

Researchers and Advocates Make Progress in Multiple Myeloma

BY ELIZABETH WHITTINGTON

With his upcoming wedding, Brian Novis decided to increase his life insurance—a decision that required a simple blood test among other tests to gauge his physical well-being. The results showed multiple myeloma, a cancer of the bone marrow that produces too many abnormal plasma cells. And in 1988, the prognosis and treatment for multiple myeloma wasn't promising.

When he was diagnosed, Brian was told he had three to five years to live. He stayed busy during the next four years before his death in 1992. He married his fiancée Susie and started the International Myeloma Foundation.

Susie remembers how Brian asked her to carry on the foundation. "Brian said, 'You know Susie, one person can make a difference, two people can make a miracle.'" After her husband's death, Susie Novis made the foundation her own mission to educate patients and fund research.

Plasma cells are produced by the bone marrow, and for patients with multiple myeloma, these cells begin multiplying at an abnormal rate. The unhealthy plasma cells tend to crowd out other types of blood cells, including oxygen-carrying red blood cells and infection-fighting white blood cells, which can result in anemia and an increased risk of infection. Myeloma can also damage the kidneys and decalcify bones, making them weak and at increased risk of breaks and fractures.

The American Cancer Society estimates that in 2007 there will be approximately 19,000 new cases of multiple myeloma and 10,790 deaths in the United States. However, newer treatments, such as Thalomid® (thalidomide), Revlimid® (lenalidomide) and Velcade® (bortezomib), have shown benefit and are extending remission times and survival.

Approved in 2003, Velcade works by inhibiting proteasomes—enzyme molecules that act as a cellular garbage disposal, destroying damaged proteins. Researchers also believe it may inhibit a protein called nuclear factor κB, which is partly responsible for the process of stimulating growth and preventing cancer cell death. Revlimid and thalidomide kill myeloma cells by reducing blood vessel growth and angiogenesis in the bone marrow.

In 1988, the standard treatment for Brian Novis was steroids and chemotherapy, and little support or patient education available. In response, Brian and his

doctor, Brian Durie, MD, started a foundation to reach out not only to patients, but also to doctors. Knowing he had limited time, Brian worked for the next two years developing a foundation and raising awareness of the disease.

Seventeen years after the International Myeloma Foundation was started, it has grown to include more than 165,000 members in 113 countries worldwide. Dr. Durie, an attending physician at Cedars-Sinai Medical Center in Los Angeles and National Program Director for Multiple Myeloma and Related Disorders at Aptium Oncology, and Susie Novis, now president and cofounder of the IMF, work collaboratively to educate newly diagnosed patients about the disease and to help them find effective treatments. Dr. Durie and Susie recently answered *CURE's* questions about the disease and recent advances in the field.

Q: Why has multiple myeloma been so hard to treat?

Brian Durie, MD: Until 1998, we had limited drug treatment options. The mainstay of treatment was alkylating agents, such as melphalan and Cytoxan® (cyclophosphamide). Since melphalan was the best drug we had, it was used in combination with other drugs and at very high doses with stem cell rescue, which produced added benefit. With the availability of Thalomid in 1998 and subsequently Velcade and Revlimid, a whole new era began. These new targeted therapies produced much better responses with lesser toxicity.

Q: What goes into the decision of choosing treatment?

Brian Durie, MD: For patients over 65 years of age, the combination of melphalan and prednisone with Thalomid (using 100 mg by mouth daily) has produced remarkable responses and improved survival. For patients who are transplant candidates, Revlimid plus dexamethasone and Velcade plus dexamethasone produce initial response in 90 percent of patients.

The major question now is how important is it to achieve higher-level response? Is there longer remission if multi-drug combinations are used? An additional question is does high-dose therapy with, for example, melphalan add to the benefit achieved with initial frontline novel combinations? There are now many ongoing trials designed to answer these questions. However, we now know that high-dose melphalan can combine with novel approaches to improve the chance of achieving a complete response.

The current major need is to learn which combinations and what sequences produce the best short-term and longer-term results. These issues are a priority even before identifying and introducing additional new agents in phase I or II trials. With the drugs we have it is possible for many patients to achieve chronic disease control-in some cases beyond 10 years. Thus, achieving "chronic" is an important step on the path to developing curative therapy.

Q: How can patients learn more about these clinical trials and if they are right for them?

Susie Novis: One of our board members, who is a 16-year multiple myeloma patient, came up with the Myeloma Matrix, which is available on our website and in print. It lists all the drugs in preclinical studies, human clinical trials and drug approvals, and includes indications, manufacturers and contact information. We encourage patients to take that to their doctors to discuss if any of those trials

are appropriate for them. We also have a hotline. We're the only myeloma organization that has National Cancer Institute—trained coordinators to answer any questions patients may have.

