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UCLA establishes CAR T-cell therapy program

UCLA's Division of Hematology-Oncology has launched a new program to deliver chimeric antigen receptor (CAR) T-cell therapy to select patients with certain types of hematologic cancers. In August 2017, the Food and Drug Administration approved the first CAR T-cell therapy, tisagenlecleucel (Kymriah), for patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) who have disease refractory to treatment or in second or later relapse. ALL is the most common pediatric cancer. Most patients achieve long-term remission with standard treatments, however, CAR T-cell therapy provides patients who have relapsed or have not responded to conventional treatment a promising option.

In October 2017, the FDA also approved axicabtagene ciloleucel (Yescarta), a CAR T-cell therapy for adults ages 18 and older with diffuse large B-cell lymphoma (DLBCL) who have disease unresponsive to treatment or in second or later relapse.

Breakthrough immunotherapy

CAR T-cell therapy is one of the most promising forms of oncologic immunotherapy, emerging from scientific advances in immunotherapy, cell therapy and gene therapy. T cells are isolated from the patient's blood and genetically modified to express a chimeric antigen receptor that recognizes CD19, a protein found on the surface of antibody-secreting B cells and cancers originating from B cells.

Clinical expertise in an emerging treatment

CAR T-cell therapy represents a major advance in cancer treatment, says Josh Sasine, MD, clinical director of the UCLA CAR T-cell Therapy Program.

"The clinical benefit of CAR-T therapy is much greater than most treatments for cancer. For example, about half the patients in the B-cell lymphoma clinical trial remained in remission at a median duration of 15.4 months of follow up," he says. "These remarkable results were achieved with a single dose."

Few centers currently have the capability to offer CAR T-cell therapy. "We have experience with CAR T-cell products in clinical trials and are devoting significant resources to ensure our patients receiving CAR-T therapy are given state-of-the-art care delivered expeditiously and safely. We also focus on coordinating care with other providers. For patients who normally receive their medical care at other facilities or health systems, we incorporate their team of doctors into their care at every step of the way, even patients coming from outside the Southern California area," Dr. Sasine says.

Following reinfusion, the genetically modified T cells initiate an inflammatory response to destroy the malignant cells. Both tisagenlecleucel and axicabtagene ciloleucel target CD19 expressed on the surface of B-cell cancers.

Single-dose CAR T-cell therapy has shown breakthrough success in appropriately selected patients. Current data show remission at 15 to 24 months in almost half of patients with large B-cell lymphoma. For patients with ALL, 83 percent attained a complete remission within three months of infusion. This led to a probability of survival of 79 percent at 12 months, far higher than what would be expected with standard treatments. Additional large and long-term studies are needed to determine long-term remission rates and whether patients benefit from sequential dosing.

Management of side effects

CAR T-cell therapy is associated with significant side effects, including Cytokine Release Syndrome (CRS) and CAR T-cell-Related Encephalopathy Syndrome (CRES). CRS mimics septic shock, causing a systemic inflammatory response. Severe CRS can cause hypotension, respiratory distress syndrome and multi-organ failure. More than 90 percent of treated patients develop some form of these, most having mild symptoms. However, as many as 20 percent of patients will experience severe CRS or CRES, with a mortality rate of 3 to 5 percent overall. Tocilizumab was recently granted expanded approval by the FDA for the treatment of CRS related to CAR T-cell therapy for its ability to decrease the severity of the syndrome and improve patient outcomes.

Ongoing research

UCLA's Jonsson Comprehensive Cancer Center faculty have a long history of immunotherapy research, participated in clinical trials using CAR-T therapy and have several CAR-T trials ongoing. CAR T-cell therapy requires stringent quality control and extensive training of physicians and nurses to manage side effects. The program is administered by clinicians in the bone marrow transplant program who have decades of experience in adoptive cell and antibody therapies. The program adheres to a rigorous timeline to advance the patient from evaluation to treatment in about one month. Patients are typically hospitalized for at least one week following infusion and must remain in close proximity of the medical center for the first month following treatment to monitor for late-occurring side effects.

UCLA has a diverse research program in cancer immunotherapy. This includes studies aimed at identifying additional antigens that may be targets for CAR T-cell therapy and would permit use of the therapy in other types of cancer. Patients who are not candidates for currently approved CAR T-cell therapy may have access to these investigational therapies. Additionally, research is under way to optimize outcomes for more patients and to identify strategies to reduce and mitigate side effects.

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