Multi-Center Evaluation of the Prognostic Significance of Measurable Residual Disease (MRD) Testing Prior to Allogeneic Transplantation for AML

CIBMTR® (Center for International Blood and Marrow Transplantation®) study in collaboration with the Laboratory of Dr. Christopher Hourigan at the National Heart, Lung, and Blood Institute: Pre-MEASURE

Highlights for Physicians:

Measurable residual disease (MRD) assessment before allogeneic hematopoietic cell transplantation (alloHCT) can be a powerful relapse and survival predictor in patients with acute myeloid leukemia (AML), but standardization is lacking. Relapse prevention for adults with AML in first remission is the most common indication for alloHCT. Next-generation sequencing (NGS)-based MRD testing pre-transplant may identify AML patients at high risk for subsequent relapse.

- **This study included the largest cohort of patients with AML with retrospective NGS-MRD testing on samples collected prior to alloHCT,** which provides valuable insight into MRD as a predictive tool for individualizing treatment plans and informing decisions regarding transplantation.
- **AML patients in first remission but with FLT3-ITD or NPM1 mutations still detectable had increased relapse and worse survival** compared to those without mutation persistence.
- **NGS-MRD testing of remission blood pre-transplant in patients with FLT3-ITD and/or NPM1 mutated AML can identify differential risk of subsequent relapse.** This supports the need for future precision medicine approaches to develop standardized DNA sequencing testing for MRD variants to help improve patient outcomes.

Results at a Glance:

Pre-MEASURE: N=1075 (N=454 discovery cohort transplanted between 2013-2017, N=621 validation cohort transplanted between 2018-2019), patients aged 18 and older who underwent first alloHCT for AML in first remission and had an FLT3, NPM1, IDH1, IDH2, and/or KIT mutation at diagnosis with pre-transplant remission blood available from the CIBMTR repository

- There were no differences in 3-year relapse rates (29% vs. 28%) or overall survival (OS) rates (61% vs. 61%) between the discovery and validation cohorts.
- In the discovery cohort, 17.3% of patients with the persistence of NPM1 and/or FLT3-ITD mutation variants had significantly higher relapse (59% vs. 24%) and lower OS (34% vs. 66%) at 3-years post-transplant than patients without persistent variants.
- Of the 451 patients in the validation cohort, 17.3% with persistence of NPM1 and/or FLT3-ITD mutation variants also had higher relapse rates 3-years post-transplant (68% vs. 21%) and decreased OS (39% vs. 69%).
- Myeloablative conditioning (MAC) regimens were associated with lower relapse and improved survival compared to reduced intensity conditioning (RIC).

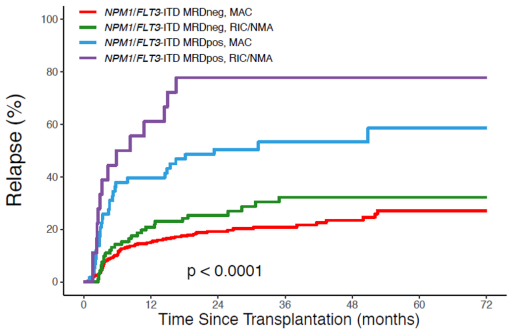

Figure: Relapse based on conditioning intensity and pre-transplant NGS-MRD in patients <60 years.

Advancing Practice and Improving Outcomes:

The National Marrow Donor Program®/Be The Match® and the CIBMTR are committed to patients thriving after transplant. The development of standardized approaches for monitoring MRD before and after alloHCT for AML can support a personalized treatment plan for each patient. This is the aim of the multi-center, prospective MEASURE protocol (NCT0522466), following up on Pre-MEASURE results. Our research programs are evaluating novel treatment strategies that can improve outcomes and care for all patients.

You can support your patient's journey both pre- and post-transplant by:

- Discussing treatment options early with your patients
- Examining your center's protocols for NGS-MRD testing and monitoring
- Coordinating care between transplant centers and hematology/oncology physicians to improve communication and optimize treatment plans for your patients

Read the full Pre-MEASURE results in the *Journal of the American Medical Association* (DOI: 10.1001/jama.2023.1363).

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