



*Accelerating
the
Search
for a
Cure*

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MYELOMA FOCUS

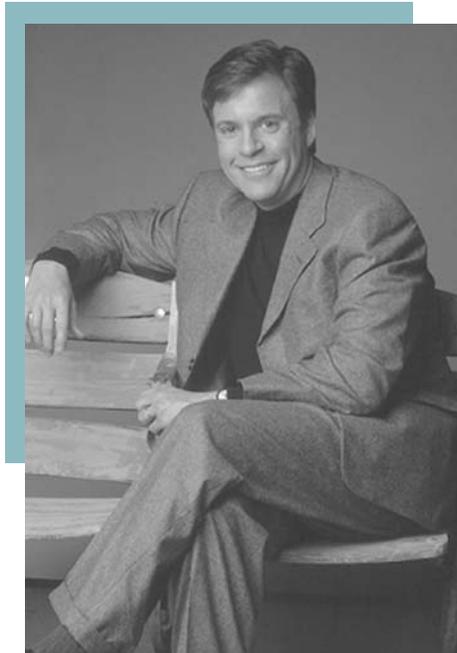
Newsletter of the

MMRF

MMRF Public Awareness Award Goes to Bob Costas

Ann Landers Research Fund Award To Be Announced

Bob Costas, award-winning broadcaster for NBC and HBO, will receive the MMRF Public Awareness Award at the 2003 MMRF Chicago Awards Dinner to be held on March 4th at the Four Seasons Hotel in downtown Chicago. The event will also include the presentation of the MMRF Ann Landers Research Fund \$100,000 Award to a Chicago-based myeloma institution in memory of the legendary advice columnist. The award is being sponsored by Chicago Tribune Company, publisher of Ms. Landers' long-time home newspaper.

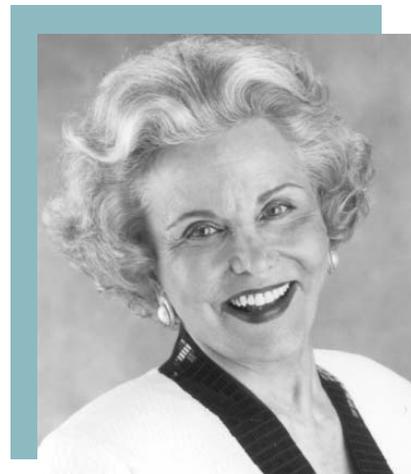


Bob Costas
award winning broadcaster

Mr. Lester B. Knight, founding partner of RoundTable Healthcare Partners, will serve as the Event Corporate Chairman. Joining Mr. Knight on the event leadership team is Ms. Susan Crown, Vice President, Henry Crown and Company; Mr. Harry Kraemer, CEO, Baxter International; Mr. Ron Labrum, Executive Vice President, Cardinal Healthcare; Mr. Andy McKenna, CEO, Schwarz; Mr. Bill Osborn, CEO, the Northern Trust Company; Mr. Philip Purcell, CEO, Morgan Stanley; and Mr. Patrick Ryan, CEO, Aon Corporation.

Bob Costas has been a long-time supporter of the Multiple Myeloma Research Foundation, serving as the emcee of the 2001 New York City Awards Dinner, and he also serves as an Honorary Board Member for the MMRF. Mr.

Costas has done a tremendous amount to heighten cancer awareness. In 1998, the Bob Costas Cancer Center opened at Cardinal Glennon Hospital in St. Louis, MO to honor Bob for his dedication to the children in St. Louis and beyond. Through Bob's efforts, more than \$10 million has been raised to deliver some of the most advanced medical care available in the world. For more information on the event, please contact Craig Robertson, MMRF Director of Development, at robertsonc@themmrf.org



Ann Landers
legendary advice columnist

Welcome Letter

Families Funding Research

Joan Lesnick and Steve Zatz

Dear Friends,

Last year the MMRF was proud to fund \$4 million in targeted myeloma research grants, including 19 Senior Research Grant awards and \$1.5 million to Johns Hopkins University as a 3-year Collaborative Program Grant. These MMRF grant recipients are some of the most promising myeloma researchers investigating new therapy combinations, vaccine approaches and how treatments such as Velcade work.

In addition to our own support of myeloma research, we also continue to work closely with the National Cancer Institute (NCI) to ensure improved federal support of myeloma research. Since the MMRF was founded, the NCI's myeloma funding level has grown from \$10.8 million to \$22 million in fiscal year 2003. This growth has helped to stimulate advances in myeloma treatments and therapies that have greatly improved patients' lives. But as we all know, more needs to be done.

