Use of venetoclax in transplant conditioning regimen shows promise in myeloid cancers

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Jacqueline S. Garcia, MD. Credit: Dana-Farber Cancer Institute

For patients with high-risk myeloid cancers undergoing a donor stem cell transplant, adding the targeted drug venetoclax to a reduced-intensity drug regimen prior to transplant is safe and does not impair the ability of the donor cells to take root in recipients' bodies, a study led by Dana-Farber Cancer Institute researchers suggests. The study will be presented today at the 61st American Society of Hematology (ASH) Annual Meeting.

The findings provide support for the use of venetoclax prior to transplant as a way to increase the chances of transplant success in this group of patients, said Jacqueline S. Garcia, MD, physician in the Adult Leukemia Program at Dana-Farber and first author of the study.

While a donor stem cell transplant can cure myeloid malignancies such as acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS), patients whose tumor cells carry certain genetic mutations or chromosomal abnormalities have a high risk of relapsing after transplant. A variety of approaches to lowering the chance of relapse are under study. One involves using venetoclax, which prompts cancer cell death by blocking the BCL-2 protein, as part of the conditioning regimen patients receive in preparation for a donor stem cell transplant.

The new study focused on patients who underwent reduced-intensity conditioning regimens, which use lower, less toxic doses of chemotherapy and radiation therapy. While such regimens kill fewer cancer cells than traditional "myeloablative" treatments, they are milder on the body and are used in patients over age 60.

"In previous research, we have shown that adding venetoclax to leukemia drugs produces a very large increase in anti-leukemia activity," Garcia remarked. "We hypothesized that venetoclax would promote the anti-

leukemic effect of conditioning chemotherapy and therefore reduce the risk of relapse without producing undue toxicity."

The study involved nine patients with high-risk AML or MDS who were recommended for a donor stem cell transplant. In a phase I clinical trial, they received venetoclax along with the chemotherapy drugs fludarabine and busulfex as a conditioning regimen and then underwent a donor stem cell transplant.

"We found that venetoclax can be safely added to standard reduced-intensity conditioning without impeding the ability of donor neutrophils [a type of white blood cell] to engraft," Garcia stated.

Because patients are just six months removed from transplant, it is too early to know if the new regimen reduced the chance of relapse, Garcia noted, but the fact that the donor cells have engrafted—evidenced by patients' blood counts—is an encouraging sign. There has not been a signal of toxicity in excess of what is expected with standard reduced-intensity conditioning, including rates of graft-versus-host disease. To further minimize the potential for relapse, the trial is under an amendment to allow trial participants to receive post transplant maintenance therapy of low dose venetoclax and the chemotherapy drug azacytidine.

More information: ash.confex.com/ash/2019/webpro … ram/Paper126172.html

Provided by Dana-Farber Cancer Institute

https://medicalxpress.com/news/2019-12-venetoclax-transplant-conditioning-regimen-myeloid.html