Early infusion of donor T cells prevents graft versus host disease in blood cancer patients
3 February 2011

For blood cancer patients at high risk of relapse, hematopoietic stem cell transplantation (HSCT), the transplantation of blood-forming stem cells, is one of best options for treatment and a potential cure. Unfortunately, the most common complication of HSCT is graft-versus-host disease (GVHD), a serious and often deadly post-transplant complication that occurs when the newly transplanted donor cells recognize the recipient's own cells as foreign and react by attacking the cells in the patient's body.

A study published today in Blood, the Journal of the American Society of Hematology, highlights updated results for a potential new strategy for preventing GVHD and promoting the patient's immune system recovery after transplant.

Patients who do not have a compatible donor in the family or in donor registries must rely on a transplant from alternative sources, such as a partially matched donor, as their only hope for cure. To ensure the success of transplants from partially matched donors, the donated stem cells must be treated before they are transplanted into the patient. This treatment depletes the donor's T cells, which are critical for promoting immune recovery after transplant but can also trigger severe and potentially fatal GVHD. Therefore, managing the dual function of T cells is critical before and after the transplant procedure.

In a trial conducted at the University of Perugia in Italy by a group that has pioneered the use of partially matched donors, researchers explored the use of a population of T cells called regulatory T cells (Tregs) that control immune reactions. Regulatory T cells have been widely studied in animal models and have been shown to promote the acceptance of organ grafts and control abnormal immune reactions associated with GVHD. They have not yet been tested in humans prior to this study, which enrolled 22 patients with acute myeloid leukemia (AML), five patients with acute lymphoid leukemia (ALL), and one patient with high-grade non-Hodgkin lymphoma. Four days before HSCT, the 28 patients were infused with donor Tregs, and on the day of the transplant, they were infused with normal T cells in an effort to simultaneously prevent GVHD and promote immune system recovery.

“Our aim was to determine if patient outcomes could be improved if Tregs were introduced early in the transplantation process,” said senior study author Massimo F. Martelli, MD, Full Professor and Head of the Umbria Region Bone Marrow Transplantation Program at the University of Perugia.

Results of the study revealed that 26 patients achieved full-donor engraftment, meaning that all of the transplanted donor cells were able to reproduce into new, cancer-free cells. Only two of the 26 patients that were evaluated developed acute GVHD, and at median follow-up of 11.2 months none of the patients had developed chronic GVHD. The immune system of these patients was restored to normal levels, better than other patients who had not received the T cell infusions. There were also fewer episodes of the reactivation of Cytomegalovirus (CMV), a common virus known as a major cause of morbidity and mortality after HSCT due to a weakened immune system, and no patient developed CMV disease. Furthermore, early Treg infusion was not associated with an increased incidence of leukemia relapse; only one relapse had occurred at median follow-up of 12 months in a patient with AML. One patient died from adenoviral infection and GVHD and one died from GVHD; at median follow-up of 12 months, 12 patients (46.1 percent) were alive and disease-free.
"This is an update of the first study in humans that demonstrates that regulatory T cell-based therapy ensures that hematopoietic stem cell transplant is successful, without triggering GVHD, by reconstituting the patient's immune system faster than standard transplant methods," said Mauro Di Ianni, MD, senior study co-author and Researcher at the Hematology and Clinical Immunology Section at the University of Perugia.

Provided by American Society of Hematology