We can only keep the pace we've set if everyone pitches in -- and there are so many ways to do that this year. With six MMRF Race for Research events and three corporate fundraising events scheduled across the country, there are many ways to be a part of the MMRF cause. By supporting these events, you are directly supporting myeloma research. Please get involved and help us continue to accelerate the search for a cure. Check the MMRF calendar of events on page 11 for details.

Kathy Austin

When Joan Lesnick learned of her mother's myeloma diagnosis two years ago, the MMRF was one of the first places she turned to. She downloaded information from the MMRF website and read it on the plane to San Diego, where her mother, Dolores Lesnick, lives. That 3,000-mile trip was much further than she would have to travel in the months to come to support her mother and the search for a cure.

Though Dolores and Joan live on opposite coasts, the myeloma resource Joan relied on immediately was right in her own backyard. As New Canaan, CT residents, she and her husband, Steve Zatz, MD, decided that contributing to the MMRF would be the best way to support some of the most aggressive and promising new therapies for myeloma patients. Since that time they have made significant contributions to the MMRF and Joan has dedicated her time as a volunteer in the MMRF's New Canaan office.



Joan Lesnick with her mother Dolores

Joan has been able to see her contributions at work up close. She has helped the foundation organize and update its membership database and has also helped as a participant in the second Blood Cancer Advocacy Day.

"Being in the office I see just how hard everyone works, and how much of every dollar raised is going straight to research." She knows that this is in part because of volunteers like herself, who keep operating costs to a minimum and ensure that dollars go straight into the hands of researchers. She is grateful for the opportunity to give and to the MMRF for raising awareness of the disease.

Joan is thankful that her mother is receiving excellent care under the direction of James Berenson, MD, of Cedar-Sinai Medical Center, and member of the MMRF's Scientific Advisory Board. Through the efforts of researchers, the MMRF, its supporters and volunteers -- including Joan and Steve -- she knows that every day we are closer to a cure.



1-800-flowers.comSM

Order the freshest flowers, sweets and novelty items for holidays and special occasions. Use the promotional code **MMRF** when you place an order and you will be supporting the fundraising efforts to accelerate the search for a cure. Call 1-800-Flowers (1-800-356-9377) or order on-line at www.1800flowers.com.

FUNDRAISING

MMRF Race For Research 5k Walk/Run

San Francisco April 13, 2003

The 2nd annual MMRF Race for Research -- San Francisco, will be held Sunday, April 13th at Crissy Field in the Golden Gate National Recreation Area. The 5K Walk/Run begins at 8 AM with registration opening up at 6:30 AM. Proceeds from the event will go directly to fund myeloma research. This year's event chairman will be Mark Ahn, Vice President of Hematology at Genentech, Inc. Genentech, a leading bio technology company based in South San Francisco, is back as this year's flagship sponsor of the event.

Boston April 27, 2003

The 1st annual MMRF Race for Research -- Boston, will be held on Sunday, April 27th at the Esplanade. The 5K Walk/Run begins at 9:00 AM, with registration opening up at 7:30 AM. Proceeds from the event will go directly to fund myeloma research. Dr. Ken Anderson, Director of the Jerome Lipper Multiple Myeloma Cancer Center and Chairman of the MMRF Scientific Advisory Board, will serve as the Honorary Chairman. The flagship sponsor of this year's event will be Cambridge, MA based Millennium Pharmaceuticals, Inc.

To register or to get more information on these events, please contact Craig Robertson, MMRF Director of Development, at robertsonc@themmrf.org or call 203-972-1250

2003 MMRF Special Events Calendar

Join the tens of thousands of patients, family members and their friends helping the MMRF to make a difference. Plan to participate in, or volunteer at, one of the many fun and exciting MMRF special events scheduled throughout the year.

March 4 - MMRF Chicago Awards Dinner - Chicago, IL
April 10 - MMRF Laugh for the Cure - New York, NY
April 13 - MMRF Race for Research 5K Walk/Run - San Francisco, CA
April 27 - MMRF Race for Research 5K Walk/Run - Boston, MA
June 9 - MMRF New York City Awards Dinner - New York, NY
June TBA - MMRF Race for Research 5K Walk/Run - Cleveland, OH
July 19 - MMRF Race for Research 5K Walk/Run - Seattle, WA
August TBA - MMRF Race for Research 5K Walk/Run - Philadelphia, PA
September 14 - MMRF Race for Research 5K Walk/Run - Chicago, IL
October 25 - MMRF Friends for Life Fall Gala - Greenwich, CT
October TBA - MMRF Race for Research 5K Walk/Run - Atlanta, GA

PEPSICOLA, NA HEADLINES 2003 FALL GALA

The MMRF is excited to announce that the 2003 Fall Gala will be chaired by Dave Burwick, SVP and Chief Marketing Officer of Pepsi-Cola North America, the refreshment beverage unit of PepsiCo Inc. The Gala will be held on Saturday, October 25, 2003, at the Greenwich Hyatt in Greenwich, CT.



