

Researchers test drug combinations to prevent graft vs. host disease

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Researchers at Moffitt Cancer Center have conducted a clinical trial aimed at preventing graft vs. host disease (GVHD) in patients who have received hematopoietic (blood) cell transplants (HCT). The study, comparing the drug tacrolimus (TAC) in combination with either methotrexate (MTX) or sirolimus (SIR), found that the sirolimus/tacrolimus (SIR/TAC) combination was more effective in preventing grades II-IV acute GVHD and moderate-severe chronic GVHD after allogeneic blood cell transplantation.

The study randomized 74 patients, ages 16 to 70, to receive either SIR/TAC or MTX/TAC. Patients were stratified by donor relation (siblings or matched, unrelated individuals) and age.

Their study was published in a recent issue of *Haematologica*, the journal of the European Hematology Association.

"Graft vs. host disease poses major health problems for patients who have received hematopoietic [cell transplants](#) and threatens the long-term success of their transplant," said Joseph Pidala, M.D., M.S., a medical oncologist and study principal investigator. "Existing pharmacologic strategies do not adequately prevent acute graft vs. host disease following allogeneic hematopoietic (blood) [cell transplantation](#), and effective acute GVHD prevention is an important clinical goal necessary to ensure the long-term success of transplantation."

According to the authors, their study design mandated at least one year

of sirolimus therapy in order to both limit the risk from chronic GVHD development and to promote the patients' [immune tolerance](#) based on the "reconstitution" of the patients' immune cells, called regulatory T cells, or "Tregs."

"Our hypothesis was that SIR-based [immune suppression](#) would suppress alloreactive T cells, support the recovery of the immune system's Tregs, and more effectively prevent GVHD," explained Pidala.

Results showed that on days 30 and 90 post transplantation, SIR/TAC-treated patients had "a significantly greater proportion of [regulatory T cells](#) among the CD 4 [immune cells](#) in their peripheral blood" and their regulatory Tregs were "functional."

The authors suggested that the "net benefit" observed in Treg reconstitution with SIR/TAC-treated patients was likely due to both the suppression of immune systems' non-Treg CD4 T cells by sirolimus, as well as the lower tacrolimus exposure for these patients as compared to patients on the MTX/TAC arm of the study.

Provided by H. Lee Moffitt Cancer Center & Research Institute

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