New drug combo may improve family-donated stem cells as blood cancer treatment

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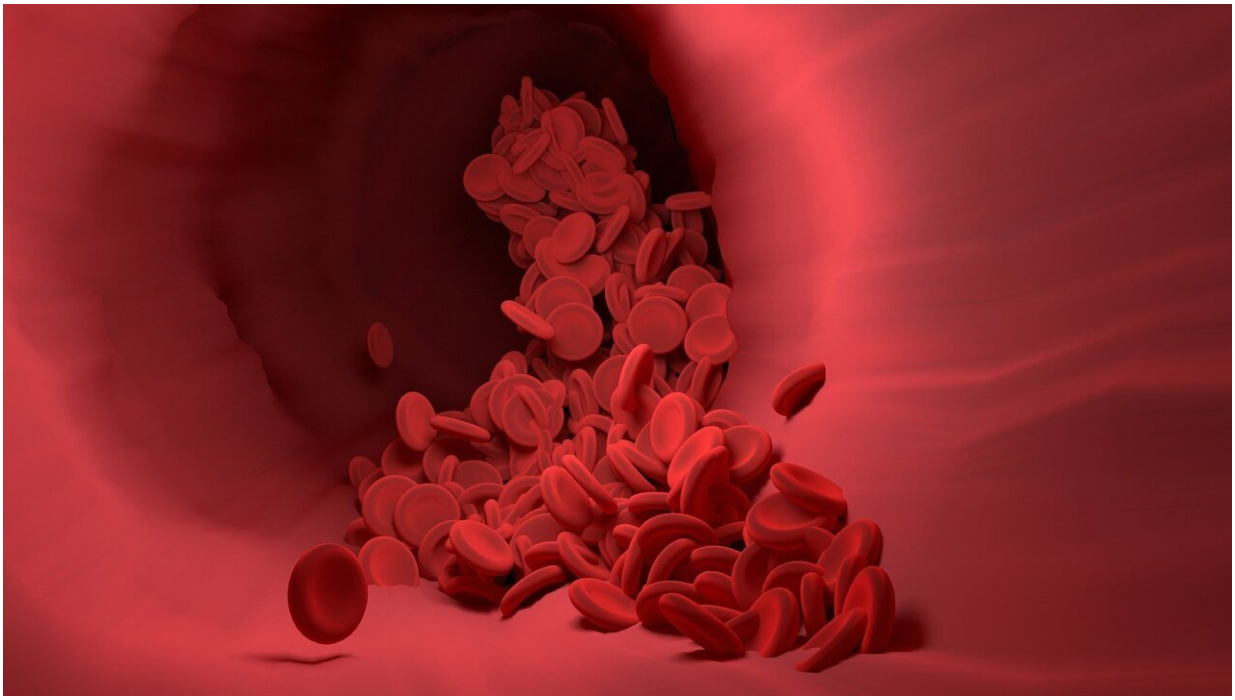

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A drug combination can safely prevent transplanted stem cells (graft) from attacking the recipient's (host) body, allowing them to develop into healthy new blood and immune cells, a new study shows.

Researchers say stem cell transplantation, especially from members of the same family, has transformed the treatment of leukemia, a disease

that afflicts nearly a half-million Americans. And although the treatment is successful for many, half of those who undergo the procedure experience some form of graft-versus-host disease (GvHD). This happens when the newly implanted immune cells recognize their host's body as "foreign" and then target it for assault, much like they would an invading virus.

Most cases of GvHD are treatable, but an estimated one in 10 can be life-threatening. For this reason, researchers say, immune-suppressing drugs are used to prevent GvHD by the donated cells, and patients, who are mostly unrelated, are matched whenever possible with donors beforehand to make sure their immune systems are as similar as possible.

Led by researchers at NYU Langone Health and its Laura and Isaac Perlmutter Cancer Center, the new and ongoing study showed that a new regimen of immune-suppressing drugs, cyclophosphamide, abatacept, and tacrolimus, better addressed the problem of GvHD in people being treated for blood cancer.

"Our preliminary results show that using abatacept in combination with other immune-suppressing drugs is both safe and an effective means of preventing GvHD after stem cell transplantation for blood cancers," says study lead investigator and hematologist Samer Al-Homsi, MD, MBA. "Signs of GvHD with abatacept were minimal and mostly treatable. None were life-threatening," says Al-Homsi, a clinical professor in the Department of Medicine at NYU Grossman School of Medicine and Perlmutter Cancer Center.

Al-Homsi, who also serves as director of the blood and marrow transplant program at NYU Langone and Perlmutter Cancer Center, is presenting the team's findings online Dec. 13 at the American Society of Hematology's annual meeting in Atlanta.

The investigation showed that among the first 23 adult patients with aggressive blood cancers given the posttransplant drug regimen over a period of three months, just four showed early signs of GvHD, including skin rash, nausea, vomiting, and diarrhea. Another two developed reactions weeks later, mostly skin rashes. All were successfully treated with other medications for their symptoms. None developed more severe symptoms, including liver damage or difficulty breathing. However, one patient, whose transplant failed, died of recurring leukemia. The rest (22 men and women, or 95 percent) remain cancer free more than five months after their transplant, with donated cells showing signs of producing new, healthy, and cancer-free blood cells.

Along with increasing donor options for all patients, the study results have the potential to address racial disparities in stem cell tranplantation. Given the nature of the donor pool to date, Blacks, Asian Americans, and Hispanics are less than one-third as likely as Caucasians to find a completely matched stem cell donor, leaving family members as the most reliable donor source. Some 12,000 Americans are currently listed and waiting on the national bone marrow program registry, Al-Homsi notes.

The current study involved stem cell transplantations from closely related (half-matched) donors and patients, including parents, children, and siblings, but whose genetic make-up was not identical, with the drug combination increasing the likelihood of successful transplantation.

"Alternative drug regimens are urgently needed to prevent GvHD, especially among those for whom finding a close match is challenging," says senior study investigator and hematologist Maher Abdul Hay, MD, an assistant professor at NYU Grossman School of Medicine and Perlmutter Cancer Center and director of its clinical leukemia program.

"By improving the odds against developing graft-versus-host disease, we

can expand the pool of family members who can safely serve as stem cell transplant donors for people with blood cancers, regardless of their ethnic background," says Al-Homsi.

The new regimen replaces the traditionally used drug mycophenolate mofetil with abatacept. Al-Homsi says abatacept is "more targeted" than mycophenolate mofetil and prevents immune T cells from becoming "activated," a necessary step before these immune cells can attack other cells. Abatacept is already widely approved for treating other immune disorders, such as arthritis, and has been successfully tested in preventing GvHD with closely matched, unrelated donors. Until now, fully matched donors have shown better results in preventing graft-versus-host disease than half-matched family, or so-called haploidentical, donors.

Also, as part of the revised treatment, researchers shortened the treatment time for tacrolimus to three months, from the original treatment window of six to nine months. This was due to the drug's potential toxic side effects on the kidney.

More information: This poster presentation at the annual meeting of the American Society of Hematology, Abstract #3906, Session #722, Is titled Posttransplant Cyclophosphamide, Abatacept, and Short-Course Tacrolimus Combination (CAST) is Safe and Seems Highly Effective in Preventing Graft-Versus-Host Disease Following Haploidentical Peripheral Blood Stem Cell Transplantion.

Provided by NYU Langone Health