that we made all those years ago, applied to a relatively small data set, are still true today.

Another example of a concept that has remained relevant is that myeloma can enter a plateau phase. Would you please tell us about that?

In 1980, *THE LANCET* published my paper on the plateau phase in myeloma. Intrinsically, myeloma is not always actively growing. The plateau phase is an indolent phase during which no new myeloma growth is occurring. It is possible to stop treatment during the plateau phase, with the disease remaining stable for two or three years or sometimes longer. That's an important concept in terms of maintenance therapy and, yes, that crucial point has persisted to the present time. For patients in the plateau phase, the "standard of care" is **no maintenance** because maintenance therapy does not offer clear added advantage.

In the years that followed, you worked on understanding amyloid, Sβ2M, and osteoclast activating factors and bone disease.

In the 1970s, Gregory Mundy and I worked on osteoclast activating factors. That work was the first recognition of myeloma-derived factors triggering bone disease. At that time, we did not know exactly what those factors were, but we were able to demonstrate that when fluid from myeloma is added to bone it causes bone destruction, and that the extent of the bone disease is quantitative. Our paper was published in the *British Journal of Haematology* in1981 and was the starting point for subsequent studies looking at myeloma bone disease. Greg Mundy went on to identify several of the bone resorptive factors.

In 1982, the *New England Journal of Medicine* published my paper on amyloid production in human myeloma stem-cell culture. By observing myeloma stem-cell cultures in the lab, we were able to show, by electron microscopy, amyloid synthesis (production) as a result of myeloma cells' macrophages.

CONTINUES ON PAGE 6

2009 WALDENSTRÖM'S AWARD — continued from page 5

My work on serum beta2-microglobulin (Sβ2M) plus albumin, which was the result of collaboration with Régis Bataille, showed that Sβ2M reflects myeloma biology. Our paper was published in *Blood* in 1986 and, 20 years later, served as the basis for the International Staging System (ISS) of myeloma.

In 1988, I published a paper in the *British Journal of Haematology* on overcoming multi-drug resistance (MDR) in myeloma with verapamil. This was not the result of a protocol I was working on, but rather the outcome of my experience with a myeloma patient who had to be treated with verapamil for her high blood pressure while she was receiving VAD chemotherapy for her myeloma. I subsequently worked with cyclosporine, a drug that was even better at overcoming MDR than verapamil, and I published several papers on this together with Pieter Sonneveld.

In 1989, I started collaborating with Howard Urnovitz on the SV40 polyomavirus (found in the rhesus monkey kidney cells used to make the polio vaccine) and circulating RNA in microvesicles in myeloma. Our work led to a more detailed evaluation of RNA sequences present in the blood of people with myeloma. The project is moving forward with new technology that has made it possible to detect all of the sequences present in blood. Now, having looked at all the sequences using the new technique, we have been able to confirm that the sequence we had found in the late 1990s using what amounts to calculated guesswork is in fact the relevant sequence for myeloma. The on/off "switch" for myeloma varies from patient to patient, and this work is bringing us much closer to identifying the molecular signature of myeloma on an individual patient basis.

In the 1980s and 1990s, I studied all sorts of things with the soft agar culture – drug sensitivity, labeling index, etc. We had the first cytogenetics lab devoted exclusively to myeloma and related diseases, and we studied cytogenetics on each of our myeloma patients. Many papers were published as a result of our research, and many sank like a stone thrown into a dark well.

How is that possible?

It is not unusual for valid ideas to languish for decades. By definition, new concepts may not directly fit in with what others in the myeloma field are working on so, unless you continue to work on the concepts yourself, the ideas may not be picked up by others for many years.

In 1984, the *British Journal of Haematology* published my work on myeloma heterogeneity, which examined whether myeloma is or is not a monoclonal disease. In that paper, I pointed out that while myeloma cells tend to continue to produce the same monoclonal protein, the disease is heterogeneous and evolves over time. This point is confirmed by patients who become non-secretory and those who develop extra-medullary myeloma in the course of their disease. We see heterogeneity in disease that becomes resistant to treatment. When a patient becomes resistant to a previously effective treatment, we see that the presence of the monoclonal protein is deceptive, because it makes you think that the disease is the same, while in fact the genetics have changed. I was able to show this at a molecular level. In 1984, I demonstrated that myeloma is polyclonal from the genetic perspective, manifesting sequential clonal evolution. The cells don't even look the same over time. Today, when myeloma researchers are looking at chromosomal deletions and translocations, it is clear that we are dealing with sequential clonal changes and a disease that is actually heterogeneous. It is crucial that we acknowledge that there is a tendency for this to happen, because it is myeloma's strong heterogeneity that makes it a tricky disease and accounts for its bad prognostic features.

Along the same lines, we can look at my collaboration with Benjamin Van Camp in the 1980s, when he worked in my lab in Arizona. We looked at the myeloma phenotype and reported that myeloma is CD56 positive. This was substantiated by two separate labs, including one that was a repository for the Southwest Oncology Group (SWOG), one of the largest of the National Cancer Institute-supported cancer clinical trials cooperative groups in the US. When we submitted our paper for publication in *Blood*, it was initially rejected because it was considered "not possible" for myeloma to share an antigen present on nerve cells. So we supplied further data from the world's two top labs confirming our findings with methods employing immunogold markers, and the manuscript was finally published in 1990, with the image from the rejected manuscript used for the cover photo! It took us years to convince others that the publication was valid and that the assertion in our original paper was in fact correct.

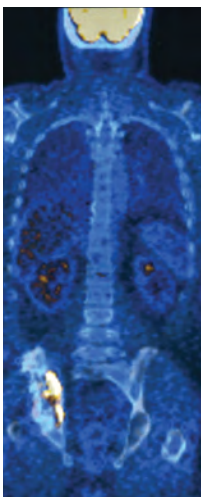
There are many other examples, as these experiences are not unique. New ideas are often rejected initially if they show an unexpected result. There have been several instances where I would be contacted by someone who had done the same research I did many years ago but who was unaware of my work until after they had completed their own research and did a literature search and found my published papers.

Has this dynamic persisted to the present day?

At present, the dynamic in the field of myeloma is dramatically different, as we have worked hard to establish very active collaboration. The International Myeloma Working Group (IMWG) is the result of those efforts. Now, a promising new idea in myeloma will be immediately investigated and validated by others. In fact, over the last five or six years, important projects have been initiated in collaboration with the IMWG, which have produced a whole series of manuscripts.

You have also worked on PET scanning for many years. In fact, you received the 1st prize award for Best Nuclear Medicine Paper of 2002.

I started work with FDG (fluoro-2-deoxy-D-glucose) PET (positron emission tomography) scanning in 1997 and published the paper you are referring to in the *Journal of Nuclear Medicine* in 2002. PET scans can improve disease staging and treatment planning, and can significantly change the course of treatment for many myeloma patients. With PET scans doctors can visualize the whole body to see the full extent of disease on initial diagnosis, follow the response to treatment more accurately, and better determine when further treatment is needed and when it is not.



Recently, PET scanning in myeloma was finally approved by Medicare for insurance coverage. It took a decade to get this accomplished. As you might imagine, Medicare waged a battle of attrition against the approval: they called for meetings

CONTINUES ON PAGE 10

XII INTERNATIONAL MYELOMA WORKSHOP

Excerpts from text by Lynne Lederman, PhD

Introduction

The XII International Myeloma Workshop (IMW) was held from February 26 to March 1, 2009 in Washington, DC. Approximately 1000 attendees exchanged ideas during the meeting sessions, symposia, poster sessions, and working breakfast and lunch sessions, and at two dinner events. This meeting was originally scheduled to be held in India, but was moved to the US subsequent to the tragic events in Mumbai. Meeting organizers Drs. Nikhil Munshi, Vincent Rajkumar, Sundar Jagannath, and Vinod Raina, along with colleagues Drs. Mammen Chandy and Atul Sharma, hope to have the opportunity to organize the workshop in India at a future date.

Overview

Topics presented included myeloma molecular and signaling pathways, myeloma immune and antibody targets, the bone marrow microenvironment, clinical trial results, pathogenesis, risk stratification and prognostics, new therapeutic agents, and transplantation in myeloma. Oral clinical presentations covered clinical trials, new agents, and clinical care; basic biology sessions covered novel and potential therapeutic targets. The Consensus Panel presentations discussed Guidelines for the Uniform Reporting of Clinical Trials in Myeloma, Guidelines for Risk Stratification in Myeloma, and Guidelines for Standard Investigative Work-up in Myeloma. There was a presentation on Statistical Issues in the Design and Analysis of Clinical Trials in Myeloma, along with several sponsored symposia and poster sessions. The final day of the conference included pro and con discussions, presentation of Phase II studies and plenary abstracts, and a future perspectives session. This write-up summarizes some of the key issues discussed during the IMW meeting. Please visit the IMF website www.myeloma.org to read the full report.

Molecular Pathways

The opening session included Dr. Rafael Fonseca's discussion of chromosomal fluorescent *in situ* hybridization (FISH) and its association with pathophysiologic events, prognostic value at baseline disease diagnosis, and its predictive value in therapeutic outcomes. He compared the value of emerging gene expression profiles versus FISH as prognostic factors. This session confirmed a number of genetic markers associated with poor prognosis; but it was noted that, as new therapies emerge, alterations in the prognostic value may shift. These approaches will reach their full potential once demonstrated as effective in clinical trials.

Phase III Studies

The US/DFCI approach – novel agents as part of new combinations – focus on relapsed myeloma

Dr. Ken Anderson presented on behalf of Dr. Paul Richardson. He commented that bortezomib, lenalidomide, thalidomide, and pegylated doxorubicin shouldn't be called "new" any more. He noted that since the introduction of these agents, median survival of patients with myeloma has been prolonged from 3 to 7 years. Using these agents in combination should increase efficacy, avoid resistance, and result in a more favorable side effect profile.

Early combination studies – new combinations for multiple myeloma

Dr. Antonio Palumbo observed that in the Phase III trial of bortezomib plus pegylated doxorubicin, the addition of the second agent increased efficacy. Three-drug combinations that have been tested show increased response rates. However, it is unclear which is the best three-drug combination. Four-drug combinations are also promising. Randomized studies are needed.

