Novel Regimen Greatly Reduced Chronic GVHD After Stem Cell Transplants

Fred Hutch's Phase II study of blood cancer patients is a "game changer" in preventing graft-versus-host disease after transplantation.

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Chronic graft-vs.-host disease (cGVHD) can be debilitating for people who have had an allogeneic stem cell transplant. In GVHD, the transplanted donor cells recognize the recipient's tissues as foreign and attack them. This can cause a variety of problems throughout the body, from skin rashes to organ damage.

A novel drug regimen tested for the first time by researchers at Fred Hutch Cancer Center has shown great promise in preventing moderate to severe cGVHD after transplant in people who received nonmyeloablative or reduced-intensity conditioning to treat a blood cancer. In a randomized Phase II study, the Fred Hutch team compared the effects of two drug combinations given to prevent GVHD by suppressing the immune system: sirolimus, cyclosporine and mycophenolate mofetil (SIR/CSP/MMF) and sirolimus, cyclosporine and post-transplant cyclophosphamide (SIR/CSP/PTCy).

The rate of moderate to severe cGVHD one year after transplant was 1% in the latter group, who received PTCy, compared to 28% in the control group. Estimated one-year cGVHD-free relapse-free survival was also better in the PTCy group — 76% vs. 55%.

Fred Hutch clinical researcher Masumi Ueda Oshima, MD, MACourtesy of Fred Hutch News Service

“PTCy has been a game changer for chronic GVHD, and our novel combination of drugs may work even better than previous combinations of drugs with PTCy,” said Masumi Ueda Oshima, MD, MA, lead researcher for the study and associate professor in Fred Hutch’s Clinical Research Division, who was pleased to see that the reduction in cGVHD was not offset by an increased risk of the patient’s cancer returning.

Ueda Oshima will present the results, including updated data with longer follow-up of patients, on February 14 at the Tandem Meetings in Honolulu, a joint conference of the American Society for Transplantation and Cellular Therapy (ASTCT) and the Center for International Blood and Marrow Transplant Research. Tandem selected Ueda Oshima’s abstract as one of the best submitted to the conference.

Another Fred Hutch researcher, Filippo Milano, MD, PhD, will be joining ASTCT’s Board of Directors as Director at Large. He is the director of the Cord Blood Transplant Program at Fred Hutch. Additionally, Mary Flowers, MD, professor emeritus in the Clinical Research Division, will be honored at the Tandem Meetings, where she will receive an ASTCT Public Service Award. Flowers is a world-renowned expert in the study and treatment of cGVHD.

Exciting results for both HLA-matched and HLA-mismatched transplants

“I don’t think any other study so far has combined PTCy with sirolimus and cyclosporine. The rate of chronic GVHD in our PTCy cohort is lower than in studies that have used PTCy with other combinations of drugs, traditionally cyclosporine or tacrolimus and mycophenolate mofetil,” said Ueda Oshima.

The researchers enrolled 145 adults who received an HLA-matched or HLA-mismatched transplant at Fred Hutch using stem cells from an unrelated donor between November 2017 and May 2024.

HLA typing is a way to compare a recipient’s and donor’s immune systems and tissues before transplant. This reduces the chance of selecting a donor whose cells will see the recipient’s cells as foreign. In a fully HLA-matched transplant, recipients and donors match on 10 out of 10 markers. This study also included recipient-donor pairs who matched on only 9 out of 10 markers, the “mismatched” group.

The fact that the SIR/CSP/PTCy regimen worked well in a trial including patients getting a mismatched transplant is of particular value for people who have trouble finding a full match. This includes certain ethnic groups who are underrepresented in donor registries, including African Americans, Asian Americans, Native Hawaiians, Pacific Islanders and Latinos. In transplantation, ethnicity is relevant as it relates to tissue types we inherit from our ancestors.

Building on past research and looking to the future

The new PTCy research builds on an earlier multicenter study led by Brenda M. Sandmaier, MD, which found that adding sirolimus to cyclosporine and mycophenolate mofetil significantly reduced acute GVHD (which develops in the first three months after transplant) and improved overall survival. Sandmaier is deputy director of the Translational Science and Therapeutics Division. In her study, rates of chronic GVHD (which typically develops three months to three years after transplant) didn’t drop with the addition of sirolimus. The next step then, said Ueda Oshima, was to focus on reducing cGVHD by keeping sirolimus in the mix but trying PTCy in place of mycophenolate mofetil.

There’s more work to be done. Ueda Oshima plans to confer with colleagues at the Tandem Meetings about the possibility of a conducting a multicenter study testing the SIR/CSP/PTCy regimen in more people to see if they get the same promising results.

Infection is one focus of further study. Viral and other infections were more common in the patients receiving PTCy, but reassuringly, this did not lead to higher rates of treatment-related death. Further study may help researchers understand why infections were more common and optimize the SIR/CSP/PTCy regimen to reduce infection risk, said Ueda Oshima.

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support.

Fred Hutch at Tandem Meetings

View highlights of Fred Hutch faculty members' presentations at Tandem from February 12–15.

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