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CAR-T therapy for multiple myeloma is on the horizon

Bispecific antibody therapies are also in development

by ROSANNA SUTHERBY, PHARM.D.

Multiple myeloma is a form of cancer characterized by the proliferation of plasma cells in the bone marrow. Although relatively rare, accounting for less than 2% of all cancer cases each year, multiple myeloma is the second most common blood cancer in the United States. The National Cancer Institute estimates that approximately 34,500 cases will be diagnosed this year and that 12,640 people in the U.S. will die from the multiple myeloma.

Clinicians and patients have a growing number of treatment options for multiple myeloma from which to choose, both for patients whose disease comes back after responding to treatment (relapse) and isn't responding to treatment (refractory). A cohort of newer treatments featuring innovative mechanisms of action are currently under development, including chimeric antigen receptor T-cell (CAR-T) therapy and bispecific antibodies.

Off the shelf

CAR-T therapy has involved using the patient's own T cells to attack cancer cells. The T cells, which are the mainstays of the body's immune system, are collected from the patient's blood and re-engineered in a laboratory to produce proteins on their surfaces that recognize and attach to specific antigens on the surface of cancer cells. These proteins are called chimeric antigen receptors (CARs). Millions of CAR-altered T cells are grown in the laboratory, then infused back

into the patient, where they seek out and bind to antigens on cancer cells and destroy them. Typically, CAR-T-cell therapies target CD19 antigens or B-cell maturation antigens (BCMAs). CAR-T therapy is complicated and expensive; the price of the primary treatment and the associated treatment typically exceeds \$500,000.

Poseida Therapeutics, a San Diego biotech company, is developing an allogeneic version of CAR-T therapy. Instead of using the patient's own cells, the allogeneic version of CAR-T uses T cells from donors to create CAR-T cells for use in multiple patients. Allogeneic products carry an increased risk of host-graft and graft-versus-host reactions, but they can be created more easily to meet off-the-shelf demand. Poseida's product, provisionally named P-BCMA-ALLO1, is currently in a phase 1 study evaluating its safety in patients with relapsed/refractory multiple myeloma. Preliminary results are expected in June 2023.

Cartesian Therapeutics, based in Gaithersburg, Maryland, is developing the first CAR-T cell therapy to potentially treat newly diagnosed multiple myeloma. The investigational agent, Descartes-08, is currently in a phase 2 study evaluating its use in patients with high-risk multiple myeloma. Primary study results are expected in February 2023.

OriCAR-017, developed by Shanghai-based OriCell Therapeutics, is a second-generation CAR-T cell therapy targeting GPRC5D, a surface receptor on myeloma cells.

The findings from a phase 1 trial were presented at the 2022 American Society of Clinical Oncology (ASCO) annual meeting in June. Efficacy results were positive with no dose-limiting toxicities reported.

Matchmaking tumor, T cells

Bispecific antibodies are monoclonal antibodies with two targets. Typically, one is on tumor cells and the other on the surface of cells the immune system. Bispecific antibody targets include BCMAs on myeloma cells and CD3 proteins on the surface of T cells.

Pfizer's elranatamab is a BCMA, CD3-targeted bispecific antibody under investigation for the potential treatment of relapsed/refractory multiple myeloma. The FDA has granted the drug an orphan drug and fast-track designation. Interim results from a phase 2 were presented at the 2022 ASCO meeting. Patients with refractory multiple myeloma received a 76-milligram dose of elranatamab weekly via subcutaneous injection. Of the 94 patients evaluated, 90% responded positively to the treatment. Based on results, Pfizer says it plans to move ahead with the drug. Also moving through the pipeline is Cartesian's Descartes-25. This novel bispecific antibody targets BCMA and the cytokine interleukin-12. The drug is currently in a phase 1/2 study as a treatment for relapsed/refractory multiple myeloma. ■

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