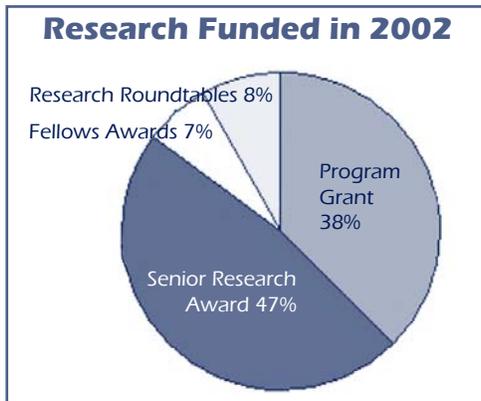
Dave Burwick

As the MMRF is the world's leader in funding myeloma research, PepsiCo is the world leader in convenient foods and beverages. Both organizations share a passion for making a difference. With its world headquarters located in Purchase, NY, PepsiCo has a long history of corporate citizenship. Its people feel a responsibility to contribute to the quality of life in the communities where they work and live. This philosophy is put into action through support of social agencies, projects and programs. The scope of this support is extensive -- ranging from sponsorship of local programs and support of employee volunteer activities, to contributions of time, talent and funds to programs of local and national impact. The MMRF is proud to have PepsiCo as our corporate partner for the 2003 Fall Gala. For further information or for volunteer and donation opportunities, please contact Jennifer McMahon at 203-972-1250.



MMRF FUNDS \$4 MILLION IN RESEARCH

The MMRF committed an unprecedented \$4 million to funding cutting-edge myeloma research in 2002, including one Collaborative Program Grant for \$1.5 Million, 19 Senior Research Awards for \$100,000 each and seven Fellows Awards for \$40,000 each. We finalized six year-end Senior Research Awards on New Year's Eve, which were made possible by 2002's successful fundraising efforts. Thank you to all who supported the Foundation and made it possible for us to continue to fund research that is designed to improve our understanding of the disease and accelerate the availability of new, effective treatments.



in their proposal, remissions induced by allogeneic lymphocytes highlight the anti-tumor immune response as the only therapy currently capable of fully eradicating the malignant clone.

Project 1, led by Drs. Levitsky and Borello, builds upon preliminary studies of marrow infiltrating lymphocytes (MILs) obtained from patients in their ongoing myeloma tumor-cell based vaccine trial. The frequency, avidity and function of myeloma-specific T

cells within this population will be examined, and strategies for the ex vivo expansion of such cells will be optimized for use in adoptive immunotherapy.

2002 Collaborative Program Grant

The MMRF announced in October that a team of researchers led by Hyam Levitsky, MD, was the winner of our second Collaborative Program Grant. The grant provides \$1.5 million in funding over three years, and is designed to foster unique collaborations among researchers and institutions to help bring new therapies to clinic quickly.

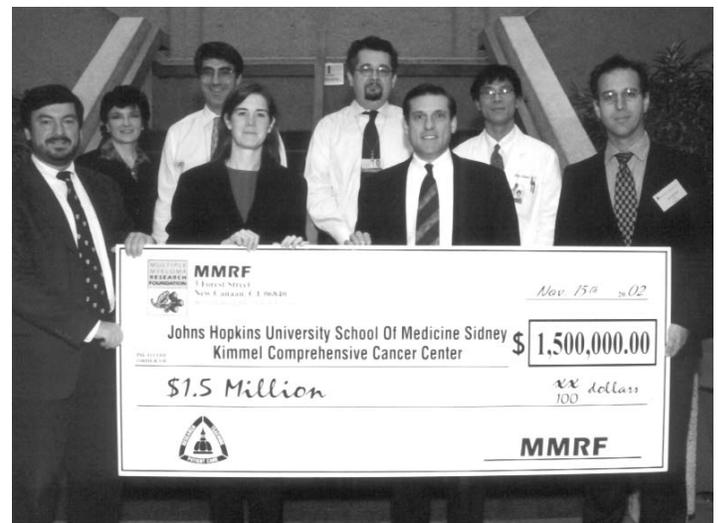
"The MMRF Collaborative Program Grant really helps to synergize the research of physician-scientists in the fields of cancer immunotherapy, bone marrow transplantation, and cancer stem cell biology. This award enables a critical mass of investigators at Johns Hopkins to focus on multiple myeloma in a way that was previously not possible," said Dr. Levitsky.