Anti-angiogenic agents

Dr. Shaji Kumar reviewed the role of angiogenesis. He cited two paradigms of drugs which are known to have anti-angiogenic properties. Dr. Kumar concluded that bone marrow endothelial cells in myeloma were a valid target, although it was likely that this strategy may not work alone, so a combination approach with myeloma cell-targeted therapy plus EC targeted might work best.

Transplant

Dr. Sergio Giralt presented "New mobilization and conditioning strategies (Autografting for myeloma in 2009)." He said that the use of novel agents for induction does affect outcome, and that researchers were starting to address issues about the quality and amount of cells that are being collected. Dr. Giralt suggested a refocus on improving the stem cell product, determining the minimum number of cells to collect, looking at the effect of infused cell numbers on reduction of the still-considerable symptom burden, and improving immune reconstitution, noting that lymphocyte recovery is associated with better outcome.

Dr. Donna Weber discussed "Timing of transplant in the era of new drugs." Before novel agents, transplants offered the advantage of better survival. Dr. Weber observed that it will take powerful studies to determine if transplantation is still needed with currently available therapies. She thinks that some form of maintenance consolidation after transplant seems warranted. Other questions to be answered include the length of induction and the best combinations of agents.

Dr. Michele Cavo discussed "Single or double autologous stem cell transplantation (ASCT) before and after the era of novel agents." He reviewed the history of ASCT for myeloma from the recognition that there was a dose response to melphalan, to the observation of increased CR rate and OS with a single ASCT vs. conventional chemotherapy, to the investigation in Phase III trials of double or tandem ASCT as a way to further improve outcome.

Dr. Bart Barlogie presented "Total therapy (TT) for multiple myeloma." He reviewed the past 20 years of TT which he characterized as an "evolution from palliation to cure." He maintains that there is a role for tandem transplants in myeloma.

Continues on Page 14

PLERIXAFOR AND TRANSPLANTATION IN MULTIPLE MYELOMA

Myeloma Today in conversation with Dr. Sergio Giralt

Please give us a brief overview of transplantation in multiple myeloma.

In the early 1980s, Tim McElwain (Professor of Medical Oncology at the Royal Marsden Hospital in the UK) made a seminal observation that by giving myeloma patients high doses of melphalan, we could overcome the resistance of their disease to standard doses of melphalan therapy and regain control of their myeloma, albeit for a short period of time. The other thing he demonstrated was that the toxicity of melphalan primarily affected the bone marrow, the organ in the bone that produces the red and white blood cells and the platelets, which carry oxygen to the body, protect us from infection, and prevent bleeding. Some patients who received very high doses of melphalan died from complications due to the marrow toxicity. It was Bart Barlogie's concept to take out the patients' marrow and freeze it before giving them high doses of melphalan, then re-infuse the marrow to help patients recover more quickly from the melphalan therapy. That's how the whole field of bone marrow transplantation (BMT) for myeloma began.

Sergio Giralt, MD
Professor, Deputy Chair,
Stem Cell Transplantation
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The University of Texas
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Houston, TX

Initially, BMTs were performed on patients who had exhausted their other options. Later, transplantation became a frontline therapy option. There was much controversy in this arena, but most studies showed that patients who underwent transplantation had a higher complete remission (CR) rate and lived longer without disease than those who did not.

In the late 1980s, it was discovered that bone marrow stem cells, which give birth to all mature cells, circulate in the blood after the patient undergoes chemotherapy. The stem cells could be collected from the bloodstream after patients received high doses of Cytoxan® (cyclophosphamide). At the same time, white cell growth factors such as Neupogen® (filgrastim), Neulasta® (pegfilgrastim), and Leukine® (sargramostim) were becoming commercially available to help patients receive chemotherapy with less marrow toxicity than before. Investigators in Europe demonstrated that the combination of chemotherapy and these granulocyte-colony stimulating factors (GCSF) "mobilized" the release of stem cells from the bone marrow into the bloodstream. It was no longer necessary to put patients under general anesthesia to harvest cells by direct penetration and aspiration of the marrow from the bones. We could collect large numbers of patients' stem cells directly from the blood, as if it were a blood donation. This is how autologous bone marrow transplantation (BMT) was replaced by autologous stem cell transplantation (ASCT).

What is the current place of ASCT in myeloma?

As with other forms of therapy, the goals of ASCT are to achieve the maximum depth and duration of response leading to the best overall survival. Myeloma is the most common indication for high-dose chemotherapy with ASCT in North America today. It remains the treatment associated with the highest CR rate in myeloma and, when compared to conventional chemotherapy regiments, ASCT is associated with improved survival.

Is this likely to remain the case in the context of available novel agents?

We have seen a continued increase in the number of ASCTs performed for myeloma, even after the approval of thalidomide, Velcade® (bortezomib) and Revlimid® (lenalidomide). The role of high-dose therapy in the context of these novel anti-myeloma therapies and combinations is being re-explored, but it is likely that high-dose therapy will remain an important component of frontline and relapsed myeloma therapy. Discussions continue regarding ASCT and stem cell mobilization in myeloma in the context of new therapies.

What about single versus double ASCT?

It is interesting that you ask this. The Italian and French studies have shown that if you respond well to the first transplant, you do not benefit from the second. But that conclusion was made based on a very small number of patients in an analysis that was not really planned so, in my opinion, this assertion is not statistically valid.

The Blood and Marrow Transplant Clinical Trials Network (BMT CTN), a cooperative group funded by two divisions of the U.S. National Institutes of Health – the National Cancer Institute (NCI) and the National Heart, Lung, and Blood Institute (NHLBI) – is conducting a randomized clinical trial of 750 patients who will all receive one transplant with high-dose melphalan, followed by either four cycles of novel therapy or a second transplant, or maintenance alone. We encourage all patients and physicians to consider participating in this study. The results of this study should show us, in the context of novel therapies, if one transplant is as good as two.

Let's return to the topic of stem cell mobilization.

Mobilization is the process by which we get the stem cells from the marrow into the bloodstream. Stem cell procurement for ASCT has most commonly been performed with stem cell mobilization using GCSF with or without prior chemotherapy.

What are the determining factors in whether a myeloma patient is mobilized with or without chemotherapy?

This often depends on whether the patient has active myeloma, the extent (and type) of prior therapy, and disease duration. Sometimes the determination is based upon the program in which the patient's physician is participating. Modern technology allows for about 95% of myeloma patients to be successfully mobilized with enough cells for one or two transplants. Most clinical trials suggest that more cells can be collected after chemo-mobilization, but chemo-mobilization has not demonstrated superior outcomes while being associated with more toxicity, and the failure rate with chemo-mobilization is similar to the failure rate with GCSF alone.

What are the options for the myeloma patients who are not mobilized successfully?

Years ago, the patients who were poor mobilizers, who failed to mobilize despite multiple attempts, were never able to proceed to transplant. Most

CONTINUES ON PAGE 10

PHASE II STUDY OF CARFILZOMIB IN PATIENTS WITH RELAPSED MYELOMA

Myeloma Today in conversation with Dr. Sundar Jagannath

At the 2009 annual meeting of the American Society of Clinical Oncology (ASCO), IMF spoke with Dr. Sundar Jagannath, the principal investigator of a Phase II study of carfilzomib in patients with relapsed and refractory multiple myeloma.

Sundar Jagannath, MD
Chief, Multiple Myeloma Program,
Bone Marrow and Blood
Stem Cell Transplantation
St. Vincent's Comprehensive
Cancer Center
New York, NY

Dr. Jagannath, at the recent ASCO meeting you presented the final results of your study of carfilzomib, a new agent being investigated in myeloma. Would you please tell us more about this agent and your study findings?

Carfilzomib (CFZ) is a novel proteasome inhibitor of the epoxyketone class that exhibits a high level of proteasome selectivity and demonstrats anti-tumor activity in bortezomib-resistant myeloma patients in Phase I studies.

Our study, PX-171-003-A0, was an open-label, single-arm, multicenter study that enrolled myeloma patients who had relapsed from more than two prior therapies, failed on therapy with bortezomib (Velcade®), and failed at least one immunomodulatory agent (thalidomide or lenalidomide). The enrolled patients were refractory to last treatment while on, or within 60 days of last therapy, or had <25% response to last therapy. Patients received CFZ 20mg/m^2 intravenously two days per week for three weeks (on days 1, 2, 8, 9, 15, and 16) of a 28-day cycle, for up to 12 cycles. Again, let me stress that all study participants had exhausted all treatments currently available to them and their disease had progressed on their last therapy.

Forty-six patients were enrolled in the initial phase of the study, including 78% with progression on/within 60 days of last therapy and 22% with no response to last therapy. Thirty-nine patients completed at least one cycle of CFZ, had measurable M-protein, and were evaluable for response. All patients had received prior bortezomib therapy, 91% had prior thalidomide and 89% prior lenalidomide, and 83% had prior stem cell transplant. All had failed combinations including anthracyclines (80%) and/or alkylating agents (94%).

What conclusions did you reach as a result of the initial phase of this carfilzomib study?

I feel that CFZ is a very active and very well-tolerated anti-myeloma agent. Eight out of ten patients achieved response during cycle one, and 72% of participants experienced either improvement or stabilization of their disease. Median time to progression (TTP) was 6.2 months. Close to one out of five patients responded to treatment.

Single-agent CFZ achieved a TTP of >6 months in relapsed and refractory myeloma patients who failed available therapies. We are quite excited that the drug seems to be tolerated very well. Patients stayed with this study for a median of eight months, which demonstrates that most study participants tolerated the treatment well and that most of the toxicities were manageable. The most common adverse events were fatigue, anemia, thrombocytopenia, nausea, upper respiratory infection, increased creatinine, and diarrhea. As with most of the other side effects, peripheral neuropathy (PN) occurred in less than 10% of participants. Importantly, exacerbation of pre-existing PN was rare, and 80% of study participants had pre-existing PN.

What is the next phase for this carfilzomib study?

The study has been expanded to enroll an additional 250 patients in this unmet medical need population at an escalated dose, and treatment has been extended beyond a year. If this compound continues to prove to be an effective treatment for myeloma in the next phase of the study (PX-171-004), we are hoping that the expanded trial will help expedite the drug approval process for the use of CFZ in myeloma. **MT**

Editor's Note: For more information, please see below, visit www.myeloma.org, or call the IMF Hotline at 800-452-CURE (2873).

