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HEALTH & WELLNESS

New Weapons in the Fight Against Multiple Myeloma

Hope and more options for patients after the FDA's approval of three drugs for the blood cancer

By **RON WINSLOW**

Few types of cancer research have witnessed more progress in the past decade than the fight against the blood cancer known as multiple myeloma.

There are 10 multiple myeloma treatments on the market, including three that won Food and Drug Administration approval during a remarkable 15-day span in November. Other medications in the pipeline hold promise to meet patients' hopes for even further gains.

Patients on average can now expect to live about seven years after diagnosis, and doctors expect the newest drugs may help extend that to a decade or more. By comparison, prospects for patients diagnosed with multiple myeloma just over a decade ago were grim. Chemotherapy was essentially their only drug-treatment option and the average survival period was three years.

"Of all the cancers, in terms of progress in the last 10 years, multiple myeloma is at the top of the list," says S. Vincent Rajkumar, professor of medicine and a hematologist/oncologist at the Mayo Clinic, in Rochester, Minn.

Nearly 27,000 people in the U.S. were diagnosed with multiple myeloma in 2015, and more than 11,000 died of the disease, according to National Cancer Institute estimates. There is no cure and patients' experiences vary widely. Current treatments enable some patients to live mostly normal lives for prolonged periods, while others live with pain and relapse quickly. About 15% get little or no benefit from available drugs.

Multiple myeloma is a cancer of the plasma cell, which lives in the bone marrow and makes antibodies that

help fight infections. As cancerous cells accumulate in the bone marrow, they displace healthy cells, ultimately leading to kidney problems, bone pain and fractures, anemia and a vulnerability to infections.

There are potentially serious side effects from the drugs. Some may cause heart damage, while others carry risk of nerve pain in the hands and feet. They are also expensive: Treatments can average between \$8,000 and \$14,000 a month.

Still, the sheer number of options enables patients who relapse on one medicine or combination treatment to shift to another, and then to another. The serial treatments help account for a much longer survival benefit than would be expected from a single drug.

"If I'm going to get this disease, I'm so fortunate to get it now as opposed to 15 years ago," says Bob Dickey, 49, who was diagnosed with multiple myeloma in 2011. Mr. Dickey, of Menifee, Calif., says he is in partial remission and "within a short distance of being in full remission." He spends lots of time at the gym and is training for an ascent later this month of Africa's Mount Kilimanjaro with a team that includes three other myeloma patients on a fundraising expedition for the Multiple Myeloma Research Foundation.

The disease, whose cause is unknown, is more common among men and more than 60% of patients are 65 or older. African-Americans face double the risk of the overall population.

Journalist Tom Brokaw revealed his battle with multiple myeloma in May in his book "A Lucky Life Interrupted." Geraldine Ferraro, the congresswoman and vice presidential candidate, and

Wal-Mart founder Sam Walton are among prominent people who have died of the disease.

Treatment strategies vary widely depending on such factors as the stage of the disease at diagnosis, the patient's general health and recommendations of oncologists, who often disagree on the best approach.

Many patients undergo a stem-cell transplant at some point in their treatment in a bid to root out the malignant plasma cells. But even when that procedure results in a complete remission—when no disease can be detected—the cancer often eventually comes back.

The flurry of new drugs, triggered by scientific advances and spurred in part by an active patient-advocacy community, build on the progress initiated by Celgene Corp.'s Thalomid and its sister drug Revlimid, and Takeda Pharmaceutical Co. Ltd.'s Velcade. Those treatments changed the landscape for multiple myeloma when they were approved in the mid-2000s.

Takeda's Ninlaro, an oral formulation of the company's Velcade, was among the three agents the FDA approved between Nov. 16 and 30, an unusual string of approvals for a single cancer. The other new drugs are Johnson & Johnson's Darzalex and Emlliciti from Bristol-Myers Squibb Co. and AbbVie Inc. The new medications halt progression of the disease for a relatively modest five to eight months longer than regimens they were compared against.

Researchers say Ninlaro is an important, patient-friendly improvement on Velcade, while the other two drugs hit new targets against the cancer. "The field would get greater mileage from a new class of drugs than another of the

(over please)

older drugs,” says Madhav Dhodapkar, hematology section chief at Yale Cancer Center, in New Haven, Conn.

Multiple myeloma can come on with little warning. The first sign for many patients is a broken bone. Mr. Dickey, a self-described gym rat, considered himself “extremely healthy” when, in September of 2011, he picked up a barbell to warm up for a workout and snapped three vertebrae in his spine. The diagnosis: Stage 3 multiple myeloma, the most advanced form.

“Those vertebrae looked like Swiss cheese,” Mr. Dickey says. “That’s the only sign I had.”

He initially tried Velcade and then Revlimid (along with a steroid), with mixed results. In July 2012, he underwent a stem-cell transplant that put his disease in remission for about two years. Then a blood test indicated his disease was worsening. In 2014, he signed up for a clinical trial of Ninlaro, which he says has proven effective against his disease.

The new treatment options present challenges for clinicians and patients. “We need to understand the optimal use

of the drugs and the optimal combinations,” says Kathy Giusti, a myeloma patient and founder of the Multiple Myeloma Research Foundation.

As with other cancers, sequencing the DNA of tumors shows “there are many kinds of myeloma,” Ms. Giusti says. That calls for devising so-called precision medicine strategies designed to target genetic variants that drive an individual patient’s malignancy.

The MMRF, which has raised more than \$275 million to support research since its founding in 1998, recently completed enrollment in a \$40 million, 1,000-patient study called CoMMpass to build a database that links genetic data with clinical information. By tracking patients over time, part of the study’s mission is to help determine “which patients are benefiting from what drug and what combination,” Ms. Giusti says.

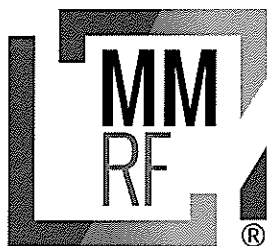
The effort is bearing fruit. At the annual meeting of the American Society of Hematology in December, researchers analyzing CoMMpass data reported that a combination of Velcade, Revlimid and dexamethasone

is more effective than either Velcade or Revlimid separately with the steroid.

Meanwhile, companies including Novartis AG and Celgene, in collaboration with Cambridge, Mass.-based Bluebird Bio Inc. are developing new treatments designed to directly enlist the body’s immune system into attacking the aberrant plasma cells.

Jenny Ahlstrom, a mother of six in Salt Lake City, hopes medical advances will continue against multiple myeloma. The 48-year-old founder of advocacy group myelomacrowd.org was diagnosed with the disease in 2010. She underwent so-called tandem stem-cell transplants—two procedures within a few months of each other that proponents say is associated with a durable remission.

She is free of the disease and not taking any medication for it. But she says she is on the lookout for the next potential treatment. “I don’t want just 10 more years,” she says. “I have an 8-year-old. I want to be around for my kids.”



MULTIPLE MYELOMA
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