This Collaborative Program, entitled Analysis and Therapeutic Manipulation of Myeloma Specific Immunity, brings together experts in the field of tumor immunology, stem cell biology and bone marrow transplantation to focus on understanding the immunobiology of myeloma and manipulating the immune response to eradicate this disease. In addition to Dr. Levitsky, the principal investigators are: Ivan Borello, MD, Ephraim Fuchs, MD, Richard Jones, MD, Leo Luznik, MD, and William Matsui, MD.

This research focuses on three critical aspects of myeloma biology and the anti-myeloma immune response, and each seeks to augment the therapeutic efficacy and specificity of the response. The three projects are bound by the strong evidence of immune recognition of multiple myeloma from animal models and analysis of patient samples. As the researchers point out

Project 2, led by Drs. Jones and Matsui, studies the phenotype and antigenic profile of myeloma progenitor cells, which are the ultimate target for any curative therapy.

Project 3, led by Drs. Fuchs and Luznik, examines the relative efficacy of allogeneic and post-transplant vaccine-induced tumor-specific immunity as well as the role of host and donor T-cells in anti-tumor immunity after non-myeloablative allogeneic bone marrow transplant for multiple myeloma.



Anne Quinn Young, MPH, MMRF Program Director and Scott Santarella, MMRF Executive Director, present Dr. Hyam Levitsky (front row, far left) and his team with a check for \$1.5 million at the November 15 Institutional Insights Symposium at Johns Hopkins.

2002 FALL SENIOR RESEARCH AWARDS

The MMRF is funding six Senior Research Awards. These winning researchers represent the most highly rated grants and have at least five years of experience in blood cancer research. Each recipient will receive a one-year \$100,000 grant.



Robert G. Fenton, MD, PhD University of Maryland, Baltimore
Anti-Apoptosis Mechanisms of Mcl-1 in MM

Our laboratory has shown a protein called Mcl-1 helps keep MM cells alive; blocking Mcl-1 production induces the rapid death of MM cells through apoptosis. We will analyze the mechanisms through which Mcl-1 protects the MM cells from apoptosis to generate a model of Mcl-1 function. The knowledge gained will be used to develop an experimental system to identify small molecule inhibitors of Mcl-1 with the potential of becoming potent anti-myeloma drugs.



Jonathan D. Licht, MD Mount Sinai School of Medicine
Functional Characterization of the MMSET Domain Protein

A recent discovery that MM cells harbor shuffled, rearranged genes may lead to changes in gene function and the development of the disease. We are studying one such gene, MMSET, which we

believe makes a protein that in turn represses other genes in the cell. We will try to lower MMSET levels within myeloma cells to determine if MMSET levels within myeloma cells might represent a new therapeutic target.



John A. Lust, MD, PhD Mayo Clinic
Inhibition of IL-1 in the Myeloma Micro-environment

We are focused on the role of cytokines in the transition from MGUS to smoldering MM (SMM) to active MM. We found that the IL-1 β produced by patients with progressive disease induces IL-6 levels that are significantly higher than the levels generated by patients with stable disease. We have developed a clinical trial using IL-Ra in patients with SMM who are at high risk for progression to active myeloma.



Constantine S. Mitsiades, MD, PhD Dana-Farber Cancer Institute
The IGF/IGF-1R System as a Major Therapeutic Target for Myeloma

We seek to increase the anti-myeloma (MM) effects of standard or new therapies by blocking the activity of insulin-like growth factors (IGFs). IGFs, which are present in the bone marrow (BM) of MM patients, decrease the anti-MM effect of current therapies. We will define new strategies to decrease the production of IGFs in the BM and block the protec-

tive effect of IGFs on MM cells against therapy to improve the outcome of patients with MM.



G. David Roodman, MD, PhD University of Pittsburgh
p62ZIP and Myeloma Bone Disease

Myeloma cells produce factors that increase osteoclasts, the cells that destroy bone. We will characterize the role of a recently identified member of the NF κ B signaling pathway, p62ZIP, in osteoclast formation and myeloma cell growth, and determine if blocking or deleting the p62ZIP gene in mice decreases osteoclast formation and the capacity of cells to support the growth of myeloma cells.



Frits van Rhee, MD, PhD University of Arkansas for Medical Sciences
Immunotherapy with Myeloma-specific Cytotoxic T Lymphocytes

Bone marrow transplantation and chemotherapy can cure myeloma in some patients, but in most, the disease eventually returns because of drug-resistant myeloma cells. To eliminate drug-resistant cancer cells, we plan to activate patients' immune cells to recognize and kill myeloma cells by expressing genes or proteins unique to cancer and myeloma in a subset of immune cells called dendritic cells.



INDUSTRY UPDATE

Millennium Submits NDA for Velcade®

Millennium Pharmaceuticals, Inc. recently announced that it has submitted a New Drug Application (NDA) with the Food and Drug Administration for approval to market its proteasome inhibitor Velcade (bortezomib) for injection (formerly known as PS-341) as a treatment for relapsed and refractory myeloma. (See page 10 for more information about NDAs and the drug approval process.)