Open-label, Single-arm, Phase II Study of Carfilzomib in Patients with Relapsed Multiple Myeloma: Carfilzomib given at increasing doses with dexamethasone (PX-171-004)

Trial description: This is a single-arm study for patients who have relapsed, refractory or progressive disease after at least one but no more than 3 prior treatments for myeloma. The initial dose of carfilzomib will be increased if the drug is well tolerated. Both patients never treated with Velcade® and patients previously treated with Velcade® will be studied.

Trial Objectives: To evaluate the best Overall Response Rate after 6 cycles of carfilzomib.

Inclusion criteria:

- 18 years or older
- Adequate ability to perform acts of daily living
- Symptomatic myeloma with measurable disease
- Relapsed, refractory or progressive disease after at least one, but no more than three treatments or regimens for multiple myeloma

Exclusion Criteria:

- Non-secretory multiple myeloma or myeloma only measurable by serum free light chain (SFLC) assay
- Not responsive to standard front line therapy
- Systemic myeloma treatment within 3 weeks of study, radiation therapy or immunotherapy within 4 weeks of study or localized radiation therapy within 2 weeks of study
- Significant neuropathy (Grade 3, 4 or Grade 2 with pain)
- Acute active infection requiring systemic antibiotics, antivirals or antifungals within 2 weeks of study

Locations and Trial Coordinator Telephone Contacts:

Mayo Clinic, Scottsdale, AZ: 480-301-4890
Barnes-Jewish Hospital, St. Louis, MO: 314-454-8377
Hackensack University Medical Center, Hackensack, NJ: 210-336-8020
St. Vincent's Compr. Cancer Center, New York, NY: 212-604-6026
MD Anderson Cancer Center, Houston, TX: 713-792-9559
Princess Margaret Hosp, Toronto, Ontario, Canada: 416-946-4501, x 5931

This study continues to expand, adding new locations weekly, so please visit **www.myeloma.org** or call the IMF Hotline at **800-452-CURE** (2873) for the most up-to-date list of trial sites.

CHARLES NEWMAN — continued from page 4

I understand that you are involved with the IMF cell phone collection program.

The program has been a "win-win" initiative for all: it generates funds for the IMF, provides donors with a tax deduction, places phones in the hands of people in less developed nations, and protects the environment by saving older cell phones from ending up at the garbage dump. I am in the cell phone reuse business, so when the IMF decided to initiate its cell phone donation program several years ago, my people were there to offer any support they could provide.

What is your outlook for the future?

First, the IMF must continue to secure financial resources in order to continue serving the myeloma community, and it is one of the Board's tasks to help the Foundation in this regard. The IMF must continue to educate more and more patients and physicians about myeloma. Through the IMF, I have personally counseled 100-200 people in an effort to help them better understand the available options so that they might have the standard of care that my wife has had. There is now so much more information about this disease than when it first entered our lives, but there is still much work to be done to help improve patient outcomes while continuing to make strides towards finding a cure for myeloma. **MT**

2009 WALDENSTRÖM'S AWARD — continued from page 6

upon meetings where I had to plead the case for the use of PET scanning in myeloma. In the beginning, I would see representatives of many other cancer groups at the Medicare meetings who were trying to get PET scanning approved for various diseases. At the last meeting, I was the only one representing myeloma, and the only other person in attendance representing a disease group was an advocate for ovarian cancer. She and I were the only ones there to present our cases and, in the end, Medicare approved PET scanning only in myeloma and ovarian cancer. Clearly, perseverance paid off! The cancer groups that had given up were denied approval, although the technology might have been useful for them as well.

What do you see as you look toward the future?

Luc Montagnier, who first identified the AIDS virus, is working with Howard Urnovitz and me on sequencing DNA and RNA in the blood; Luc has called these circulating nucleotides "Voyager DNA" and "Voyager RNA." It is possible to identify molecular patterns of disease that will be an important way to both diagnose and monitor myeloma on an individual patient basis. I am very interested in this project as I believe it will lead to new approaches to cancer therapy. This would be a very important way forward.

Innovation is always challenging. In addition to the usual difficulties, the present economic climate has placed additional challenges in our path. But we must remain focused on our key goal – improving outcomes for our patients – so we must consider not only the cost of myeloma therapies but the cost **effectiveness** of therapies.

The stimulus for me as a clinician continues to be working with patients, thousands of patients over the years. They continue to be my inspiration. **MT**

SERGIO GIRALT — continued from page 8

retrospective studies addressing mobilization have identified patient age, method of mobilization, time to stem cell mobilization, number of prior regimens, and prior melphalan and/or radiation exposure as predictors of patients failing to achieve a minimal dose. Parallel to this, other studies have been exploring the biology of myeloma and the mechanism of how cells move out of the bone marrow. The science is very elegant, with parallels between how stem cells find their home in the bone marrow. Stem cells are designed to live as long as we live, and they are there to produce all the blood cells and platelets that we need for our lifespan. The stem cells "stick" with what are called adhesion molecules, the glue that holds the stem cells against the walls of the bone marrow to prevent them from being released. Today, novel mobilization strategies are disrupting the "glue" so the stem cells can separate themselves and circulate in the blood to improve collection yield and efficiency.

This is where plerixafor steps into the picture?

Plerixafor (also known as Mozobil®) is a drug that was originally developed for AIDS. During the clinical trials conducted with plerixafor for AIDS, an observation was made that patients taking this drug had very high white blood cell counts. Further studies showed that plerixafor breaks the bond between stem cells and the walls of the marrow cells, thereby releasing more stem cells into the bloodstream.

In myeloma and lymphoma, two important clinical trials have shown that plerixafor is safe and effective in combination with GCSF and results in increased stem cell mobilization in fewer apheresis days compared to GCSF alone.

Also, plerixafor showed to be effective in mobilizing adequate stem cells in two thirds of the patients who had failed traditional mobilization techniques as demonstrated in the compassionate use protocol. In patients with myeloma, plerixafor in combination with GCSF has also been shown to be more effective as an initial mobilizing regimen than GCSF alone. More studies need to be done with this agent to better define its role in the treatment of myeloma, but we have found the use of plerixafor to be both safe and predictable (in terms of cell yields) as a mobilization agent.

Plerixafor is a major advance in ASCT in myeloma. It has a very manageable toxicity profile, with the most common adverse events being injection-site reaction and mild GI upset. It allows us to more efficiently collect larger numbers of cells from good responders, to mobilize patients who have failed mobilization, to help save patient resources, and to study if transplanting very high numbers of stem cells can improve outcome for patients.

Any closing comments?

High-dose melphalan is still recommended for eligible patients, and stem cell collection early in the course of therapy should be considered in all patients eligible for ASCT. The decision of whether or not to pursue ASCT must be made by the patient in consultation with their treating physician. If a patient chooses to undergo ASCT, they don't necessarily need to incorporate plerixafor into their mobilization regimen but it can be very helpful if they fail to mobilize without it.

In closing, I would recommend that patients discuss with their doctors the benefits of plerixafor in combination with GCSF, as opposed to using GCSF alone, especially since plerixafor does not add the significant toxicities associated with stem cell mobilization using chemotherapy. **MT**

IMWG STUDIES PATIENTS WHO HAVE EXHAUSTED THEIR TREATMENT OPTIONS

Myeloma Today in conversation with Dr. Shaji Kumar

Dr. Kumar, we would like to hear about your current research project on behalf of the International Myeloma Working Group (IMWG), but first please tell us about the 1999 Mayo Clinic study of myeloma patients whose disease relapsed?

Up until approximately 10 years ago, there were relatively few therapies available for treating multiple myeloma, and most of those therapies had been developed during the preceding 30 years. In 2000, investigators at the Mayo Clinic analyzed data pertaining to myeloma patients who were treated at the Clinic and whose disease came back after initial therapy. Here at Mayo, we have long-term follow-up on our patients, so we looked at patient outcomes from each time their disease relapsed from previous treatment. After each relapse, we measured how long the patient responded to subsequent treatment, and how long they lived after the treatment failed.

Shaji Kumar, MD
Associate Professor of Medicine
Division of Hematology
Mayo Clinic
Rochester, MN

What was the significance of that study?

That was a very interesting study because until that time we had not examined in detail what happened to myeloma patients post-relapse. Most of the investigations performed prior to that study focused on what happed after initial treatment up until the first relapse.

Please tell us about the study follow-up.

To follow up, we initiated a new study at Mayo Clinic in 2007, and our findings were published in *Blood* in early 2008. We looked at data from nearly 3,000 patients treated at the Clinic over a 36-year period. We separated the patients into six groups, based on the year of diagnosis. In the first four groups, which included patients diagnosed prior to 1994, we saw very little improvement in patient survival. We saw improvement in the survival of patients who were diagnosed between 1994 and 2000, with the data on the survival of patients diagnosed since 2000 being even better than for those who were diagnosed between 1994 and 2000.

How did you interpret those findings?

We think that what changed related primarily to two things: wider use and availability of stem cell transplantation, and the introduction of three novel anti-myeloma agents (thalidomide, lenalidomide, and bortezomib) that are very effective at treating the disease. We know that both these components played a role in our findings, because we saw improved survival in newly diagnosed patients and also in a smaller subset of patients who relapsed following a stem cell transplant. Of the three novel agents, lenalidomide and bortezomib have been proven to improve overall survival, both when used as part of initial anti-myeloma therapy and in the relapse setting.

Now please tell us about the analysis you are currently performing on behalf of the IMWG.

The IMWG project was undertaken to find out what happens to myeloma patients who have exhausted all their treatment options.

Over the last 10 years, we have seen a major shift both in available treatments and in the outcomes for patients with myeloma. In 2009, we are looking at a very different landscape of available anti-myeloma therapies. Over the past decade, survival of newly diagnosed patients has more than doubled. Data show survival improvement for each year following 2000, which is directly related to the role played in myeloma treatment by the three novel agents I mentioned earlier.

But we know that none of the three novel agents are curative, because the myeloma invariably comes back sooner or later. And the introduction of the novel agents has also brought forth new challenges. Because we have significantly improved the outcome for patients, the problem that we face today is that newer medications that need to be studied for myeloma have a much higher hurdle to overcome to demonstrate to the regulatory authorities that a new drug warrants investigation because it is likely to make a difference for patients. This means that it has become more difficult to show that newer drugs are able to improve survival ever more than the currently available medications. Clinical studies now require larger groups of patients, who must be followed for longer periods of time.

