Germline predisposition traits in allogeneic hematopoietic stem-cell transplantation for myelodysplastic syndromes

WHAT?

The Chronic Malignancies Working Party (CMWP) of the European Society for Blood and Marrow Transplantation (EBMT) set out to understand current practices in Europe and establish consistent guidelines for the testing and treatment of patients with myelodysplastic syndromes (MDS) who have specific inherited genetic changes (germline variants).

WHY?

- Certain germline variants could make a person more likely to have certain types of blood cancers and blood disorders, such as MDS. Understanding if a patient or donor has these genetic changes could impact a doctor's treatment plan for a patient who needs an allogeneic blood or marrow transplant (BMT). Allogeneic BMT uses blood stem cells from a related or unrelated donor.
- There are no international guidelines to standardize the treatment approach for patients with MDS when specific genetic changes are detected through molecular testing.

WHO?

- A CMWP MDS subcommittee and Practice Harmonization and Guidelines committee surveyed EBMT transplant centers with high expertise in BMT for MDS as well as an international panel of experts with worldwide representation.
- An international panel of hematologists, transplant physicians, pediatricians, nurses, and experts in molecular biology and genetics who have experience in MDS came together to discuss the survey results and establish the guidelines.

WHEN?

- Survey work began in February 2023. The CMWP published a position paper and suggested guidelines in October 2023.

RESULTS

- The survey showed variation in many areas such as access to and use of next-generation molecular testing, criteria used in deciding which patients to screen, access to a dedicated genetic counselor, and whether detection of a genetic trait led to use of a different donor or different patient conditioning strategies.
- The published guidelines outline many recommendations for patients with MDS who will have BMT such as: criteria to screen patients for germline variants; how to test, confirm and interpret germline variants; genetic counseling and surveillance of donors and families with inherited traits; conditioning regimens and GVHD prevention strategies; and follow-up after BMT to screen for complications like donor-derived leukemia.

Read the study abstract published in The Lancet Haematology: https://doi.org/10.1016/S2352-3026(23)00265-X

IMPACT

- Following the recommendations outlined in the guidelines could improve BMT outcomes for patients with MDS who have specific germline variants.

FROM THE EXPERTS

"We recognize that when hematopoietic stem cells with deleterious germline variants in certain genes are used for allogeneic stem cell transplantation, several poor outcomes result: poor mobilization, poor engraftment, poor graft function, donor-derived leukemias, and leukemia developing in the donor. We also know that individuals with deleterious germline DDX41 variants are susceptible to severe graft-versus-host disease even with wild-type donors unless T-cell suppression provided by post-transplant cyclophosphamide is used. Additional critical questions to address for the future include developing a comprehensive list of deleterious germline variants that result in poor allogeneic transplant outcomes; whether some such variants are permissive to successful transplants; and whether germline testing for cancer risk and bone marrow failure conditions should become routine for all donors whether related to the patient or not."

Lucy A. Godley, MD, PhD
Jeffrey and Marianne Silver Family Professor of Oncology
Director, Silver Family Blood Cancer Institute
Clinical Director of Cancer Genetics
Robert H. Lurie Comprehensive Cancer Center
Division of Hematology/Oncology
Northwestern University

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