The NDA filing for Velcade is based primarily on the results of the Phase II SUMMIT trial, final results of which were reported at the American Society of Hematology (ASH) in December and covered in our Special Edition newsletter. This trial included 202 patients with advanced relapsed and refractory disease who had received an average of 6 previous therapies. An overall response rate of 35% was seen with Velcade therapy and 59% of patients experienced a response or stable disease. Velcade was generally well tolerated and adverse events were predictable and manageable.

The Phase III APEX study, an international, multicenter trial of Velcade is currently underway. It will include a total of 600 patients with progressive disease.

Doxil®: A Potential New Treatment Option for Myeloma

Doxil (doxorubicin liposome injection, Ortho Biotech) is a new formulation of doxorubicin being investigated for use in myeloma. It is being evaluated as an alternative for Adriamycin, a brand of doxorubicin, in VAD (vincristine, Adriamycin, dexamethasone) therapy. It is also being tested in combination with vincristine, dexamethasone, and thalidomide (DVD-T).

Results of a Phase II study of Doxil, vincristine and reduced-dose dexamethasone in patients with newly-diagnosed myeloma were recently reported by the Cleveland Clinic (see the table below). The study showed that the regimen has fewer side effects, including cardiotoxicity, than conventional doxorubicin while maintaining effectiveness.

The Doxil formulation packages doxorubicin inside microscopic fat bubbles called liposomes. The liposomes are surrounded by a layer of hair-like strands of a substance called

polyethylene glycol, a process called pegylation, which allows Doxil to stay in the blood for a longer period of time. There, it has more time to reach tumor tissue, where the drug is slowly released from the liposome. Both agents are given intravenously and physicians must keep track of the total amounts of doxorubicin administered to a patient over time. With the VAD regimen, doxorubicin is administered by continuous infusion for 4 days, requiring insertion of a central line and a pump. Use of Doxil in the regimen is more convenient, as it is administered in a 2 to 3 hour injection once every 4 weeks.

Response	Percentage of Patients (n=33)
Overall response	88%
Complete response	12%
Major response	55%
Minor response	21%
Stable disease	9%

Visit Clinical Trials Monitor (CTM) on the MMRF's web site (www.multiplemyeloma.org) for more information on Velcade and Doxil trials.

The MMRF Thanks
the following corporations for their support of Myeloma Focus

Celgene



Chugai Pharmaceutical



Millennium



Ortho Biotech



MYELOMA FOCUS

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The information herein is not intended to replace the services of trained health professionals (or to be a substitute for medical advice.) You are advised to consult with your healthcare professional with regard to matters relating to your health, and in particular, regarding matters which may require diagnosis or medical attention.

MMRF ANNOUNCES

The MMRF Clinical Trials Monitor (CTM) currently lists more than 80 trials at more than 100 sites worldwide. CTM is continuously updated to include the most cutting-edge pharmaceutical and single-institution trials. Information about these and other trials can be found on the MMRF website at www.multiplemyeloma.org.

Trials Posted on CTM

Phase III Open-Label Study of VELCADE Versus High-Dose Dexamethasone/ Assessment of Proteasome Inhibition for Extending Remission (APEX) at 50 locations worldwide

Phase III Trial of Thalidomide + Dexamethasone Versus Dexamethasone for Newly Diagnosed Myeloma – Mayo Clinic (MN)

Phase II Study of Arsenic Trioxide as Maintenance Therapy in Patients with Multiple Myeloma Following High-dose Chemotherapy and Stem Cell Transplant – Jewish Hospital (OH)

Phase II Trial of Autologous Stem Cell Transplant Followed by Miniallogeneic Stem Cell Transplant in Lieu of Standard Allogeneic Bone Marrow Transplantation for the Treatment of Multiple Myeloma – H. Lee Moffitt Cancer Center (FL)

MMRF Announces CME- Accredited MMRF Case Studies Program

On January 14, the MMRF launched its CME-accredited MMRF Case Studies program for healthcare professionals. Dr. Ken Anderson from the Dana-Farber Cancer Institute, Chair of the program, will send an email to registered professionals with a link to a new case study of a myeloma patient each month. This free program is designed to teach professionals about current evolving treatment options for MM, as well as share recent data and scientific developments. The program is also designed to formulate treatment decisions based on the data presented. Visit the MMRF's website today to view the first two cases and sign up to receive the next case directly to your desktop!

Combined Federal Campaign



The MMRF has been approved for the Combined Federal Campaign (CFC) and is eligible for inclusion on the 2003 CFC List. The CFC is the annual fundraising drive conducted by Federal employees in their workplace every fall raising millions of dollars to benefit thousands of charities.