Doesn't that delay the process of getting the next promising anti-myeloma drug to patients?

That is exactly our concern. The three novel drugs currently available took four to five years to get to the marketplace. If the newer drugs follow the same path, it might take even longer to get them approved! Clearly, that is just too long to wait.

How does that relate to the current IMWG study?

We hope that by analyzing the outcome of patients who have failed on all available therapies the current IMWG study will accelerate the process of drug approval. If we can show that the newer drugs being studied offer a clear survival benefit to patients who have no remaining approved treatment options, this can become the new benchmark for evaluating newer compounds in clinical trials. This would help expedite bringing new useful compounds to market.

For this research project, we are collecting data on a group of patients who have become nonresponsive or refractory to all the novel agents available to them. The data is being provided by investigators at 13 myeloma centers (six in the US plus seven in Europe). The availability of novel agents varies from country to country, but the data gives us a broad global spectrum of the impact of the newer medications. We are looking at how these patients have been doing from the time they became unresponsive to available treatments.

Based on prior studies, we are targeting a group of 300 patients who have active myeloma and no remaining means to control the disease. We feel that this would give us enough data for a strong study leading to a good conclusion. The patients are not "enrolled" in this study in the traditional sense, as what we are doing is analyzing existing medical records of nonresponsive patients retrospectively, and tracking what happened to those patients over time.

Continues on Page 16

HONORING PROF. JEAN-LUC HAROUSSEAU AND HIS WORK

The Award

Nearly a century ago, Dr. William Mayo set the standard for treatment of patients at Mayo Clinic with these words: "The needs of the patient are the only needs to be considered." In 2003, the IMF bestowed the first annual Lifetime Achievement Award to a physician whose work against multiple myeloma reflects the dedication and compassion inherent in Dr. Mayo's vow. The IMF chose to name this award for Dr. Robert Kyle, whose life and work give new meaning to Dr. Mayo's words.

Dr. Robert Kyle

In his more than 40 years at Mayo Clinic, Dr. Kyle has never wavered from his commitment to the needs of patients with myeloma. He has devoted his life's work to them. He has gained recognition the world over as a pioneer and respected leader in the advancement of research, clinical treatment, and education about myeloma.

When Brian Novis sought to learn more about his disease, he was looking for the finest doctor available to help him. When he heard about Dr. Kyle, Brian didn't know at the time that Dr. Kyle was considered to be the "grandfather" of myeloma treatment.

Later, when Brian Novis and Dr. Brian Durie decided to create an international foundation dedicated to helping others with myeloma, Dr. Kyle was the first person they contacted. Dr. Kyle agreed to collaborate with the two Brians, and became a founding member of the International Myeloma Foundation's Board of Directors and chairman of its Scientific Advisory Board, a position he still holds today.

Dr. Kyle is a sought-after presenter at IMF clinical conferences and workshops, and is the most frequently requested speaker at IMF Patient & Family Seminars. Through IMF programs, Dr. Kyle has made himself accessible to thousands of myeloma patients and their families around the world. His guidance and encouragement are as important to the IMF today as when the IMF first began.

When Dr. Kyle was first approached about receiving the Robert A. Kyle Lifetime Achievement Award, his response to Susie Novis was, "I'm not done yet." His humility, dedication, sense of humor, and caring and compassionate nature are among the many reasons for which the IMF named this award in his honor.

Left to right: Prof. Mario Boccadoro, Susie Novis, Prof. Jean-Luc Harousseau, Florence Harousseau, and Dr. Brian G.M. Durie

The Seventh Annual Robert A. Kyle Lifetime Achievement Award

The Recipient

Prof. Jean-Luc Harousseau

Professor of Hematology and Director of the Cancer Center René Gauducheau at Nantes, France

Prof. Harousseau was born in Nantes in 1948, where he has spent almost all his personal and professional life. He joined the faculty of medicine in Nantes in 1965, and moved to Paris in 1972, where he spent four years as Interne des Hôpitaux de Paris. He was then appointed as Assistant in the Department of Hematology chaired by Prof. Jean Bernard at Hôpital St-Louis. During this period he trained in hematology and his main topic was the treatment of acute leukemias.

In 1980, at the age of 32, he became the youngest professor of hematology in France. He returned to Nantes where he created the department of hematology of the University Hospital, including the Pediatric Onco-Hematology Unit and the Bone Marrow Transplantation Unit, with the help of Prof. Noël Milpied. He became Head of Department when he was only 36. At that time he was mostly involved in autologous and allogeneic stem cell transplantation, and he created the multicentric French group GOELAMS initially focused on the treatment of acute myeloid leukemia.

Prof. Harousseau's interest in myeloma started in 1983 with the publication in *Lancet* of "High-dose melphalan in high-risk myeloma" by Drs. MacElwain and Powles. He became one of the pioneers of high-dose therapy in myeloma, and was also one of the founders of the Intergroupe Francophone du Myélome (IFM) with Prof. Michel Attal and Prof. Thierry Facon. The IFM has conducted a number of randomized trials that have contributed significantly to the major improvements in the prognosis of myeloma in the past 20 years.

Prof. and Mrs.Harousseau

The major contribution of IFM trials was initially in the field of high-dose therapy (conventional chemotherapy versus autologous transplantation, conditioning regimen, single versus double transplantation, tandem auto versus mini allogeneic transplantation). More recently, the IFM introduced novel agents in frontline therapy (thalidomide as maintenance, MP-thalidomide versus MP in elderly patients, bortezomib in the induction treatment). The large number of

Lifetime Achievement Award

patients recruited for the IFM trials also permitted analysis of prognostic factors and of the impact of complete or very good partial response achievement.

In the early 1990s, Prof. Harousseau convinced Dr. Régis Bataille, who was already a world-renowned researcher in myeloma, to join him in Nantes and build a Center for Research on Myeloma "from bench to bedside." Their work has ranged from laboratory research on the phenotype of the malignant plasma cell, bone disease, and mechanisms of apoptosis and resistance with Dr. Martine Amiot and Dr. Catherine Pellat; to clinical trials with Dr. Philippe Moreau; to translational research, including FISH, gene expression profile, and more recently SNP-arrays, with Hervé Avet-Loiseau.

Prof. Harousseau is the author or co-author of more than 400 peer-reviewed articles, including papers in high-impact factor journals (*New England Journal of Medicine*, *Blood*, *Journal of Clinical Oncology*) and of a number of book chapters. He is very involved in the life of the French Society of Hematology, and is a member of several scientific societies. He has a passion for education and is proud of having created in Nantes one of the best French teams of coworkers in the field of hematology. In October 2008, he left the department of hematology he created and developed, and has been appointed as Director of the Cancer Center of Nantes.

The Ceremony

The Seventh Annual Robert A. Kyle Lifetime Achievement Award ceremony took place on May 15 in Monte Carlo, Monaco. Along with many of his colleagues from around Europe, Prof. Harousseau was in Monte Carlo participating as faculty for the already-scheduled New Developments in Multiple Myeloma Clinical Conference. The Fairmont Hotel was the perfect venue for both the conference and the award ceremony.

Dr. Brian G.M. Durie

A trio of classical musicians greeted Prof. Harousseau, his wife Florence, and their invited guests for a celebratory glass of champagne and hors d'oeuvres. Susie Novis and Dr. Brian Durie gave a short welcome to the more than 150 colleagues and friends in attendance before announcing the commencement of the special dinner in Prof. Harousseau's honor.

After dinner, Drs. Kyle and Durie spoke about the importance of Prof. Harousseau's many contributions to myeloma research and treatment. During the ceremony,

Prof. Jean-Luc Harousseau (left) being congratulated by Prof. Jesús San Miguel

Dr. Kyle asked both Prof. Heinz Ludwig and Prof. Mario Boccadoro to stand for a nice round of applause to recognize them as being previous recipients of the Robert A. Kyle Lifetime Achievement Award.

Prof. Philippe Moreau, who has worked closely with Prof. Harousseu for many years, gave a moving speech about the importance of Prof. Harousseau's contribution to the field of myeloma, his legacy as co-founder of the Intergroupe Francophone du Myélome, the French national myeloma research consortium, and his tremendous dedication to myeloma patients in France and around the world. **MT**

Prof. Philippe Moreau of the CHU de Nantes gave an extensive and entertaining speech about Prof. Harousseau's remarkable tenure there

Dr. Catherine Pellat and Dr. Brain G.M. Durie

Dr. Michel Delforge and Greg Brozeit

Prof. Heinz Ludwig and Prof. Jean-Luc Harousseau

David Girard, Susie Novis and Prof. Antonio Palumbo

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IMW — continued from page 7

Dr. William Bensinger discussed "Allogeneic donor transplants for multiple myeloma in Seattle." He presented the results of allo-ASCT in 278 patients treated from 1977 to 2008. Dr. Bensinger suggested that post-transplant maintenance therapy with one of the novel agents and more targeted conditioning regimens might improve outcomes.

Dr. Thierry Facon presented "Post-transplant maintenance." He said that the advent of novel agents and their use in combination therapies have contributed to achieving optimal regimens for post-transplant consolidation and maintenance therapies. Dr. Facon reviewed trial results for maintenance therapy with thalidomide. Bortezomib and lenalidomide are also being tested for consolidation/maintenance as single agents and in combinations. He addressed Phase III trials to assess the role of consolidation and maintenance post-transplant, which may answer some of the outstanding questions concerning post-transplant consolidation and maintenance.

Pro and Con Sessions

Simultaneous versus Sequential use of Novel Agents

Dr. Morie Gertz argued for simultaneous use of novel agents in induction therapy and Dr. Joan Bladé argued for sequential use. The concept of conventional therapy is changing, and there are no data showing that sequential treatment is inferior to combination therapy. It was also noted that different populations of patients may require different approaches.

Risk Stratification

Dr. Angela Dispenzieri favors basing therapy on risk stratification, which is based on patient characteristics, including age, performance status, renal function, and co-morbidities; and on tumor characteristics. Dr. Jesús San Miguel is against basing therapy on risk stratification, but says treatment can be individualized. In the ensuing discussion, Dr. Rajkumar stated that this was not the time for risk stratification, and urged putting patients in trials, doing a biologic analysis up front, carefully analyzing response, then tailoring treatment to specific patients. He suggested offering a high risk treatment approach to patients who wouldn't benefit as much as those with standard risk disease.

