[Clinical Trial Identifies New CAR T-Cell Therapy to Fight Leukemia](http://blog.fisherbioservices.com/clinical-trial-identifies-new-car-t-cell-therapy-to-fight-leukemia)

Posted by [Dan H. O'Donnell](http://blog.fisherbioservices.com/author/dan-h-odonnell) on Jul 28, 2015 11:00:00 AM

Two of our previous blogs, [Viral Cell Therapies Fighting Cancer](http://blog.fisherbioservices.com/viral-cell-therapies-fighting-cancer) and [Researchers Learn How to Turn Cancer Cells into Macrophages](http://blog.fisherbioservices.com/researchers-learn-how-to-turn-cancer-cells-into-macrophages), discussed the challenges associated with Acute Lymphoblastic Leukemia (ALL) and some of the medical breakthroughs being used to fight this difficult disease. A recent article in [Blood Journal](http://www.bloodjournal.org/content/125/26/4017?sso-checked=true) explains how recurrent ALL is very difficult to treat, but suggests there is real hope for finding a lasting curative therapy for refractory patients. Let's explore the studies findings and uncover additional information on the research into potential ALL [cell therapy](http://connect.fisherbioservices.com/fisher-bioservices-cell-therapy-solutions)treatment modalities.

Although the overall survival rate for children diagnosed with ALL is high (85%), those who relapse are far more difficult to treat. Investigators Maude et al. (2015) demonstrate how the adoptive transfer of T-cells can be engineered to express a chimeric antigen receptor (CAR) that has emerged as a powerful targeted immunotherapy, showing striking responses in highly refractory populations.

The concept of using CARs was first introduced over 25 years ago and is now in a third generation phase. Pre-clinical studies showed some evidence of possible success and after fine-tuning to optimize in-vitro and in vivo T-cell proliferation, researchers determined the first generation CAR ready for clinical trials.

Second generation CARs added CD28 or 4-1 BB to the CD3 intracellular signaling domain of the T-cell receptor of the first generation and in the third generation added CD27 and ICOS. Early clinical trials targeted high risk CLL (Chronic Lymphocytic Leukemia) and demonstrated such positive results that researchers progressed to studying the efficacy of their treatments for ALL.

There are at least three groups actively pursuing CARs related therapies specifically for ALL and although results vary to some extent, they report that using different CD19 CAR designs have produced up to a 90% CR rate in both pediatric and adult populations with relapsed/refractory ALL.

The most encouraging news is that all results from the three groups working independently produced similar responses. There is some concern about a toxicity that presents as inflammatory CRS (cytokine resistance syndrome). Preliminary evidence however suggests that patients who develop the CRS symptoms actually respond better to treatments than those who do not and researchers are investigating various cytokines designed to reduce inflammation and toxicity.

The research relies on gene transfer technologies to engineer T-cells that express CARs and then employ various transfer techniques to effect permanent modification to the genome. Because CD19 is a B-cell protein expressed in nearly all B-cell malignancies including CLL, ALL and non-Hodgkin lymphomas, it is an ideal target for the CARs study.

CD19 directed therapies are the most advance T-cell therapies currently being studied and have demonstrated outstanding results. Initial reports demonstrated remission for refractory and relapsed ALL patients.

Several groups have now demonstrated durable efficacy with the best results showing a 45% remission rate for advanced relapsed and refractory CLL patients extending beyond four years. All CLL patients who responded had persistent B-call aplasia and many develop the Cytokine Release Syndrome. For an unknown reason, the CRS is more prevalent in CLL than in ALL patients.

With successful studies now published by the three groups previously mentioned, researchers feel they have sufficient information to advance to more mature follow-ups. They see a need for more data from adult patients and especially want to test patients with highly proliferative gene-modified T-cells.

The most important challenges remaining for the therapies include the development of more widespread and [improved delivery mechanisms](http://www.fisherbioservices.com/services/distributiontransport/distribution-of-cellular-therapies), reducing the amount of comprehensive training currently required for administering the treatments, and the development of [a standardized approach](http://connect.fisherbioservices.com/cell-therapy-project-consultation-request).

While significant progress is being made, there are still cases of relapse after CAR T-cell therapy and investigators continue to research why the recurrences occur and how they might address them in the future. Several of the groups are now working together to combine multiple approaches into a consistent and durable curative option.