The MMRF's code number for this campaign is 1048.

Medical Corner

Immunotherapy: Harnessing the Immune System Against Myeloma

Guest Editors:



Derek Hart, MBChB, DPhil, Professor and Director, Mater Medical Research Institute, Queensland, Australia



Larry W. Kwak, MD, PhD, Head, Vaccine Biology Section, National Institutes of Health

Immunotherapy is an active area of myeloma research. This issue's **Medical Corner** provides insight into this exciting field.

What is Immunotherapy?

Immunotherapy is the manipulation of the immune system in order to prevent or treat a disease. One of the most well known examples of immunotherapy is the use of vaccines to prevent infectious disease. Cancers like myeloma, being different from normal tissues, are also theoretically susceptible to this strategy when it is used in combination with other standard treatments. Immunotherapy, particularly vaccination, is being used increasingly in myeloma. Other types of immunotherapy include cytokines and monoclonal antibodies, as well as manipulation of immune cells.

How Does Immunotherapy Work?

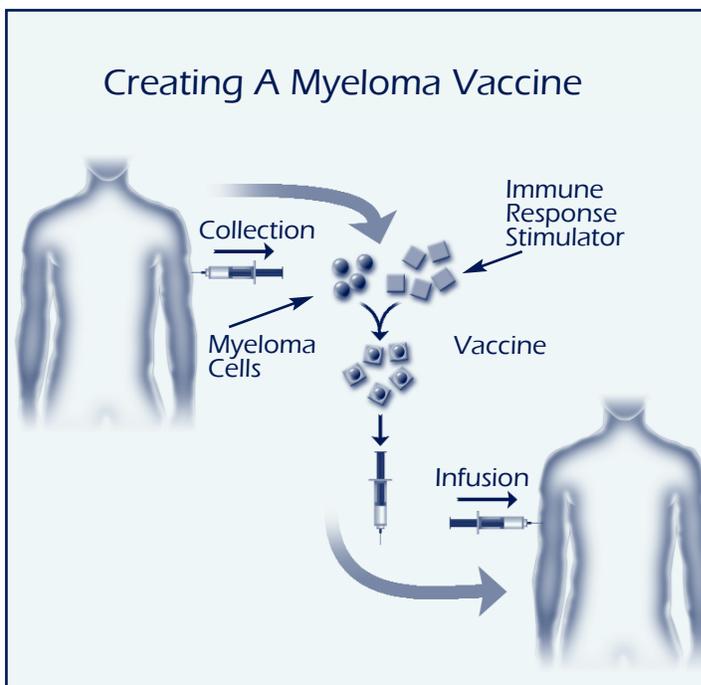
The body's immune system works to defend it against disease and infection. Typically, when a cancer cell arises in the body, the body's immune system recognizes it as abnormal and destroys it before it can spread. However, in some instances and for reasons not yet clear, the body may not recognize the cancer cell and it continues to grow. In myeloma, patients often do not mount a strong immune response against their myeloma cells. The goal of using immunotherapy is to help the body elicit an "active" immune response to attack myeloma cells or

to substitute an alternative "passive" response prepared outside the body.

Immunotherapy is likely to be most effective after high-dose chemotherapy and transplantation when the number of myeloma cells in the body has been minimized. Immunotherapy seeks to destroy the remaining cells, which are thought to be responsible for relapse after therapy. However, immunotherapy may also have other indirect anti-myeloma effects, such as slowing myeloma cell growth, making myeloma cells more vulnerable to destruction by other therapies, or affecting the bone marrow microenvironment to make it less hospitable to myeloma cell growth.

Myeloma Vaccines

Several of the immunotherapies being investigated in myeloma are active vaccines. These vaccines are created using the patient's own myeloma cells or proteins. They are usually combined with a stimulus or adjuvant that increases the body's own immune response. The patient is then immunized with this myeloma vaccine to stimulate his or her immune system to fight the disease. Several types of myeloma vaccines are being



Medical Corner

Immunotherapy: Harnessing the Immune System Against Myeloma *cont.*

investigated, including various physical/chemical adjuvants, dendritic cell vaccines, DNA vaccines and gene-modified myeloma cells.

Dendritic cell vaccines utilize dendritic cells, immune cells that play an important role in initiating and regulating immune responses. These vaccines contain dendritic cells that are combined with myeloma idiotypes (the unique portion of a patient's monoclonal protein) or other proteins, or are fused with entire myeloma cells. Preliminary results with this strategy are promising. One example of this type of vaccine is Mylovenge® (Dendreon), which uses dendritic cells that are loaded with a patient's specific idiootype. Results of Phase I/II clinical trials indicate that Mylovenge is safe, well tolerated and may cause tumor stabilization. In one study, Mylovenge was administered following reduction of tumor cell burden with autologous stem cell transplantation.

use a virus to transfer specific genes into a patient's plasma cells. These genes stimulate the production of growth factors that enhance the immune response against the tumor.