Allogeneic Transplantation

Dr. Jayesh Mehta favors using allogeneic transplantation while Dr. Jean-Paul Fermand is against it. The transplant-associated mortality for allo-SCT is 12% vs. 5% for ASCT at 2 years. Improvement should focus on methodology, including new drugs, reducing GvHD, and keeping GvM. Dr. Mehta said allo-SCT should be based on prognostic factors and be used to treat patients with very high risk disease and poor prognosis.

Consensus Panels

Guidelines for the Uniform Reporting of Clinical Trials in Myeloma

Dr. Vincent Rajkumar discussed issues concerning response criteria. The IMWG Uniform Response Criteria are recommended for use in future clinical trials. PET (positron emission tomography) and MRI (magnetic resonance imaging) will not be incorporated formally into the response criteria for assessing the depth of response but additional single center clinical studies are encouraged. The time at which each response assessment was conducted should be reported, and should be made before initiation of subsequent therapies. Time to best response should be reported, otherwise studies can't be compared.

Dr. Jesús San Miguel discussed additional definitions, including the distinction between relapsed-refractory and primary refractory disease. It was suggested to add a qualifier describing which type of therapy or drug(s) to which the disease was refractory or non-responsive. Efficacy results for Phase III trials should include OS (overall survival), TTP, PFS (progression-free survival), DOR (duration of response), and, if possible, TNT (time to next therapy, defined as time from registration on a trial to the next treatment or death due to any cause, whichever comes first), 5-year OS and 10-year OS.

Guidelines for Risk Stratification in Myeloma

Dr. Nikhil Munshi said that the main purpose of risk stratification at this time should be to update prognostic factors in the era of novel therapies, not to make a decision about treatment. Because there is evidence that risk factors change at relapse, patients can be reassessed, and if they have acquired high risk features, they should be reclassified. He also said that the International Staging System (ISS) needs to be validated for newer agents, and some modifications in the future should be expected.

Although the Durie-Salmon staging system for determining tumor mass is still the standard, it could be replaced by CRAB (calcium elevation, renal insufficiency, anemia, bone lesions) criteria. Using MRI for response evaluation requires further study. Genomic studies, including gene expression profiling (GEP), single nucleotide polymorphism (SNP) arrays, and comparative genomic hybridization (CGH) have their place in research, but are not sufficiently validated for general clinical use.

Guidelines for Standard Investigative Work-up in Myeloma

Dr. Robert Kyle reviewed the minimum tests required at diagnosis and for prognostic evaluation for patients. These include a history and physical, which should detect any co-morbidities such as heart disease, thrombosis, hypertension, renal, liver, or lung disease, or other conditions that would affect treatment. Blood tests include a complete blood count (CBC), differential, and peripheral smear; chemistry panel with calcium, creatinine, electrolytes, liver function tests, urea, albumin (preferably using nephelometry), serum protein electrophoresis (SPEP), immunofixation electrophoresis (IFE), and serum FLC; and urinalysis, including a 24-hour urine test for protein, creatinine clearance, urinary protein electrophoresis (UPEP), and IFE. Bone marrow aspirates or biopsies are mandatory to confirm a diagnosis of multiple myeloma (>10% clonal plasma cells).

Beta-2-microglobulin is needed to determine the ISS stage, and LDH is also useful for risk assessment. Other useful tests include standard cytogenetics, and FISH on sorted bone marrow plasma cells. Imaging tests include a skeletal survey; MRI of the spine and pelvis are mandatory, particularly to rule out spinal compression. There is no definite role for PET-CT, which may be helpful for extramedullary disease. **MT**

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.

New compound enters myeloma research pipeline

CEP-18770, a boronic-acid based compound, is a new research drug being developed by Cephalon as a possible new treatment for multiple myeloma. One compound from this drug class that has already been approved for use in myeloma is bortezomib (Velcade®). In pre-clinical (animal) studies, CEP-18770 showed superior activity in myeloma models versus Velcade. Most importantly, it was able to overcome Velcade resistance. In addition, CEP 18770 showed a safety profile with significantly less toxicity to the nervous system compared to Velcade.

The first in human (Phase I) study with CEP-18770 is being conducted in Italy and Switzerland. The research study is enrolling patients with multiple types of cancers. The trial's goals are to:

- determine the safety of the drug (side effects)
- determine if patients are able to take the drug without too many side effects (the tolerability of the drug)
- measure the amount of drug in the patient's blood [pharmacokinetics (PK) and pharmacodynamics (PD)]

Data from the Phase I study set the highest dose at which the study drug should be given (maximum tolerated dose). It also looked at the PK, PD and safety profile. This study will also test if CEP-18770 is effective and safe for patients with multiple myeloma.

Cephalon is planning to conduct an open-label, Phase I/Phase II research study with CEP-18770 in patients with relapsed and refractory multiple myeloma. The Phase I portion of the trial will set the dose needed for this patient population (maximum tolerated dose). Once the Phase I of the trial is completed, the Phase II portion will start. This portion will look to see if CEP-18770 in patients with relapsed and refractory multiple myeloma is effective and safe.

The Phase II portion of this trial will have two stages. Stage 1 will enroll 23 patients and if enough patients have a response to CEP-18770 the trial will begin stage 2. Thirty-two patients will be enrolled during stage 2. All patients will receive CEP 18770 intravenously in a 21 day cycle, for up to 8 cycles (24 weeks). During this Phase II portion of the trial, patients with poor response to CEP-18770 will have low dose dexamethasone (a man-made adrenocortical steroid) added into the regimen.

After 8 cycles of initial therapy, patients with responding or stable disease may continue CEP-18770 maintenance treatment for another eight 21-day cycles. Seventy to ninety patients in total will be enrolled in this Phase I/Phase II study. Thirty clinical centers in the USA, Canada and Europe will be used. Spain, Belgium, and France may participate in the trial. The study will likely start by December 2009.

Medicare to cover PET scans

The decision by the Centers for Medicare and Medicaid Services (CMS) to cover the use of positron emission tomography (PET scans) in multiple myeloma can significantly change the course of treatment for many patients. The case for using PET scans in myeloma was published in the *Journal of Nuclear Medicine* and presented to CMS by IMF chairman and medical director Dr. Brian G.M. Durie with the support of Dr. Barry Siegel, co-chair of the National Oncologic PET Registry, a comprehensive national study of PET scans in cancer.

"With PET scans doctors can visualize the whole body to see the full extent of disease on initial diagnosis, follow the response to treatment more accurately, and better determine when further treatment is needed and when it is not," said Dr. Durie. "In the national demonstration project, the course of treatment for myeloma was changed almost half the time with the use of PET scans. That's the highest impact for any cancers in the project."

Dr. Siegel added, "There are times when standard testing indicates patients are in complete remission, but with PET scans we can see that lesions, areas of cancer, are present, indicating that more or more aggressive treatment is required. Likewise, when we can be certain there is no detectable cancer, we can help patients avoid needless and expensive treatments. We are pleased to have contributed to this change in Medicare coverage."

PET scans utilize a sugar analogue that concentrates in cancer cells and emits a radioactive tracer that can be detected and located by the scan. Whole body PET scans can be used to detect unsuspected or new outbreaks of multiple myeloma both to aid in initial diagnosis and to assess ongoing treatment. PET scans have been approved for several cancers including breast, colon cancer and lymphoma. The new decision adds myeloma and ovarian cancer to the list.

"This is not only great news for patients, it is cost effective," said Michael Katz, board member of the IMF. "PET scans can cover the entire body and in our experience with myeloma patients, depending on their insurance coverage, PET scans can cost significantly less than other imaging techniques such as CT or MRI and provide better information when used as whole body scans. We believe many private insurers will now follow this lead and with more widespread use, we believe the full potential of this important medical technology can be realized. The IMF is pleased to have played a leading role in encouraging this decision."

Pesticide exposure and MGUS

As reported in *Blood* (18 June 2009, Vol. 113, No. 25, pp. 6386-6391), pesticides are associated with excess risk of multiple myeloma, albeit inconclusively. The study looked at 678 men (ages 30 to 94) to assess the risk of monoclonal gammopathy of undetermined significance (MGUS). Age-adjusted prevalence estimates of MGUS were compared with MGUS prevalence in 9,469 men from Minnesota, and associations between pesticide exposures and MGUS prevalence were assessed by logistic regression models adjusted for age and education level. Among 555 study participants older than 50 years, 38 were found to have MGUS, yielding a prevalence of 6.8%. Compared with men from Minnesota, the age-adjusted prevalence of MGUS was higher among male pesticide applicators. Increased risk of MGUS prevalence was observed among users of the chlorinated insecticide dieldrin, the fumigant mixture carbon-tetrachloride/carbon disulfide, and the fungicide chlorothalonil. The prevalence of MGUS among pesticide applicators was twice that in a population-based sample of men from Minnesota, adding support to the hypothesis that specific pesticides are causatively linked to the origins of myeloma. **MT**

IMF HOTLINE COORDINATORS ANSWER YOUR QUESTIONS

The IMF Hotline 800-452-CURE (2873) is staffed by Paul Hewitt, Missy Klepetar, Nancy Baxter, and Debbie Birns. The phone lines are open Monday through Thursday, 9am to 4pm, and Friday, 9am to 2pm (Pacific Time). To submit your question online, please email TheIMF@myeloma.org.

I recently viewed a news item from the University of Rochester Medical Center about a clinical trial for patients with a history of non-healing bone fractures who were given FORTEO® and then healed rapidly. Can this drug be given to patients with multiple myeloma who have lytic lesions and/or fractures to help heal their bones?

Paul Hewitt, Missy Klepetar, Nancy Baxter, and Debbie Birns

FORTEO® (teriparatide for injection) is synthetic parathyroid hormone (PTH) approved in 2002 by the FDA for the treatment of men and women with osteoporosis who are at risk of bone fracture. PTH stimulates the formation of new bone and increases bone mineral density and bone strength.

The Medication Guide for patients that accompanies each prescription for FORTEO states: "As part of drug testing, teriparatide, the active ingredient in FORTEO, was given to rats for a significant part of their lifetime. In these studies, teriparatide caused some rats to develop osteosarcoma, a bone cancer… It is not known if humans treated with FORTEO also have a higher chance of getting osteosarcoma."

