New T cell–based immunotherapy shows promise for lethal stem cell transplant complication

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More than 60 percent of patients with Epstein-Barr virus–associated lymphoproliferative disorder (EBV-LPD) that was not responding to standard rituximab (Rituxan) treatment responded to a new type of immunotherapy called Epstein-Barr virus–specific cytotoxic T lymphocyte (EBV-CTL) therapy, according to data from two clinical trials presented at here the AACR Annual Meeting 2015, April 18-22.

"One of the most concerning complications of blood stem cell transplantation, which has transformed the lives of many patients, including those with leukemia and lymphoma, is EBV-LPD," said Richard J. O'Reilly, MD, chairman of the Department of Pediatrics and chief of the Pediatric Bone Marrow Transplantation Service at Memorial Sloan Kettering Cancer Center in New York. "In the absence of effective therapy, these patients have an average survival time of only 16 to 56 days. The purpose of our clinical trials was to see if giving T cells from a normal-immune individual that were expanded in culture and stimulated to respond to multiple proteins from the Epstein-Barr virus could provide a safe and effective treatment.

"The good news from our two clinical trials is that EBV-CTLs generated from either the patient's transplant donor or from the bank of normal donor T cells developed at Memorial Sloan Kettering put aggressive EBV-LPD that had failed to respond to rituximab into long-lasting remission in more than 60 percent of patients," continued O'Reilly.

On March 2, 2015, the U.S. Food and Drug Administration granted breakthrough therapy designation to Memorial Sloan Kettering Cancer Center for the development of EBV-CTLs generated from the blood of third-party donors for the treatment of patients with rituximab-refractory EBV-LPD.

In the first clinical trial, 26 patients received EBV-CTLs generated from blood from their transplant donor and 13 received HLA-matched, EBV-CTLs from the Memorial Sloan Kettering Cancer Center bank of EBV-CTLs generated from third-party healthy donors.

O'Reilly explained that good treatment results were observed in this trial for patients receiving EBV-CTLs from both the sources, and because EBV-CTLs from the bank are available immediately when a patient is in need, he and his team, which includes Susan E. Prockop, MD, assistant attending in the Pediatric Bone Marrow Transplantation Service at Memorial Sloan Kettering Cancer Center, used only EBV-CTLs from the bank when treating the 18 patients enrolled in the second clinical trial.

Among the 39 patients enrolled in the first clinical trial, 23 had a complete response and two had stable disease. According to O'Reilly, 16 of those who achieved a complete response are still doing well, with eight of these patients alive more than five years after their EBV-CTL treatment and one alive more than 10 years after treatment.

Among the 18 patients enrolled in the second clinical trial, nine had a complete response, three had a partial response, and one had stable disease. All those who achieved a complete response continue to do well and the researchers will be following them long-term, said O'Reilly.

"We are looking forward to working with our collaborators at Atara Biotherapeutics and regulators to plan the next steps," said O'Reilly. "The EBV-CTLs work well for the majority of recipients. However, the responses became clinically evident only after the T cells expanded in vivo, which took about seven to 14 days. We are

rigorously pursuing the development of biomarkers or other tests to predict response earlier."

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