Cytokines

Cytokines have a wide variety of effects on the immune system and on myeloma cells. Examples of cytokines that are being evaluated in combination with other therapies include interferon, interleukin 2 (IL-2) and interleukin 12 (IL-12), which help activate tumor-fighting immune cells known as T-cells.

Manipulation of Immune Cells

Another means of attacking myeloma is to generate a cellular immune response outside the body and infuse it back into the patient. One experimental technique being investigated as part of the MMRF's 2002 Collaborative Grant (see page 4) involves harvesting immune cells from the bone marrow. These immune cells, known as marrow infiltrating lymphocytes (MILS), appear to be more effective at killing myeloma cells than immune cells in the blood. MILS will be stimulated and grown in the lab and then returned to the patient, a technique referred to as adoptive immunotherapy.

Monoclonal Antibodies

Monoclonal antibodies are man-made antibodies that target specific substances and are used as passive immunotherapy to treat disease. One monoclonal antibody being evaluated in myeloma trials is known as MRA (Chugai Pharmaceuticals). MRA is an antibody that is directed against the interleukin 6 (IL-6)

receptor. IL-6 is a major growth factor for myeloma cells, so the blockade of this receptor may prove effective in limiting myeloma cell growth.

Another monoclonal antibody in clinical trials is AHM (anti-HM1.24 monoclonal antibody, Chugai). HM1.24 is a marker expressed on myeloma cells. Antibodies to HM1.24 have been shown to induce killing of myeloma cells in the lab and in animal models.

Agent	Phase	Description
Mylovenge® (APC8020i) Dendreon	II	Dendritic cell vaccine made with patient-specific idiootype; being tested alone and in combination with thalidomide
Gvax® Myeloma Vaccine Cell Genesys	I/II	Irradiated patient myeloma cell vaccine administered with cells that secrete a cytokine that stimulates immune responses
AHM Chugai Pharmaceutical	I	Monoclonal antibody directed against the HM1.24 marker expressed on myeloma cells
MRA Chugai Pharmaceutical	I	Monoclonal antibody directed against the IL-6 receptor

Cellular vaccines utilize the patient's myeloma cells to stimulate an immune response. One such vaccine combines a patient's irradiated myeloma cells with Gvax® Myeloma Vaccine (Cell Genesys), which are cells that secrete a cytokine that stimulates immune responses. Gvax is administered before and after autologous stem cell transplantation.

DNA vaccines are composed of fragments of DNA that encode specific myeloma proteins or markers and substances to help further activate the immune system. Gene-modified vaccines



ASK THE EXPERT

This issue's **Ask the Expert** features Patty Delaney, Associate Director of the Cancer Liaison Program and the Office of Special Health Issues at the Food and Drug Administration (FDA).



1. I read that Millennium filed an NDA for Velcade®. What does this mean?

When a company files an NDA (New Drug Application), it is submitting the efficacy and safety results of their clinical trials seeking approval to market the drug in the U.S. for use in the population in which it was tested (see chart above). The FDA then reviews the data and determines whether the drug should be approved for that usage. In 2002, the average time for approval of a standard NDA was 15.3 months.

Keep in mind that the FDA cannot disclose information regarding drugs in development; FDA regulations require that this information be held confidential. The FDA is only able to discuss information that a company has publicly disclosed about its product.

2. Velcade was previously awarded fast-track designation. Does this mean that the drug will be approved faster?

Fast-track designation is a status assigned by the FDA to a drug in clinical trials that is intended to treat a serious or life-threatening condition and that demonstrates the potential to address an unmet medical need. The designation means that the FDA will facilitate and expedite the development and review of the

NDA for approval of the drug candidate. One way in which the FDA does this is that it reviews clinical trial results and parts of the application that a company submits on an ongoing basis rather than only at the end of pivotal Phase III trials when the application is complete. This helps speed up the process.

In addition, agents given fast-track designation ordinarily meet the FDA's criteria for priority (expedited) review. Priority review is a determination made when the NDA is filed that sets a target date of 6 months for the FDA to review the application. However, fast-track status does not guarantee priority review.

3. What does the Oncologic Drug Advisory Committee (ODAC) do?

The FDA sometimes uses advisory committees to obtain outside advice and opinions from expert advisors regarding the data in an NDA. Cancer drug NDAs are frequently presented to an Oncologic Drug Advisory Committee (ODAC) for

their input. At this time, the company and the FDA present the data to the committee, who can then ask questions. Based on the information, the committee may recommend approval or rejection of the drug candidate. However, the FDA is not bound to follow the committee's recommendation.