The warning that is included with the Medication Guide states that, "patients should not use FORTEO if they have ever been diagnosed with a bone cancer or with other cancers that have spread (metastasized) to the bone."

Because of the fear of stimulating the growth of cancer, says Dr. David Roodman, head of the myeloma program at the University of Pittsburgh and noted researcher in the area of myeloma-related bone disease, FORTEO has not been used in patients with cancer. It was tested in a mouse model of myeloma at the University of Arkansas for Medical Sciences by Dr. Shmuel Yaccoby, who found that PTH increased bone formation in the myelomatous bone. There was no evidence that FORTEO increased the growth of myeloma cells.

Dr. Noopur Raje, who is head of the myeloma program at Massachusetts General Hospital, and who is also involved in research with myeloma-related bone disease, cautions that myeloma patients avoid using Forteo, given the complete lack of clinical data in the myeloma setting. Dr. Raje and her group are currently conducting research with bone growth-stimulating agents ACE-011 and BHQ880, an anti-DKK-1 antibody.

There have been no trials with FORTEO in myeloma patients. FORTEO should therefore not be taken by myeloma patients outside the context of a clinical trial. At the present time, there is no clinical trial to test FORTEO's safety and efficacy in myeloma patients. **MT**

SHAJI KUMAR — continued from page 11

The project is ongoing. We have already developed a very detailed case report form to collect data regarding these patients, Dr. John Crowley and the investigators at Cancer Research And Biostatistics (CRAB) will analyze this data. We are hoping to have enough data analyzed in time to submit our findings for presentation at the 51st Annual Meeting and Exposition of the American Society of Hematology (ASH).

For a patient to have failed on all available anti-myeloma therapies, does that mean that proportionately more of the patients you are studying are longer-term survivors?

No, not necessarily. Much is determined by disease biology. Myeloma patients with very aggressive and nonresponsive disease might reach the point of exhausting their treatment options within a one- or two-year period post-diagnosis. Myeloma patients with indolent disease may arrive at the same point of non-responsiveness after a decade or more post-diagnosis. While such two patients have different disease biology and history, they are similar that they have no remaining treatment options.

Given the data you have examined so far, what is the overall trend you are seeing and what is your personal outlook for the near future in the field of myeloma?

We know that people who are living with myeloma today are likely to survive longer and to maintain a higher quality of life than patients from decades past.

Unfortunately, we still have no cure for myeloma at present so, sooner or later, all patients will relapse. We are hoping that the ongoing research will make it possible to provide each patient with an effective treatment option whenever their disease relapses.

We are getting closer to myeloma becoming a chronic disease that can be kept under control, and we are continuing to press ahead towards curative solutions that will change the biology and the natural history of the disease. It is conceivable for the cure to be the result of combining currently available therapies, but we need to continue to develop new medications. Also, myeloma is not just one disease – it is a heterogeneous illness – and one approach may not be enough to cure it, so we need to continue to improve our understanding of its biology.

There are many ongoing studies using new cutting-edge techniques to better understand myeloma from a genetic perspective. It is our hope that if we better understand the genetic changes that occur in myeloma, we might be able to find where we can intervene in the process of disease development, either before or after the disease becomes cancer. This is probably more true for myeloma that for many other diseases given the variety of changes we see in the myeloma cells.

The quest continues. Given the progress made in the field of myeloma over the past decade, I am optimistic of what we will be able to accomplish in the years to come. **MT**

A PATIENT SEEKS CONTINUED MM EDUCATION

Myeloma Today in conversation with Joan Marx

Was the recent Patient & Family Seminar in San Francisco the first IMF educational meeting you've attended?

No. The first time I attended an IMF seminar was in January 2006, also in San Francisco. I was initially diagnosed with smoldering myeloma in 2001 but, until early 2006, I was told that the disease did not require treatment. Shortly before the 2006 San Francisco seminar, the standard laboratory markers showed that my numbers had changed, and my oncologist told me that it was time to start treatment for my myeloma. After speaking with my doctor, I sought a second opinion, then another "second" opinion. Although those opinions came from doctors at respected institutions, none of them were expert in the field of myeloma. In fact, the last consult was terrible – it made me feels like the doctor was simply nudging me towards a bone marrow transplant. Luckily, by that time I had found the online myeloma listserv forum and had also joined the local Bay Area Multiple Myeloma Support Group. During group meetings, I learned about the PET scan and the Freelite assay, neither of which had ever been mentioned by my doctor, and I had both tests performed. Then one of my fellow support group members, Dave Brown *(see page 21)*, who by that time was already a long-term myeloma survivor, advised me to attend the IMF seminar.

What was your experience at your first IMF seminar?

I found the experience to be extremely valuable. It was really wonderful. The IMF Patient & Family Seminar program gathers together terrific faculty members, whose presentations are always interesting and informative. But, in my opinion, the question and answer periods that follow the sessions are equally educational and offer a glimpse into a wide variety of myeloma patient experiences. In addition, I found that the IMF meeting environment offered me an unprecedented opportunity to speak with the myeloma specialists who were part of the seminar faculty.

Specifically, at the first IMF seminar I attended, my husband approached Dr. Mort Coleman after the doctor's breakout session. I found the two of them talking in the hallway and joined the discussion about my case. I got more individual attention from Dr. Coleman, right then and there standing in that informal setting, than I had ever received from any physician during any medical appointment! As a result of my mini-consult with Dr. Coleman, and my subsequent telephone consultation with Dr. Brian Durie, it was established that treatment was not needed for my myeloma at that time. In fact, I have yet to require any anti-myeloma therapies. I feel so blessed to have had the opportunity to benefit from the intervention of these two doctors.

In general, what aspects of the seminar experience have you found to be of greatest benefit to you as a patient?

First, I'd like to reiterate that having direct face-to-face contact with the myeloma experts who present at these seminars is truly invaluable. I have found them to be very receptive to questions and very willing to offer information when a patient requires further explanation in response to his or her question.

The variety of topics presented at IMF seminars is quite impressive. In listening to the different doctors' presentations, it quickly becomes clear that different physicians follow different philosophical approaches to treating myeloma. For example, Dr. Durie's philosophical approach seems to be more about finding the lowest effective dose of treatment rather than about firing the biggest guns in a patient's potential anti-myeloma arsenal, and this approach resonates with me. Another patient might find more resonance with a different approach to the disease. I feel that it is important for all patients to arrive at the realization of just how individual myeloma and its treatments are, and to choose a path that best suits their thinking and their lifestyle.

Has exposure to other patients been useful to you?

Yes. The IMF seminar environment is great for meeting other patients. Intrinsically, exposure to other people is very useful, and the variety of opinions and experiences represented at the IMF seminar is hard to match elsewhere. I find that I store information in my brain for possible future use, and I've collected a lot of helpful info from the many patients who have shared their experiences at IMF seminars. It's hard to cite just one example because there have been so many. But meeting long-term myeloma survivors has been particularly encouraging. Even now, eight years after my diagnosis, I find their stories reassuring and inspiring. They help me keep an eye on what is possible for me to achieve, statistics notwithstanding. Those who were diagnosed with myeloma before me did not have the treatment options that I am likely to have, and yet I have met many patients who have had the disease for 20+ years and they are doing well. Of course, when I meet such patients at IMF seminars or at the meetings of my local support group, I am aware that these are people who clearly value myeloma education.

How do IMF seminars help keep you up to date on developments in the field?

IMF seminars are a great resource for the latest information about myeloma. They help patients and caregivers get a more clear sense of where expert medical opinion is at the present moment. We need to know what key questions are being addressed by myeloma researchers and clinicians. At some point, all of us need to ask, "Am I better off opting for treatment now, or saving treatment options for later? If I choose treatment with a combination of novel anti-myeloma agents, should I reserve at least one of those agents for a later time in case I might have a relapse or if my disease becomes refractory to other drugs?" The IMF seminars have been very helpful to me in getting a handle on those topics.

Do you plan to continue attending IMF seminars in the future?

My first experience was so wonderful that I've decided to keep going back both to learn what's new and to deepen my understanding of what I already know. The seminar environment encourages patients to be active participants in their own care. The most important lesson I've learned from attending IMF seminars is that the ultimate responsibility for making decisions about myeloma treatment rests with each individual patient, not with his or her doctor. And this is the lesson I would most like to share with your readers. **MT**

"CANCER PATIENT STATEMENT OF PRINCIPLES" UNVEILED AT ASCO MEETING

A coalition of cancer patient advocacy organizations led by the International Myeloma Foundation (IMF) and the Myelodysplastic Syndromes Foundation (MDSF), unveiled a patient "Statement of Principles" at the annual meeting of the American Society for Clinical Oncology (ASCO) in Orlando, Florida. The principles, issued on behalf of patients and caregivers, state:

- Prevention is the key to reducing the burden of cancer
- Continuing innovation is critical to early diagnosis and better treatment
- Equality of access to care is imperative
- Early approval of new treatments for deadly cancers is essential
- Patients who have exhausted approved therapies need simplified access to experimental agents whenever possible

Susie Novis and Dr. Brian G.M Durie sign the Statement of Principles at ASCO

"The application of these principles is especially important to patients diagnosed with any of the eight lethal cancers, those that have five-year survival rates of less than 50 percent," said Susie Novis, president and co-founder of the IMF. "These cancers, including multiple myeloma, will cause nearly half the 560,000* cancer deaths projected in America this year. This is one of the key reasons we must assure that all patients have access to well-trained specialists and that we continue to develop newer, better treatments until there is a cure."

"When patients are diagnosed with cancer, their concern should be managing their disease, not reimbursement for their treatments," said Kathy Heptinstall, BSN, RN, operating director and co-founder of the Myelodysplastic Syndromes Foundation. "Oral drugs should have the same coverage as hospital-based procedures; research and innovation must be encouraged and supported; and for fatal diseases, the criteria for drug approvals should emphasize expedited approval and ready access to them."

The patient advocacy organizations supporting these principles believe they can make initial progress working to resolve the critical disparity in insurance coverage. Medicare and many private insurance programs require higher deductibles and co-payments for oral drugs than for intravenous drugs and hospital-based procedures. Because private insurance is regulated at the state level, Oregon, Indiana, and now Iowa have laws requiring equal coverage for oral and intravenous drugs, with similar laws pending in several additional states and federal legislation introduced in Congress.

