

Antibody Therapy Eradicates Traces of Multiple Myeloma in Preliminary Trial

Lynozyfic could offer patients more durable responses than transplants, perhaps providing a functional cure.

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Treatment with an immune and cancer cell-targeting antibody therapy eradicates residual traces of the blood cell cancer [multiple myeloma](#), according to interim results from a clinical trial conducted by researchers at [Sylvester Comprehensive Cancer Center](#), part of University of Miami Miller School of Medicine.

None of the 18 patients who completed up to six cycles of treatment with the antibody linvoseltamab [Lynozyfic] had detectable disease on highly sensitive tests. This preliminary success suggests linvoseltamab, a bispecific antibody, could allow patients to avoid [bone marrow transplants](#), which involve intense, high-potency chemotherapy. It also points to the long-term possibility of improving patients' odds against this disease.

Lead researcher [Dickran Kazandjian, MD](#), a Sylvester physician and professor in the [Myeloma Division](#) at the Miller School, presented updated results today at the American Society of Hematology meeting in Orlando. Dr. Kazandjian conducted the research in collaboration with [C. Ola Landgren, MD, PhD](#), director of Sylvester Myeloma Institute.

"These patients received modern and effective, up-front treatment that eliminated 90% of their tumor," said Dr. Kazandjian. "Usually, patients like these would receive high-dose chemotherapy and transplant. Instead, we give them a treatment with the drug linvoseltamab."

Dr. Landgren, professor and chief of the Myeloma Division at the Miller School, called the results so far "extremely impressive" and said the disappearance of the lingering myeloma cells bodes well for patients' futures.

"Based on my experience, I would predict that after having such a good response after such a short time, the disease most likely could stay away for many years," he said. "Could it never come back in some patients? I would say it's possible."

Finding and Suppressing Lingering Cancer

Multiple myeloma arises from antibody-producing immune cells called plasma cells. These cancerous cells build up, interfering with normal blood cells and causing damage. There is no established cure. The U.S. National Cancer Institute's Surveillance, Epidemiology, and End Results Program estimates that, in 2022, more than 192,000 Americans were living with the disease. This year, 36,000 new cases will be diagnosed.

Currently, most newly diagnosed multiple myeloma patients receive a three- or four-drug combination. In some cases, this therapy eradicates the myeloma cells. But sometimes the cancer remains. These traces of the myeloma can occur at such low levels that they do not show up on standard bone marrow evaluations.

To find minute amounts of lingering cancer, physicians at Sylvester analyze bone marrow biopsies using a test that detects genetic sequences associated with the cancer. The test is sensitive enough to identify a single cancer cell out of a million normal cells.

Oncologists call these few remaining myeloma cells [minimal residual disease](#) or MRD. Those patients who test negative for MRD can expect to live [years longer](#) without their cancer returning than those positive for it, according to Dr. Landgren, who pioneered MRD's use as an indicator of effectiveness in evaluating experimental therapies.

For many years, patients with residual disease (who are MRD positive) typically receive potent, high-dose chemotherapy after completing combination therapy. While intended to wipe out the remaining myeloma cells, this chemotherapy causes significant side effects. To make this approach possible, the following day, patients receive a transplant of their own blood-forming stem cells from their bone marrow.

It's a "quite brutal therapy, which was first introduced in the U.K. in 1983," Dr. Landgren said.

Unfortunately, in most cases, the myeloma eventually comes back.

A "Functional Cure" for Multiple Myeloma

The study, a Phase II clinical trial conducted at Sylvester and its satellite sites at Coral Gables and Deerfield Beach, has so far enrolled 25 patients who have tested MRD positive after completing combination therapy. These participants receive four or six cycles of treatment with linvoseltamab.

While most therapeutic antibodies attach to a single target, bispecific antibodies attach to two. linvoseltamab binds to CD3, a protein on the T cells that destroy cancerous cells, and to a second target, BCMA, a protein on multiple myeloma cells. By bringing these two types of cells into contact, the antibody invigorates the body's immune response to the cancer.

A few patients experienced side effects, including decreases in white blood cells called neutropenia and upper respiratory infections. But all these events fell within an acceptable safety profile, according to Dr. Kazandjian.

The researchers took preventative measures to avoid triggering two potentially dangerous reactions, cytokine release syndrome and immune effector cell-associated neurotoxicity syndrome, that can occur with immunotherapies like this one. However, thus far, no patients in this study have experienced these reactions. Afterward, they tested patients' bone marrow for MRD using two independent and highly sensitive tests. No traces of disease were found in any of those who completed the therapy.

Based on its performance so far, Dr. Kazandjian hopes linvoseltamab could offer patients more durable responses than transplants, perhaps providing long-term control over the disease — a “functional cure.”

“It’s a bold claim, but we need to aim for the stars to move the field forward,” he said. “That is what we are trying to do.”

Exploring this possibility will require more studies with many more participants who must be followed for years. The team is already taking a step in that direction. Based on the results so far, they are expanding enrollment to 50 participants.

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