

CAR-T immunotherapy may help blood cancer patients who don't respond to standard treatments

October 20 2017, by Julia Evangelou Strait

Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine in St. Louis is one of the first centers nationwide to offer a new immunotherapy that targets certain blood cancers. Newly approved by the Food and Drug Administration (FDA) for types of advanced non-Hodgkin lymphoma in adults, the CAR-T cell therapy harnesses a patient's own immune system to fight cancer.

Washington University doctors and researchers were involved in [clinical trials](#) that led to the FDA approval of the new CAR-T cell [therapy](#), called Yescarta, and are working to develop other immunotherapies that attack cancer.

"This is the beginning of a new era of cancer therapy," said Washington University oncologist Armin Ghobadi, MD, an assistant professor of medicine, who treats patients at Siteman. "With CAR-T cell therapy, we can take patients' own cells and turn them into a powerful weapon to attack cancer. It's a highly personalized, innovative therapy and one we hope also will prove to be effective against many different types of cancer."

At the heart of the [new therapy](#) are the immune system's T cells, which typically fight off disease. In cancer patients, T cells lose the ability to recognize and attack cancer cells. CAR-T cell therapy involves extracting a patient's own T cells and genetically altering – or

supercharging – those cells to home in on cancer cells and destroy them.

The first cancers to be treated with CAR-T cell therapy include certain types of large B-cell lymphomas in adults and acute lymphoblastic leukemia (ALL) in children. Diffuse large B-cell lymphoma is the most common type of non-Hodgkin lymphoma in adults. CAR-T cell therapy for pediatric ALL was approved by the FDA at the end of August and is available through Siteman Kids at St. Louis Children's Hospital. Such cancers in children and adults are characterized by the production of too many B cells, a type of white blood cell that is also a part of the immune system.

Currently, CAR-T therapy for adults with non-Hodgkin lymphoma is available only to patients whose cancer has not responded to standard treatments—including chemotherapy and [bone marrow](#) transplantation. Kite Pharma, a Gilead company, developed the new treatment.

Clinical trials of CAR-T therapy have shown what doctors have called remarkable remission rates among children with ALL and adults with lymphomas and multiple myeloma. In patients whose disease has not responded to standard therapies or has relapsed, CAR-T therapy has achieved from 40 to 80 percent remission rates. Some patients have remained in remission for several years.

"The availability of this new treatment offers a novel and very effective option for patients whose choices were once limited to joining a clinical trial of an investigational drug or entering hospice care," Ghobadi said.

If cancerous cells find ways to fly under the radar of immune surveillance, the new therapy renders these cancers visible again.

"The immune system can't always see [cancer cells](#) as threats—the T cells are sometimes blind to them," said John F. DiPersio, MD, PhD, the

Virginia E. and Sam J. Golman Professor of Medicine in Oncology and director of the Division of Oncology at the School of Medicine and deputy director of Siteman Cancer Center. "By modifying these T cells, we tell them what to look for. Now they can go right to the leukemia or lymphoma and eliminate the [cancerous cells](#)."

Over decades, an extensive body of research gradually has revealed the details of what many types of cancers look like on the cell surface. And in this new therapy, that information is, in a sense, programmed into the T cell. A patient's T cells are isolated from the blood and modified in a way that lets the T cells specifically home in on the type of cell affected by the cancer. These modified T cells have been dubbed CAR-T cells, which stands for chimeric antigen receptor T cells.

Once a CAR-T cell finds its target, it behaves as any T cell should—triggering a chain of reactions that destroys the target cell. CAR-T cells often are referred to as a living drug because they expand their numbers dramatically once in the bloodstream. And like other T cells, they remember what their targets look like, sometimes long after the offending cells have been eradicated. While long-term data is still being gathered, there is evidence that some CAR-T cells may maintain their active surveillance and ramp up again in response to cancer recurrence. The fact that CAR-T cells can be given different programming, locking them on to different cell surface features, suggests the strategy could be expanded to other cancers.

But because the therapy induces a heightened immune response, there can be a range of side effects, from fever and shortness of breath to kidney failure and seizures. Many of the side effects are manageable, but some are severe and a few can be life-threatening, which is why the first centers selected to administer the new therapy are those with extensive expertise in treating [blood cancers](#). That expertise includes long histories of success in bone marrow transplantation and management of the

sometimes severe side effects of that similarly intensive, but standard, therapy for many blood cancers.

"The toxicities of bone marrow transplantation and CAR-T cells are completely different, but we are well-equipped to manage both," DiPersio said. "We have approved therapies we can give to counter one of the primary side effects of CAR-T [cells](#) called cytokine release syndrome, which causes symptoms like low blood pressure, high fevers, chills, swelling and kidney failure. Some patients who receive CAR-T therapies also can experience life-threatening neurologic toxicities that we are still working to understand."

Washington University doctors at Siteman also are evaluating CAR-T cell therapy in a clinical trial for leukemia and soon will begin a trial in patients with multiple myeloma, another type of blood cancer, and ovarian cancer. Clinical trials currently available for sarcoma, a cancer of bones and connective tissue; lung cancer; and melanoma, a skin [cancer](#), involve therapies very similar to CAR-T cell therapy.

More information: For more information about CAR-T cell therapy, patients should visit siteman.wustl.edu or call toll free 800-600-3606.

Provided by Washington University School of Medicine in St. Louis

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