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WEB EXCLUSIVES

Progress in Treating Multiple Myeloma

BY PETER WEST

The old and the new in myeloma therapy give patients more options.

Roseann Martorell, a homemaker from Brewster, New York, knew something was wrong when her laryngitis wouldn't go away. Soon, she began to suffer fits of coughing and vomiting.

"I was under tremendous stress then because my mother was ill," says Martorell, 50. "So I ignored the symptoms until it became obvious that this wasn't merely a case of nerves."

An internist prescribed antibiotics. When the pills didn't work, the doctor sent her for gall bladder tests. The tests came back positive—but not for a gall bladder problem. "My blood cell counts were way off; they sent me right away to a hematologist."

The diagnosis: stage 3 myeloma, a potentially deadly cancer of the plasma cells. The prognosis: three years to live.

Martorell refused to accept the startling news and sought care in New York City, eventually choosing a physician affiliated with Weill Medical College of Cornell University. Three years later, following a successful autologous stem cell transplant and high-dose regimens of Thalomid (thalidomide) and other drugs, Martorell's cancer, while technically not in remission, is at least stable and symptom free.

"I am grateful for the care I received and am very hopeful for the future," she says. "Compared to where I was in 2004, I'm feeling great."

Thanks to recent advances, it is hoped Martorell's story will become more common. Doctors are making progress in treating and, in some cases, managing myeloma, using a combination of proven therapies and novel treatments.

"The good news is that we are learning more and more about [myeloma]," said Robert Z. Orlowski, MD, PhD, a noted blood cancer expert at Lineberger Comprehensive Cancer Center at the University of North Carolina at Chapel Hill, during an educational workshop sponsored by The Leukemia & Lymphoma

Society. “Our treatments are becoming more effective. That is already resulting in an improvement in overall survival as well as quality of life. I think the next five to 10 years will only see the pace of that improvement accelerating.”

Myeloma: The Basics

Scientists do not know the cause of myeloma, which strikes more than 16,000 Americans annually. Like leukemia and lymphoma, myeloma results from an acquired injury to the DNA of a specific type of cell—in this case, the lymphocyte development sequence that is destined to form antibody-producing plasma cells. The malignancy grows continuously and forms masses of malignant plasma cells, destroying normal bone tissue, causing pain, and crowding out normal blood cell production. Abnormal antibody production can also cause problems, including altering the immune system. With their weakened immune systems, patients are susceptible to infections and other secondary complications.

The major forms of myeloma are divided into several categories, which allow the physician to decide what treatment works best for a particular patient. Multiple myeloma is the most common form of the disease (about 90 percent of cases) and may involve many sites in the body. Myeloma is not just one disease, says Dr. Orlowski, and the differences come in based on the chromosomal changes in the malignant cells.

Myeloma remains the most difficult blood cancer to cure, with just a 34 percent relative five-year survival rate in the United States. The cancer occurs more often in men than in women, with the median age of diagnosis at 70. No one knows why blacks appear more prone to getting myeloma than other racial and ethnic groups in the United States. In fact, blacks have more than double the incidence (11.2/100,000 population) than whites (5.1/100,000), according to Surveillance, Epidemiology and End Results data from the National Cancer Institute.

Because myeloma cells secrete cytokines that stimulate other cells to dissolve bone, skeletal pain is a common early symptom. Most patients with this symptom feel soreness in the back or the ribs, but pain and fracturing can occur in any bone and is usually made worse by normal movements, such as walking, lifting, and even coughing. They can also have generalized osteoporosis and experience fractures in the spine, hips, and other bones. In addition, patients fatigue more easily and often feel weak, in part because of low blood counts from the plasma cells infiltrating the bone marrow. They often suffer from repeated infections because antibodies to invading viruses, bacteria, or other disease agents are not being made efficiently or in adequate amounts. Urinary tract, bronchial, lung, and skin infections are other common first signs of the disease. Abnormal antibodies can also have harmful effects on the kidneys, nervous system, and other tissues.