Former NFL linebacker Elijah Alexander, a myeloma patient and founder of the Tackle Myeloma Foundation, says this insurance inequity must end: "This unequal coverage is unreasonable and unfair. I just take a pill at home, I feel good and I'm again active in my work and with my family. As patients we should be able to take advantage of the best care, and not be limited to what our insurance will cover."

The Statement of Principles is in keeping with sessions at the ASCO conference that go beyond clinical trial data to discuss the impact of financial issues on access to, compliance with, and reimbursement for cancer therapies. **MT**

*Source: *Cancer Facts & Figures 2009*, American Cancer Society

THE CANCER PATIENT STATEMENT OF PRINCIPLES:
Prevention, Innovation, Access, and Early Approvals

PRINCIPLE 1: ***Prevention is the key to reducing the burden of cancer. We must support every reasonable attempt to encourage studies of cause and prevention to reduce the number of new cancer cases.***

- A study in the *Journal of Clinical Oncology* projects that the number of new cancer cases diagnosed each year will jump 45 percent in the next 20 years.
- In multiple myeloma an even greater increase (57%) is projected, and we are already seeing increasing diagnoses in patients under age 65 including patients in their thirties, in what was once a "rare disease of the elderly."

PRINCIPLE 2: ***Continuing innovation is critical to the early diagnosis and the more effective and safer treatment of the vast majority of patients with cancer***

- We are in full support of the tenets of the 21st Century Cancer ALERT Act and other federal initiatives that support and encourage research.
- We believe in the importance of new and better tests to ensure the early diagnosis of all clinically significant forms of cancer.
- We believe a deep, diverse pipeline of new and better treatments will lead to better outcomes and a better quality of life for all patients.
- We believe in full funding of legislation that promotes and encourages drug and biomarker research and development intended to bring new options for patients in need.

PRINCIPLE 3: ***Equality of access (and equality of insurance coverage) should be available to all patients for all approved cancer treatments.***

- Every cancer patient should have access to the treatments recommended by their physicians.
- Patients should not suffer from cost discrimination based on the type of therapy provided or the mechanism of delivery
- Oral drugs should have the same coverage as intravenous drugs, surgery, radiation, transplantation, etc.
- The Medicare donut hole is an arbitrary and unfair burden on our most vulnerable citizens.

PRINCIPLE 4: ***National policies and procedures for early approval of new treatments for cancer and other deadly diseases need to be reformed and streamlined.***

- In the interests of patients with disorders with a five-year survival rate of less than 50 percent, the emphasis should be on proof of effectiveness and early availability, with full disclosure of risk for adverse effects.
- A more efficient mechanism is needed for early approval of off-label uses of already approved medications, possibly based on registry data, actual clinical practice, peer-reviewed studies and NCCN guidelines without the expense and delay of complex and time-consuming clinical trials.

PRINCIPLE 5: ***An efficient and effective mechanism is needed to permit access to unapproved and experimental therapies for patients who have exhausted other available possibilities.***

- In the United Kingdom, in 2008, the Department of Health gave approval to a network of 19 hospital units where terminally ill cancer patients can volunteer to participate in trials of experimental cancer therapies that may be years away from approval.
- It should be easy, not difficult, for patients who have run out of other options to gain access to investigational drugs whenever possible – with appropriate clinical input.

PEOPLE HELPING PEOPLE

You are never alone in your battle against myeloma

Support groups walk Miles for Myeloma

Philadelphia was once again the site of a pioneering effort to raise awareness of multiple myeloma while raising funds for research when the Miles for Myeloma 5K Walk/Run came to town. The April 25th regional event was co-presented by the Philadelphia Multiple Myeloma Networking Group, and the Central New Jersey and Northern New Jersey Multiple Myeloma Support Groups.

Many runners, walkers, volunteers, patients, family, and friends gathered in the City of Brotherly Love to join the movement to find a cure for myeloma. Participants enjoyed the beautiful views of Boathouse Row, Kelly Drive, the Philadelphia Museum of Art, and the city skyline along the Martin Luther King Drive walk/run route.

Proceeds from the event will benefit the research initiatives of the IMF and the MMRF. The IMF thanks all who took part in this unforgettable day, with special thanks to Miles for Myeloma chairpersons Karen Horan, Marilyn Alexander, Sharon Klein, Paula Van Riper, Maddie Hunter, and Ann McNeil.

22-year myeloma survivor heads a new group

Carole Levis was diagnosed with myeloma 22 years ago. "When I was first diagnosed, my grandson was 4 years old, and my goal was to live long enough to see him graduate from high school. I've now seen him graduate from college. When I was diagnosed, my granddaughter had not yet been born. She is now 13 years old, and my goal is to be around to see the woman she becomes."

Another goal Carole set for herself as she was about to undergo her third transplant in December 2008, was to find a way to serve the local myeloma community. Since there was no myeloma-specific support group in the area, she decided to take on the task of starting one. Carole has a long history of service, from working at a senior center and styling wigs for chemotherapy patients to headlining a Red Cross blood drive and working with Down's Syndrome children.

Carole spoke with Susie Novis about starting a new support group in DuBois, PA. Susie put Carole in touch with Robin Tuohy (IMF Regional Director, Support Groups, Northeast). "The IMF and my local cancer center were a great help in getting this much-needed support group off the ground and, only six weeks later, our group was holding its first meeting," says Carole. "I know how important myeloma education is, and I feel very blessed to be able to help others who are coping with the disease that has been a part of my life for 22 years."

The first meeting of the Tri-County Multiple Myeloma Support Group took place on June 23, with 10 people in attendance. The group will continue to meet from 6 to 8 p.m. on the fourth Tuesday of each month at the DuBois Regional Medical Center West. For more information, please contact Carole Levis via c.levis@msn.com or 814-372-2428.

New Michigan group off to a good start

IMF is pleased to announce a new myeloma support group in Michigan. Members of the Flint Area Multiple Myeloma Support Group held their first meeting on February 19. The inaugural meeting proved to be an excellent way for participants to meet and interact with fellow myeloma patients, their family members, and friends, as well as learn new aspects about the treatment and management of myeloma. This group has continued to meet the on the third Thursday of each month from 6:30 to 8 p.m. at the Great Lakes Cancer Institute. For more information, or to join the growing ranks of group members, please contact Judy or Morley Biesman via judy@biesman.com or at 810-732-4738. **MT**

How to Start a Myeloma Support Group

- Secure a location for the meeting as soon as practical. Consider parking availability and handicap accessibility. Some suggestions are hospitals, community centers, libraries, and churches.
- Pick a date and time convenient to you, taking into consideration the best time for others to come to the meeting. Groups typically meet for two hours, and on a monthly basis.
- Compose a letter that you can send to doctors, clinics, hospitals, and patients and family members informing them of the group. Ask the office of your local oncologist to inform their patients about your group and post your flyer in their office.
- List your group's meeting date, time, and place in your local newspaper's health section (free). Involve local radio and TV media to help create awareness of your group.

How the IMF can assist you

- Provide direction and ongoing assistance in starting your myeloma support group.
- List your support group on the IMF website.
- Create a basic website for the group.
- Design a flyer for the group.
- Mail out a flyer to patients in the area to help with outreach.
- IMF staff can visit and provide you with free IMF publications and information.
- Provide you with an annual DVD of an IMF Patient & Family Seminar.
- Offer free IMF Patient & Family Seminar registration for support group leaders.
- Access to specific website exclusively for IMF Support Group Leaders, as well as the Support Group Leader Listserv.
- Invite you to the IMF Annual Support Group Leader Retreat.

IMFERS RAISE FUNDS TO BENEFIT MYELOMA COMMUNITY

By Suzanne Battaglia

The "JC" Golf Tournament

The 10th annual "JC" Golf Tournament was held at Wapicada Golf Course in St. Cloud, MN, on May 16, 2009. Participants of the "Best Ball-Scramble" got going with a shot-gun start shortly after noon. The afternoon of golf was followed by an evening enjoyed by both players and non-golfers. A delicious dinner was served thanks to major sponsors Green Mill Restaurant and Short Stop Custom Catering. Prizes and a silent auction kept everyone entertained before the guests hit the dance floor to the sounds of the band "Canoise."

This year's event marked a decade of celebrating the memory of Janet "JC" Johnson by raising funds to benefit the IMF and those affected by multiple myeloma. All proceeds from the "JC" Golf Tournament go to support IMF programs. Over the past ten years, the organizers have raised over $150,000 to fund research and other IMF programs that benefit the myeloma community

Our sincere thanks go out to all the sponsors, donors, volunteers, tournament participants, and dinner guest for the continued support and generosity that have helped make this event such a huge success year after year.

Music Against Myeloma

On April 25, New York City's chic BLVD bar was the site of the fourth annual Music Against Myeloma. The evening of great company, wonderful food, and sensational live music was enjoyed by nearly 150 guests who gathered to support the work of the IMF.

Thanks to performers Danielia Cotton, Dave Murphy, Matt Ostrower, and the Turn, as well as Sugar Sweet Sunshine bakery, Murray's Cheese, and the popular "Cancer Sucks" socks, the Music Against Myeloma fundraiser has had yet another stellar year.

Music Against Myeloma was co-founded in 2005 by Slava Rubin, whose father passed away from myeloma in 1993, and Matt Ostrower, whose family has also been touched by cancer. After four successful years in New York City, the two are now thinking of taking the event nationwide. All funds raised go to support myeloma research in memory of Mark Rubin.

Spring Forward Benefit

Joseph Bellomo with colleague Taraneh Naddafi

On April 25, Joseph Bellomo and colleagues at Joseph Bellomo Architects Inc. hosted an evening to benefit the IMF and the Palo Alto High School Theater Boosters. Facebook offered the use of their corporate café as the site of the fundraiser. The event featured gourmet food by Facebook Chef Josef Desimone and his team, a wine bar, and live music. Original artwork from a local artist and high fashion designer displays for a silent auction enhanced the cocktail party atmosphere for the 80 guests in attendance. Ticket sales, donations, and auction items donated by individuals and local businesses, including Joseph Bellomo Architects, contributed to the overall success of the event, but the main focus of the evening was to raise awareness of myeloma. Joseph Bellomo and his architectural firm plan to continue their work on behalf of the myeloma community by helping fund myeloma research through annual fundraising events.

