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chemotherapy and poor candidates for stem cell transplantation, which is usually effective only if the disease is in complete remission.

Now Memorial Sloan Kettering investigators report that genetically modified immune cells have shown great promise in killing the cancer cells of patients with relapsed B cell ALL. In fact, all five of the patients who have received the new therapy – known as targeted immunotherapy – have gone into complete remission, with no detectable cancer cells. The results of this ongoing clinical trial are reported [online on March 20 in the journal \*Science Translational Medicine\*](#).

“This is a very exciting finding for patients with B cell ALL and a major achievement in the field of targeted immunotherapy,” says Michel Sadelain, Director of Memorial Sloan Kettering’s [Center for Cell Engineering](#), who led the study along with medical oncologist Renier J. Brentjens.

## Engineering Precise Weapons

Targeted immunotherapy is aimed at instructing the immune system to recognize and attack tumor cells. Over the past decade, Drs. Sadelain and Brentjens, and other Memorial Sloan Kettering researchers – including Isabelle Rivière, Director of Memorial Sloan Kettering’s Cell Therapy and Cell Engineering Facility, and physician-scientist [Marco L. Davila](#) – have investigated an approach that involves removing white blood cells called T cells from patients and introducing a new gene into the cells using an engineered viral vector. Viral vectors are viruses that have been disabled so they cannot replicate and that efficiently shuttle their genetic cargo into a host cell.

After the gene is transferred and expressed, the T cells are infused back into the patient, where they multiply and cause a variety of different immune responses aimed at attacking the cancer cells. The gene used in the targeted immunotherapy for ALL codes for the creation of a receptor on T cells that enables them to recognize the CD19 protein, which is present in B cell ALL tumor cells.

Much of the early research into this approach was supported by Memorial Sloan Kettering’s [Experimental Therapeutics Center](#) and benefactors of the Center for Cell Engineering.

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## A Bridge to Stem Cell Transplantation

“We have been a leading center in developing this technology in the laboratory, and we were the first center to bring this CD19-targeted approach using viral vectors to the clinic,” Dr. Brentjens explains.

In the phase I clinical trial, five patients with relapsed B cell ALL had cancer that was detectable at varying levels in the blood. After receiving the

genetically modified T cells, all five patients achieved complete remission, and even highly sensitive molecular analyses found no cancer cells remaining.

“Patients with relapsed B cell ALL resistant to chemotherapy have a particularly poor prognosis,” says Dr. Brentjens. “The ability of our approach to achieve complete remissions in all of these very sick patients is what makes these findings so remarkable and this novel therapy so promising.”

Four of the five patients subsequently received additional therapy in the form of a [bone marrow transplant](#), the standard of care for those patients who successfully achieve complete cancer remissions after treatment for relapsed disease. To date, three of the four patients have remained in remission for between five and 24 months. One patient died from complications unrelated to the cancer therapy while in remission.

“By serving as a bridge to a stem cell transplant, this therapy could potentially help cure adult patients with B cell ALL that has relapsed and who are chemotherapy resistant. Otherwise, these patients have a virtually incurable disease,” Dr. Brentjens says. “We need to examine the effectiveness of this targeted immunotherapy in additional patients before it could potentially become a standard treatment for patients with relapsed B cell ALL.”

Further clinical trials, including a phase II study, have already been planned to test whether B cell ALL patients would benefit from receiving this targeted immunotherapy along with chemotherapy earlier in the disease stage, either as part of the initial frontline treatment or after remission has been achieved to help prevent relapse.

Read a [New York Times story](#) about this new therapy and the experience of a Memorial Sloan Kettering patient.

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