Trial Shows Deep and Lasting Responses to CAR-T Therapy for Smoldering Multiple Myeloma

All 20 patients in Dana-Farber Phase II trial were negative for minimal residual disease within two months of treatment.

April 20, 2026 By Dana-Farber Cancer Institute

Dana-Farber Phase 2 Trial Shows Deep and Lasting Responses to CAR T-Cell Therapy for High-Risk Smoldering Multiple Myeloma

Results of the single-center, Phase II CAR-PRISM (PRecision Intervention Smoldering Myeloma) clinical trial, the first to investigate Chimeric Antigen Receptor (CAR) T-cell therapy in patients with high-risk smoldering multiple myeloma, showed that all 20 patients were negative for minimal residual disease (MRD) within two months of treatment and remained MRD-negative after a median of 15.3 months of follow-up, and none experienced high-grade side effects, according to results presented at the AACR Annual Meeting 2026, held April 17-22, in San Diego, Calif.

“Within two months, all patients were MRD-negative at the deepest level we can measure, and at 15 months or so of follow up, everyone remains MRD-negative,” said presenter Dr. Omar Nadeem, clinical director of the Myeloma Immune Effector Cell Therapy Program at Dana-Farber Cancer Institute. “This is the first time this kind of result has been reported in any spectrum of myeloma and really shows the efficacy of CAR T-cells in earlier disease state.”

The results were also published in Nature Medicine.

Smoldering multiple myeloma is a precursor to multiple myeloma, which is a cancer of the bone marrow involving plasma cells. As myeloma cells build up in the bone marrow, they can cause bone fractures, anemia, kidney impairment and pain. About 50% of patients with high-risk smoldering multiple myeloma will progress to active multiple myeloma within two years.

The CAR T-cell therapy ciltacabtagene autoleucel (cilta-cel) [Carvykti] was approved by the U.S. Food and Drug Administration (FDA) in 2024 as second-line treatment for relapsed multiple myeloma. The CAR T-cells target the B-cell maturation antigen (BCMA) protein, which is found on the surface of abnormal plasma cells.

The CAR-PRISM study investigated the potential benefits of treating patients with CAR T-cell therapy even earlier in the evolution of the disease, before they are exposed to therapies that can increase the chances of drug resistance, and before they transition into full-blown multiple myeloma, which can compromise immune system function.

“The hypothesis was that CAR T-cell therapy might work better when patients have a lower tumor burden and the immune system is still able to work well against cancer cells,” said Dr. Irene M. Ghobrial, principal investigator and director of the Center for Early Detection and Interception of Blood Cancers at Dana-Farber. “We wanted to learn if it can provide deep remissions that last a very long time.”

The study enrolled patients with high-risk smoldering multiple myeloma based on the 20/2/20 criteria for stratifying patients. Using these criteria, a patient is considered to have high-risk smoldering multiple myeloma if more than 20% of the cells in their bone marrow are precursor plasma cells, blood levels of the M-protein exceed 2 g/dL and the ratio of involved-to-uninvolved free light-chain proteins in their blood is greater than 20. Patients with additional high-risk biomarkers and 10% plasma cells in the bone marrow were also allowed to enroll. The study excluded patients with greater than 40% plasma cell infiltration in the bone marrow based on evidence that this sub-group might be more likely to experience side effects.

Twenty patients were enrolled and given one infusion of one of three doses of cilta-cel after lymphodepleting conditioning chemotherapy, but no induction chemotherapy. There were no dose-limiting toxicities, and no patients experienced high grade side effects.

All patients experienced low grade cytokine release syndrome (CRS) and no patients had grade 3 or higher CRS. The most common adverse events were temporary hematologic toxicities, including grade 3 or 4 neutropenia. Non-ICANS neurologic toxicities occurred in seven patients: facial nerve palsy in four that resolved completely; and three patients with residual mild but improved symptoms.

Within two months of treatment, all 20 patients experienced MRD negativity, meaning there was no detection of residual myeloma cells in the bone marrow. All patients maintained MRD negativity at a median follow-up of 15.3 months. No disease progression or death was observed. Six patients were followed for longer than 18 months and continued to experience complete responses and maintained MRD negativity.

“Our hope is that these responses continue to be durable in the long term to the point where we can say that patients are cured,” Nadeem said.

The team plans to continue to investigate the potential of CAR T-cell therapies as well as other immunotherapies, such as bispecific antibodies, to learn more about how they might benefit patients with high-risk smoldering multiple myeloma.

“One question is whether CAR T-cell therapy works differently in high-risk smoldering myeloma than it does in relapsed multiple myeloma,” said co-first author Dr. David Cordas dos Santos,

instructor of medicine at Dana-Farber. “Studying these differences may help us understand why responses appear so deep and rapid in these patients.”

Currently, most patients with smoldering multiple myeloma are monitored and only treated when they show signs of progression. In November 2025, the FDA approved daratumumab [Darzalex], a CD38-targeted monoclonal antibody, for the treatment of high-risk smoldering multiple myeloma, marking the first approved therapeutic for patients with the disorder.

“The results of the CAR-PRISM study really set the stage for what is possible with CAR T-cell therapy for patients with high-risk smoldering multiple myeloma,” Nadeem said. “CAR T-cell therapy has the potential to be a one-time treatment that offers disease eradication.”

Funding: This study was supported by Johnson & Johnson.

This news release was published by Dana-Farber Cancer Institute on April 20, 2026.

Click here for more news from AACR 2026.
