Researchers examine specific causes of mortality after blood and marrow transplant

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Blood and Marrow Transplantation (BMT) is a potentially curative treatment for patients with leukemia or other life-threating blood diseases. With a goal of increasing survival rates, a research team led by Roswell Park Cancer Institute (RPCI) investigators verified patient outcome data submitted by more than 150 U.S. transplant centers over an 11-year period to the Center for International Blood and Marrow Transplant Research (CIBMTR). The detailed investigation — published in the journal *Biology of Blood and Marrow Transplantation* — offers insight into different causes of death. The results of this genome-wide association study led to the development of a first-of-its-kind definition of specific causes of mortality after unrelated-donor, or allogeneic, BMT.

Theresa Hahn, PhD, of the Department of Medicine and Lara Sucheston-Campbell, PhD, of the Department of Cancer Prevention and Population Sciences, both at Roswell Park, are co-principal investigators of this study, which is supported by a National Institutes of Health (NIH) award for $5.18 million, the largest R01 research grant in Roswell Park's history.

"This work is part of the personalized medicine effort at Roswell Park and more broadly part of the NIH Personalized Medicine Initiative aimed at modifying treatment based on a patient's genetic information," says Dr. Sucheston-Campbell. "It is important that we accurately define outcomes in these types of genomic studies as precisely as possible. Our work is a critical first step toward the ultimate goal of finding a better match for patients receiving an unrelated-donor blood or marrow transplant."

The investigators convened a consensus panel to review specific causes of death to reduce misclassification and to determine the impact of genetics on BMT outcomes. The panel evaluated patient outcomes data for 1,484 patients who died within one year after an allogeneic BMT.

In the cases where the transplant center reported mortality due to leukemia, Drs. Hahn and Sucheston-Campbell found almost perfect agreement between the consensus panel and transplant center, in terms of how those deaths were classified. There was less agreement for transplant-related mortality, and the level of agreement/discordance varied depending on the specific cause of death. These results indicate that transplant-related mortality needs to be better defined. This study provides a mechanism for prioritizing those BMT cases that should be reviewed.

"We need to make sure that patients who experienced similar clinical events after a transplant were consistently defined regardless of where they were treated. This is a difficult topic to consider, but we can't make progress to improve transplant outcomes without these discussions," adds Dr. Hahn.

Researchers conducting clinical trials commonly use committees to review and define endpoints. Those conducting genome-wide association studies rarely do, instead relying on center-reported outcomes, which are variable, according to Drs. Hahn and Sucheston-Campbell.

BMT patients are matched to the best possible unrelated donors through human leukocyte antigen (HLA) typing, also called "tissue typing." HLA are proteins — or markers — found on most cells in the body. The immune system uses these markers to recognize which cells belong in the body and which do not. HLA matching is important, because a close match improves the chances of a successful transplant. This research may open doors to determining better matches between patients and donors based on testing genes in addition to HLA of both the donor and the patient.

Source:
Roswell Park Cancer Institute
