

Cancer patients with rare deadly brain infection treated successfully with off-the-shelf adoptive T-cell therapy

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An emerging treatment known as adoptive T-cell therapy has proven effective in a Phase II clinical trial for treating progressive multifocal leukoencephalopathy (PML), a rare and often fatal brain infection sometimes observed in patients with cancer and other diseases in which the immune system is compromised.

The study, led by Katy Rezvani, M.D., Ph.D., professor, Department of Stem Cell Transplantation and Cellular Therapy at The University of Texas MD Anderson Cancer Center, showed marked improvement in three PML patients infused with donor T [cells](#) targeting the BK virus. Findings were published in the Oct. 11 online issue of the *New England Journal of Medicine*.

Results from the proof-of-principle study demonstrated BK, a virus similar to the JC virus which causes PML, as the basis for a potentially viable therapy. Both viruses are named for the initials of the patients in which they were first identified.

"The JC and BK viruses are genetically similar and share proteins that can be targeted by the immune system," said Rezvani. "Because of these similarities, we hypothesized that T cells developed against BK virus may also be effective against JC virus infection."

Rezvani's team developed a novel approach for the generation of BKV-

specific T cells from healthy donors and established a bank of viral-specific T cells in MD Anderson's Good Manufacturing Practice (GMP) laboratory for immediate clinical use. The study treated three patients with third-party, partially human leukocyte antigen-matched (HLA) BK virus-specific T cells, taken from the GMP. HLAs are proteins found on the cell's surface vital to immune system recognition.

PML in patients with leukemia, lymphoma and other diseases

PML is a member of the polyomavirus family and is caused by the JC virus, which, although commonly found in the general population, can be deadly or cause serious health issues in some blood cancer patients, including those with leukemia and lymphoma, people with AIDS, and patients with multiple sclerosis, rheumatoid arthritis, lupus and other autoimmune diseases treated with biologic therapies.

PML attacks white matter in the brain called the myelin sheath, which protects nerve cells. There is no current effective treatment for PML, which is fatal in the majority of patients. Symptoms can include clumsiness or loss of coordination, difficulty walking, facial drooping, vision loss, personality changes, trouble speaking and weak muscles.

Clinical trial treatment included patients with acute myeloid leukemia (AML).

PML patients infused with BK-specific virus T cells included:

- Patient 1: 32-year-old female with AML who previously received a cord blood transplantation
- Patient 2: 73-year-old female with JAK2-positive polycythemia rubra vera, a blood disorder causing over-production of [red blood](#)

[cells](#), who had been treated with the targeted therapy agent ruxolitinib

- Patient 3: 35-year-old man with AIDS who had discontinued an aggressive form of multi-drug therapy known as highly active antiretroviral therapy (HAART) due to side effects and who was no longer able to walk.

Following the first infusion, all three patients had a reduction in JC viral load in their cerebrospinal fluid (CSF). Viral loads dropped from 700 to 78 copies in the first patient, 230,000 to 5,200 in the second, and 4,300 to 1,300 in the third patient.

"After infusion of viral-specific T cells, patients 1 and 3 had clinical improvement with significant reduction in JC virus in their cerebrospinal fluid," said Rezvani. "Both patients responded despite persistent T-cell immunodeficiency, supporting the concept that the response was mediated by the adoptively infused viral-specific T cells, and there were no infusion-related reactions."

Patient 1 received two additional infusions, which resulted in clearance of the virus in the CSF and no signs of PML 27 months after the first infusion. Patient 2 received a second infusion that further reduced JC viral load, but no further improvement was seen. The patient died eight months following the first infusion. Patient 3 received additional infusions resulting in complete clearance of the JC [virus](#). The patient has regained mobility, and nine months after the first infusion, he is able to walk with a cane.

"We are encouraged that off-the-shelf, third-party partially HLA-matched BK viral-specific T cells may provide a therapy for PML," said Rezvani. "Further study in a larger group of [patients](#) is required to determine the success rate, durability and longer-term adverse events with this treatment."

Provided by University of Texas M. D. Anderson Cancer Center

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