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). **MT**

UPCOMING MEMBER EVENTS

Sept 1-30, 2009 **Salon 926 Myeloma Awareness Month** – Wilmington, DE
Kerri Marioni, salon926@verizon.net or 302-426-9926

Sept 2009 (date TBD) **Multiple Musicians Against Multiple Myeloma** – Great Neck, NY – Naomi Margolin, nmargolin@aol.com or 516-487-6712

Sept 2009 (date TBD) **Heuer Golf Tournament** – Caledonia, NY
Nancy Heuer, nheuer@cob.rit.edu or 585-538-4333

Sept 5, 2009 **Fiacco Golf Tournament** – Canton, NY
Melanie Nichols, LMNichols94@yahoo.com

Sept 25, 2009 **Misbehaving for MM** – Chicago, IL
Alexandra Zousmer, aezous@gmail.com or 858-354-9802

Sept 27, 2009 **Pytlik Memorial Walk** – North Tonawanda, NY –
Barb Pytlik, bpcb3@hotmail.com or 716-400-3698

October 11, 2009 **Coach Rob's Benefit** – Apopka, FL
Rob Bradford, rbradford@crothall.com

November 7, 2009 **Evening 4 A Cure** – East Amherst, NY
Jerra Barit, bufbarits@roadrunner.com or 716-472-1620

Fly a Virtual Kite & Gain a Donation for the IMF

Celgene has created Multiple Expressions, a website where patients and caregivers can create a "kite for a cause" and post expressions of support for friends and loved ones with multiple myeloma. When you create a virtual kite, Celgene will make a donation to the IMF. Go to **multipleexpressions.com** to add your kite and help the IMF.

MYELOMA TODAY IN CONVERSATION WITH DAVID BROWN

You have had myeloma for many years. When were you diagnosed?

In 1978, I was 40 years old and seemingly in good health. My only complaint was a pain in my back. Eventually, that back pain brought me into the office of an orthopedic surgeon, who found what he thought to be a cyst in my thoracic spine. The mass was surgically excised and biopsied. The lab result was quite unexpected: the "cyst" turned out to be multiple myeloma.

Prudy & David Brown

How did you react to the news?

Not surprisingly, I was very scared. I tried to look at my situation objectively and saw two possible paths to follow. One was to place myself in the hands of the doctors and follow whatever instructions they gave me. The other approach was to learn as much as possible about my diagnosis. I chose the former path and did everything my doctor told me to do. The orthopedist referred me to an excellent hematologist – although not a myeloma specialist – and I was given a prognosis of a two- to three-year survival. At the time, this sounded like the best news I'd heard. I had two kids in school, in fifth and eighth grade, and I was thankful to have more years with them.

After I completed a course of radiation, I put the diagnosis out of my mind and tried not to lose any sleep over it. I do remember having some silly thoughts like, "I just bought a new pair of tennis shoes. I shouldn't have done that. My wife is going to need that money!" Otherwise, I settled into life as usual. My intermittent lab tests kept coming up okay and I had no further anti-myeloma treatment for the next 15 or 16 years. In hindsight, I now realize just how very fortunate I was.

In those early years, did you keep the diagnosis private?

I told my friends about the diagnosis and discussed it freely when asked. At work, I told my supervisor and a couple of colleagues, asking them to keep the information confidential. I stated that I didn't want either any special attention or any assignment limitations. As far as I know, they honored my request.

Have you ever wondered how or why you got myeloma?

As a child, I lived in the Panama Canal Zone and was likely exposed to some environmental toxins but I am unaware of any specific exposure linked to myeloma. By profession, I am an electronics engineer specializing in designing computer software for hospital information systems.

Let's get back to talking about your history with myeloma…

In 1993 or 1994, I got a pain in my shoulder and simply assumed I had bursitis. I took some aspirin and kept playing tennis. I had lab tests performed a couple of months prior but I didn't pay much attention to my numbers in those years and don't know if there had been a trend toward my myeloma becoming active again. The shoulder pain turned out to be the result of a myeloma lesion on my cervical spine. I underwent another course of radiation and a couple of rounds of dexamethasone. Three months later, myeloma destroyed one of my ribs.

After so many years of "smooth sailing," how did you react to having to confront myeloma again?

I figured that it was time to change my philosophy. I hit the local health library and started reading up on myeloma. The information was less than cheerful to say the least. When I'd come across the word "incurable" or when the data got too depressing to deal with, I'd head to the ice cream shop located across the street from the library. Then I'd get back to doing my homework. The librarians were a huge help to me in those days. I learned a lot about the disease and also identified the best doctors in the field. I flew to Arizona to see the late Dr. Sydney Salmon. He told me I had "indolent" myeloma – my wife says "indolent" describes my personality perfectly! – and he suggested I harvest my bone marrow. I did as he advised. (By the way, that bone marrow is still in storage.)

Did you continue to gather information about myeloma?

Yes. Around the time I went to see Dr. Salmon, my wife and I attended our first IMF Patient & Family Seminar. This was in the early years of the IMF seminar program – they were not yet the grand productions they are today – but we found the meeting incredibly helpful. We have continued to attend the IMF seminars when they come to our area, both to further educate ourselves and to meet other myeloma patients and caregivers. We also occasionally attend the meetings of our local myeloma support group. In addition, I have found the online myeloma listserv sponsored by the IMF to be an incredible source of knowledge, and I review it daily.

Do you find it useful to interact with other members of the myeloma community?

Yes. For me, this is also a way of giving back. Throughout the years, friends and acquaintances have put me in touch with newly diagnosed myeloma patients, and I've tried to be helpful and encouraging to them. I also try to be helpful to fellow patients at support group meetings and at IMF seminars.

What is your myeloma status now?

I have been on one form of treatment or another since 1993 or 1994, with various combinations of radiation, melphalan, prednisone, dexamethasone, thalidomide, Biaxin®, Cytoxan®, and Revlimid®. I am now more knowledgeable about my disease, so I am more able to engage in a dialogue about my condition and treatment with my local oncologist and with Dr. Brian Durie, my myeloma specialist.

And how is your life otherwise?

I certainly don't sit around worrying about myeloma, and I don't pay attention to statistics. I believe that there is no one on Earth who knows how long I am going to live with myeloma, so I take things one day at a time. I retired from work in 1998. I try to take good care of my wife/caregiver, as I think this experience has been harder on her than on me. We travel, we play bridge, we enjoy our life – especially visiting our four grandchildren. I like reading, working out with a personal trainer, and playing tennis and hiking. I am very thankful for my good fortune, for the support of my wife and family and friends, and for the good medical care I've received over the years. It has been 31 years since my myeloma diagnosis. I have been incredibly lucky. **MT**

WHAT DO YOU GET AT AN IMF PATIENT & FAMILY SEMINAR?

Education • *Access to Experts* • *Camaraderie*

Topics Covered

- *What's New in Myeloma?*
- *Ask-the-Expert*
- *Managing Side Effects*
- *How to be a Better Patient*
- *Frontline Therapy*
- *Transplant*
- *Bone Disease*
- *Maintenance Therapy*
- *Relapse*
- *Novel Therapies*

Go to our website **www.myeloma.org** *and click on the "Seminars and Meetings" tab for more details, the most up-to-date faculty, hotels and registration information.*

Upcoming 2009 Patient & Family Seminars

Washington, DC
August 7-8, 2009

Minneapolis
August 28-29, 2009

2009 Regional Community Workshops (RCW)

If you cannot get to a P&F Seminar, consider attending a Regional Community Workshop. These half-day meetings provide Education, Access to Experts, and Camaraderie. Upcoming RCWs will be held in Arizona, Colorado, Hawaii, Kansas, Ohio, and Texas. Registration is free *but you must register*. It's a great way to learn from myeloma experts, as well as share experiences and gain strength from others in the IMF family. Find more details about the next RCW near you at our website.

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www.myeloma.org
(800) 452-CURE (2873)
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Dedicated to improving the quality of life of myeloma patients while working towards prevention and a cure.

2009 IMF Calendar of Events

Aug 7-8	IMF Patient & Family Seminar – Washington, DC
Aug 28-29	IMF Patient & Family Seminar – Minneapolis, MN
Sept 11-12	Myeloma Canada Patient & Family Seminar – Calgary, CANADA
Sept 11	IMF Regional Community Workshop – Honolulu, HI
Sept 16	IMF Clinical Conference – St. Petersburg, RUSSIA
Oct 1	IMF Regional Community Workshop – Shreveport/Bossier City, LA
Oct 3	IMF Regional Community Workshop – Longview, TX
Oct 12	IMF Physician Community Workshop – Valencia, SPAIN
Oct 13	IMF Regional Community Workshop – Murcia, SPAIN
Oct 14	IMF Regional Community Workshop – Madrid – SPAIN
Oct 15	IMF Regional Community Workshop – Pamplona, SPAIN
Oct 16	IMF Physician Community Workshop – Barcelona, SPAIN
Oct 17	IMF Patient & Family Seminar – Seville, SPAIN
Oct 17	IMF Regional Community Workshop – Cincinnati, OH
Oct 23	IMF Patient & Family Seminar – Torino, ITALY
Oct 25	Patient & Family Seminar – Heidelberg, GERMANY
Oct 26	IMF Physician Community Workshop – Stuttgart, GERMANY
Oct 30	IMF Patient & Family Seminar – Paris, FRANCE
Nov 7	3rd Annual Comedy Celebration – Los Angeles, CA
Nov 14	IMF Regional Community Workshop – Florence, ITALY
Nov 14	Southwest Symposium – Tempe, AZ
Nov 16	IMF Regional Community Workshop – Bologna, ITALY
Nov 17	IMF Physician Community Workshop – Pavia, ITALY
Nov 19	IMF Regional Community Workshop – Stuttgart, GERMANY
Nov 21	Patient & Family Seminar – Karlova Studanka, CZECH REPUBLIC
Nov 21	IMF Regional Community Workshop – Overland Park, KS
Nov 22	IMF Japan Patient & Family Seminar – Niigata, JAPAN

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.

Thank you for your continued support of the IMF. Because of your contributions, we have been able to maintain the full range and quality of the programs we offer.