Treatments: Promising New Therapies

Chemotherapy has been the mainstay of treatment for years, but achieving complete remission for long periods remains a challenge. Conventional chemotherapy with one, two, or three drugs has therefore given way to more

intensive treatment using new agents and in different combinations.

With the advent of these new therapies, several approaches can be used depending on the patient's unique situation, such as age, extent of disease, and pre-existing conditions. Frequently used drugs include:

> Adriamycin (doxorubicin)

> Alkeran (melphalan)

> Aredia (pamidronate)

> BiCNU, BCNU (carmustine)

> Cytoxan (cyclophosphamide)

> Decadron (dexamethasone)

> Doxil (liposomal doxorubicin)

> Idamycin (idarubicin)

> Oncovin (vincristine)

> Prednisone

> Roferon-A, Intron A (interferon alfa)

> Zometa (zoledronic acid; not a chemotherapy, but a bone-strengthening drug)

More recent agents, some of them under study for newly diagnosed patients, include:

> Thalidomide, often used in combination with Decadron

> Revlimid (lenalidomide), a more potent form of thalidomide with potentially broader anti-myeloma effects.

> Bisphosphonates to alleviate bone disease and potentially inhibit myeloma cell growth.

> Trisenox (arsenic trioxide) in various combinations, including melphalan and vitamin C (MAC therapy), in patients with relapsed or non-responsive disease.

The drug Velcade (bortezomib), currently approved to treat myeloma patients who have received at least one prior therapy, is now showing promise as a first-line option in combination with other drugs. Results of a phase III study announced in September showed previously untreated myeloma patients who received Velcade in combination with melphalan and prednisone—the prescribed treatment for patients not undergoing a stem cell transplant—experienced statistically significant benefit.

Stem cell transplant, usually with the patient's own stem cells, is recommended therapy for patients who can withstand high doses of pre-treatment chemotherapy and/or radiation. The good news is that transplant physicians are developing less strenuous pre-transplant conditioning regimens that may be suitable for a wider range of patients in the future. This is one treatment that at the current time is associated with prolonged remission, and possibly long-term

cure, although more follow-up is needed.

“Right now, the challenge we face sometimes is having so many and different alternatives that we don’t know exactly what the sequence of these [treatments] should be and what should we offer first to patients,” said Melissa Alsina, MD, an associate professor and myeloma expert at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, during a Society educational program. “But studies are ongoing right now to try to solve those dilemmas.”

The Future

There is every reason to believe new and better treatments for myeloma will appear in the near future. Scientists are investigating a range of intriguing therapies, such as immunotherapy, statins (normally used to lower high cholesterol), targeted radiotherapy, and antisense oligodeoxynucleotides. In five years perhaps, Dr. Alsina said doctors may have better tests that can profile a patient’s unique genetic makeup and determine which therapy he or she may best respond to.

While the future of myeloma research is promising, success will ultimately depend on the vibrancy of clinical trials and their ability to attract enough patients, says Hildy Dillon, MSW, of the Society’s Patient Services Department. Clinical trials are the proving ground for innovative therapies. “In order to continue to make progress in better understanding this complicated disease and improve therapies, more patients who reflect the population living with this disease should be enrolled in trials,” Dillon said.

The Society and other organizations are taking lead roles in encouraging patients to participate in clinical trials of potentially effective treatments. The Society’s Information Resource Center is staffed by master’s level social workers and health educators who are available Monday through Friday from 9 a.m. to 6 p.m. ET at 800-955-4572 to discuss clinical trials with patients and help them find the study that is right for them. The Society’s website (www.lls.org) is another good source for information on myeloma, treatment options (including clinical trials), and other disease-related information.

“All in all, I think patients have reason to be hopeful,” says Deborah Banker, PhD, vice president, Society Research Communications. “Medicine is moving in the right direction.”