Steps In The Drug Approval Process

Preclinical Testing

Submission of an **Investigational New Drug Application (IND)** to the FDA for permission to test the drug in humans.

Clinical Trials:
Phase I
Phase II
Phase III

Submission of a **New Drug Application (NDA)** to the FDA for permission to market the drug.

Approval for sale

IXth International Workshop on Multiple Myeloma May 23-27

The MMRF is proud to support this year's Myeloma Workshop in Salamanca, Spain. The Workshop will serve as a forum on the scientific progress made in understanding and treating multiple myeloma. While the Workshop is limited to healthcare professionals, the MMRF will make the latest news and information available to the public as the official webcaster and will publish a special edition newsletter. Researchers and Physicians - deadline for submitting abstracts and for early registration is March 1, 2003. For more details, visit <http://myeloma2003.usal.es>

MMRF INSTITUTIONAL INSIGHTS



INSTITUTIONAL INSIGHTS ON MYELOMA

The UNC program was held on October 24 and 25 with more than 140 patients and their families, and more than 45 healthcare professionals attended. In addition to Dr. Gabriel, speakers included Dr. Carlos de Castro from Duke University, Dr. Paul Richardson from the Dana-Farber Cancer Institute, Dr. Brian Van Ness from the University of Minnesota and Dr. Donna Weber from the MD Anderson Cancer Center.

The Johns Hopkins program, was held on November 14 and 15, and attracted more than 100 patients and caregivers and more than 70 healthcare professionals. Speakers included Dr. Ken Anderson from the Dana-Farber Cancer Center who is also a Johns Hopkins School of Medicine alumnus, and in addition to Dr. Borello, Drs. Rafael Fonseca and Vincent Rajkumar from the Mayo Clinic also spoke.

The MMRF would like to thank the institutions, and the speakers, for their support of these programs.

The MMRF recently held Institutional Insights symposia at the University of North Carolina at Chapel Hill (UNC) and at Johns Hopkins School of Medicine in Baltimore. Both were new sites, and the programs were well received by patients and their families, as well as by physicians. Dr. Don Gabriel served as Chair for the UNC program, and Dr. Ivan Borello served as Chair for the Johns Hopkins program.



Dr. Robert Orłowski, one of the healthcare professionals who attended, speaks with patients at the UNC Institutional Insights Program



Dr. Ivan Borello speaks with patients at the Johns Hopkins Institutional Insights Program

DATES TO REMEMBER

March 4, 2003 Chicago, IL
Chicago Awards Dinner. For more information, please contact Craig Robertson at 203-972-1250

March 25-26, 2003 Cleveland, OH
*Institutional Insights on Myeloma

April 2 - 3, 2003 Boston, MA
*Institutional Insights on Myeloma

April 13, 2003 San Francisco, CA
MMRF Race for Research 5k Walk/Run

April 27, 2003 Boston, MA
MMRF Race for Research 5k Walk/Run

May 23-27, 2003 Salamanca, Spain
IXth International Workshop on Myeloma

June, 2003 Cleveland, OH
MMRF Race for Research 5k Walk/Run

June 5, 2003 Teleconference
"Update from the IXth International Workshop on Multiple Myeloma"

June 9, 2003 New York, NY
New York City Awards Dinner. For more information, please contact Craig Robertson at 203-972-1250

June 17-18, 2003 Washington DC
Blood Cancer Advocacy Days
For more information contact Anne Quinn Young at 203-972-1250

July 19, 2003 Seattle, WA
MMRF Race for Research 5k Walk/Run

June 20, 2003 New York, NY
*Institutional Insights on Myeloma

Sept 14, 2003 Chicago, IL
MMRF Race for Research 5k Walk/Run

*For more information on Institutional Insights call (203) 972-1250 or at www.multiplemyeloma.org/events/seminars.html



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Third Annual Blood Cancer Advocacy Day

The Third Annual Blood Cancer Advocacy Day will be held on June 17 and 18 in Washington, DC. The MMRF will join forces with the Lymphoma Research Foundation (LRF) to advance blood cancer research and ensure access to quality cancer care for all blood cancer patients. The two-day event will include leadership from Geraldine Ferraro and Senator Kay Bailey Hutchison, interactive advocacy training, a Congressional reception and lobbying visits with key members of Congress from your area.



Kay Bailey Hutchison and Geraldine Ferraro team up to make a difference.

If you are interested in going to Washington DC to be an official myeloma advocate on June 17 and 18, to obtain an application please contact Anne Quinn Young at 203-972-1250 or by email at quinnyounga@themmrf.org or contact Bruce Holmberg at 301-509-4106 or by email at bpholmberg@aol.com