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Adicet 'gamma-delta' T cell therapy shows complete remissions in early study of lymphoma patients

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By Adam Feuerstein[2] [3] June 6, 2022

Courtesy ASCO/Scott Morgan

CHICAGO — Adicet Bio reported Monday that a unique, off-the-shelf therapy made from a special type of T cell induced complete remissions in patients with advanced and aggressive B-cell lymphomas, including patients with cancer who relapsed after receiving a personalized CAR-T treatment.

In the early-stage study, six of eight patients achieved complete remissions after a single infusion of Adicet's therapy, called ADI-001. Three of the patients were particularly difficult to treat because they entered the study with lymphomas that had relapsed after they received CAR-T treatments; all achieved complete remissions with ADI-001, Adicet said.

The results are preliminary with relatively short follow-up, but the data show a potentially new way of treating advanced lymphoma patients with an on-demand therapy derived from gamma-delta T cells — a type of immune cell that can recognize and kill cancerous cells like other types of adaptive T cells, but that also have certain innate immune characteristics of natural killer cells. For instance, treatments made from other types of T cells need to be genetically edited to prevent the body from rejecting it as foreign. Gamma-delta T cells do not.

The ADI-001 study data were presented Monday at the annual meeting of the American Society of Clinical Oncology by Sattva Neelapu, a physician and blood cancer expert at the University of Texas MD Anderson Cancer Center.

Adicet is the first biotech to test an off-the-shelf gamma-delta T cell therapy in patients with blood cancer. The gamma-delta field is relatively new but gained visibility in late 2021 when the Japanese drugmaker Takeda acquired privately held GammaDelta Therapeutics. Other companies developing gamma-delta T cell treatments include In8Bio, Lava Therapeutics, and Immatics.

Gamma-delta T cells are just one approach of many being used by

biotech and pharma companies to develop off-the-shelf cell therapies to treat blood cancers and solid tumors. CRISPR Therapeutics, Allogene Therapeutics, and Caribou Biosciences are developing treatments consisting of engineered T cells. Other therapies from Fate Therapeutics, NKarta, and Affimed are derived from natural killer cells.

To make ADI-001, Adicet first obtains gamma-delta T cells from the blood of healthy donors. The cells are then processed in a lab, where they are genetically engineered to recognize and kill malignant cells that express a protein target called CD20 on their surface. The cells are then grown, frozen, and ready for use in patients on demand.

Preclinical research suggested that relatively low doses of ADI-001 could be used effectively, and that turned out to be true in its first human study, said Adicet CEO Chen Schor.

Initially, Adicet administered a 30 million-cell dose of ADI-001 to three patients with aggressive B-cell lymphoma that was resistant to as many as five prior therapies. Two of the three patients achieved complete remissions. One of the patients in remission died shortly thereafter from Covid-related pneumonia, but the second patient remains in remission with seven and half months of follow up.

Adicet increased the ADI-001 dose to 100 million cells for another three patients, and again achieved two complete remissions. Both of the patients remain in remission but follow-up is relatively short at between three and six months. The highest

dose of ADI-001 used to date, 300 million cells, has been administered to two patients, and both achieved complete remissions with short follow-up.

No patients reported serious, treatment-related side effects.

The number of patients treated to date is still small and therefore the results need to be interpreted cautiously, said MD Anderson's Neelapu. But what impressed him the most was the ability to achieve complete remissions with low doses of ADI-001, and the efficacy of the treatment in patients with lymphoma that had relapsed after personalized CAR-T therapy.

One patient treated with ADI-001 and now cancer free entered the study relapsed after two prior personalized CAR-T treatments.

"Patients who relapse after autologous anti-CD19 CAR-T therapy have particularly poor outcomes, so to see complete remissions in these patients with ADI-001 is notable," said Neelapu.

One cause of relapse in lymphoma patients is the loss of the CD19 protein target on the surface of the cancer cells. When that happens, cell therapies that target CD19 no longer work. For that reason, Adicet CEO Schor said ADI-001, which goes after the CD20 protein target, has the potential to be particularly beneficial for patients with advanced lymphoma in the relapsed-CD19 CAR-T setting.

These are the same types of patients who could also be ideal candidates for treatment with so-called bispecific antibodies that

also target the CD20 protein, such as glofitamab from Roche, which will soon be filed with regulators. At the ASCO annual meeting, glofitamab showed a complete remission rate of 39% in a much larger study than anything Adicet has done to date with ADI-001.

Schor hopes to replicate or beat the glofitamab results with ADI-001, but the company will need to enroll more patients and follow them longer for durability.

About the Author

Adam Feuerstein[2]

Senior Writer, Biotech

Adam is STAT's national biotech columnist, reporting on the intersection of biotech and Wall Street. He's also a co-host of "The Readout LOUD" podcast[8].

adam.feuerstein@statnews.com [9]
@adamfeuerstein [3]

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