Q: You say a board member is a 16-year survivor. Is that unusual?

Susie Novis: Myeloma used to be described as a rare, incurable disease of the elderly. Today we know it is being diagnosed in increasing numbers with evidence that in some cases it is linked to industrial pollution. Studies have shown, for example, that the number one cancer risk for firemen is multiple myeloma and they are exposed to massive amounts of smoke and soot. We also have members who have been diagnosed in their 30s. And yes, we have a group of patients who have had access to the newer treatments who have survived 10, 12 and 15 years, so we're seeing myeloma move toward becoming a chronic, manageable disease.

Our 16-year survivor is not alone, and is one of the people to be diagnosed in his 30s. Today he's in his 50s and recently danced at his son's wedding. A milestone once never thought possible for people who were given just three to five years to live.

Q: Why did you become an advocate for multiple myeloma patients?

Susie Novis: The foundation officially started in our home in 1990. In the first two years, Brian helped plan the first clinical conference for multiple myeloma, started the newsletter *Multiple Myeloma Today*, held the first fundraiser for multiple myeloma research, we honored Dr. E. Donnall Thomas, who won the 1990 Nobel Prize in Medicine for his work in bone marrow transplantation—and then Brian died. And when he died, I had two choices: I could either walk away from this foundation that was two years old that this wonderful man gave his life for, or I could pick up where he left off.

Q: What is IMF's Bank on a Cure?

Susie Novis: It doesn't matter how much money you raise, but what you do with it. We're working very hard on multiple myeloma research with our Bank on a Cure DNA databank—an inclusive research project with centers all over the world collaborating on this databank. We've already identified genes that are linked to increased risk of deep vein thrombosis, which can be a problem with some of the new therapies. And we can identify who would be at risk for that. We've also identified genes that are linked to why patients get bone disease. We're also currently investigating why some patients respond to novel therapies and why some don't.

The IMF has a circular approach to treatment. Everything we do relates back to the patient, doctors, researchers and nurses—it's not only putting people together, but getting results.

We have been a very inclusive organization. We do an enormous amount with other doctors and researchers. Our International Working Group has over 85 members who meet regularly and work collaboratively to make things happen. They've published seven papers that have really changed the paradigm on how patients are treated, including diagnostic criteria, response criteria, osteonecrosis of the jaw, the new staging system for multiple myeloma—things that help doctors take better care of their patients today.

Q: What is the IMF doing to spread the word about multiple myeloma?

Susie Novis: This summer, the Myeloma Mobile—a 37-foot Winnebago—is being driven across the country by Michael and Robin Tuohy with their two children and their dog. Michael is a multiple myeloma patient, and Robin is one of our support group coordinators. They had the idea to drive across country and reach out to people who don't normally get information on multiple myeloma. It kicks off in June in Boston, and the point is to raise awareness about multiple myeloma and reach people who are now suffering with this disease. We have wonderful booklets and information that we'll be disseminating to people. Michael Tuohy, by the way, was diagnosed when he was just 36, so he is an example of how myeloma is no longer a disease of the elderly.

Q: What are some issues multiple myeloma patients face that may be different from other cancers?

Susie Novis: It's a rare disease and doesn't get as much attention as the major cancers. One of the things I hear is: Where is my myeloma? It's not associated with a body part; it's not like breast cancer or prostate cancer. You can't cut it out. First of all, when they're diagnosed, patients have never heard of it and they often think it's melanoma. And because it is a cancer of the bone marrow, it's hard to associate where it is and what is happening in your body.

It's also an incredibly complicated disease because it's a blood cancer. There is no cure and although we can tell people it's treatable and we can put you in a good remission, it's still there. Even with a transplant, you never really get rid of it all. It's like they are waiting for the other shoe to drop. Is it going to come back? When is it going to come back?

Q: Multiple myeloma was once considered an incurable disease. How has this changed?

Brian Durie, MD: There is a paradox in the search for the cure. It takes time to know what has been accomplished. Will a remission last three years, five years, 10 years? It's frustrating to wait to know. In the interim, one strategy is to work aggressively to improve therapy for patients with higher-risk disease identified by abnormal chromosome or molecular patterns. If we can develop therapy for these patients in whom early relapse is common, this should result in better therapy overall and maybe even a cure for some patients.

There has already been a quantum change in the outlook for myeloma patients. New innovations will undoubtedly improve on that. But it will be some years until we know if some patients are indeed cured.

Resources for patients and caregivers with multiple myeloma include:

International Myeloma Foundation
www.myeloma.org

Multiple Myeloma Research Foundation
www.multiplemyeloma.org