Immunotherapy demonstrates long-term success in treating lymphoma

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Targeted immunotherapy has been an attractive new therapeutic area for a number of cancers because it has the potential to destroy tumor cells without damaging surrounding normal tissue. New study results demonstrate high success rates using specialized white blood cells to prevent or treat lymphoma associated with the Epstein-Barr virus (EBV-lymphoma) in patients who have received a hematopoietic stem cell transplant (HSCT). This study was pre-published online today in *Blood*, the official journal of the American Society of Hematology.

Lymphoma is a cancer of white blood cells called lymphocytes that are largely responsible for maintaining the body's immunity, and EBV is one of the most common human viruses that can have a long-lasting impact on the body's immune system. Immune-compromised patients who receive HSCT, especially from mismatched donors or matched but unrelated donors, may be at higher risk of developing EBV-lymphoma than other patients. Previous studies have suggested that EBV-lymphoma occurs most often in the first few months post-transplant.

The researchers hypothesized that aggressive EBV-lymphomas may be responsive to control or eradication with EBV-specific cytotoxic T lymphocyte (CTL) treatment. (CTLs are highly specialized white blood cells that build the body's defenses against disease.) To test their theory, the team infused EBV-specific CTL lines into two groups of patients: those who were undergoing HSCT and were at high risk of developing EBV-lymphoma, and patients who had already developed lymphoma. The study reported that CTL treatment successfully prevented the

development of EBV-lymphoma in all 101 patients in the at-risk group who received the therapy prophylactically and achieved sustained complete remission in 11 of the 13 patients (85 percent) treated therapeutically (those who already had the disease).

"Therapy with EBV-specific CTLs was effective for these severely immunocompromised patients. The CTLs successfully reached tumors, multiplied, and were able to kill the tumor cells," said lead study author Helen Heslop, MD, of the Center for Cell and Gene Therapy at Baylor College of Medicine, The Methodist Hospital, and Texas Children's Hospital.

While the successful outcomes result from a number of factors in the study, the researchers attribute some of the success of the trial to the time of treatment. The CTL lines were infused soon after stem cell transplantation, when the existing white blood cell count was still low and was not quickly regenerating, allowing the infused cells to more quickly multiply and mediate anti-viral and anti-tumor effects. In addition, by marking and tracking the CTL genes, the team was able to demonstrate that the cells could survive for up to nine years in the body, conferring long-term protection.

With strong clinical outcomes, the study team is working to determine the most appropriate role and timing for CTL infusions. Some newer therapies (such as monoclonal antibodies) offer prophylactic and therapeutic options but cannot offer long-term protection. Therefore, treatment with CTLs may be reserved for the highest risk patients - those with a diagnosis of immune deficiency or a history of EBV-lymphoma, or those who develop elevated EBV levels after therapy with monoclonal antibodies.

Importantly, the study found that this type of therapy is not only effective, but economically advantageous. A preliminary analysis

showed that a patient-specific CTL line can be manufactured, tested, and infused for approximately $6,000, a cost that compares well with other modalities used in the treatment of EBV-lymphoma. Moreover, the team determined that it is possible to manufacture cells in one location and ship them to another center for infusion, with reproducible and consistent results and clinical outcomes.

"It's important to note that this promising therapy is not only effective, but it is also a cost-effective option for high-risk patients," said Dr. Heslop.

More information: www.bloodjournal.org

Source: American Society of Hematology