Can We Risk Adjust for Measurable Residual Disease in Acute Leukemia?

Wael Saber

Project #1: integration of MRD data in annual Center Specific Analysis

- Relatively few patients had definitive MRD response

Among 8200 patients with AML in CR, by high resolution testing, only

3% were MRD negative, and only 8% were MRD positive

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Project #1: integration of MRD data in annual Center Specific Analysis

- Among those with definitive data, substantial rate of discrepancy exists between different testing modalities (MFC vs. NGS), and within the same modality (NGS data) when reported at two consecutive time points with no intervening therapies (at last eval and immediately pre-HCT)

- Nearly 1300 (16%) were reported to have negative MFC at HCT but were positive for a molecular marker at last eval

- 30% had discrepant molecular data between last eval and at HCT

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- Unclear if the reported molecular data represent key driver mutations vs. germline variants vs. CHIP

Project #2 LK21-01

- LK21-01a "Impact of MRD status on outcomes of AML patients in CR1 undergoing allo-HCT".

- Only 10% (N=60) of those who relapsed any time after transplant (N=620) had a positive pre-transplant MFC test result, underscoring limited prognostic utility of registry-reported MFC-MRD testing

- Although 41% of the MRD-neg and 36% of patients in the MRD-pos group had both molecular and MFC MRD testing reported on the forms, the collected molecular MRD was not comprehensive

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Project #2 LK21-01

- LK21-01b Inter-Laboratory differences affect the prognostic value of pre-transplant flow cytometric measurable residual disease in acute myeloid leukemia: A CIBMTR Analysis.

The analysis confirmed heterogeneity in the prognostic impact of MRD by MFC across centers.

The prognostic performance may be influenced by center-specific factors, possibly including differences in assay implementation, sensitivity, or reporting practices.

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A taskforce was convened

Purpose:

- Assess the current state of MRD data collection and variable definitions within CIBMTR forms and datasets
- Identify key sources of heterogeneity and misclassification in reported MRD data
- Recommend standardized data elements and definitions for MRD testing and interpretation across leukemia subtypes based on current clinically recommended testing
- Propose revisions to CIBMTR forms and data collection workflows to improve accuracy and utility of MRD data
- Define an approach for stratifying or adjusting MRD data for analysis when different methodologies are used
- Prioritize feasibility and clinical relevance to ensure recommendations are implementable by centers of varying resources

A taskforce was convened

The membership was comprised of:

- Co-chairs of the CIBMTR leukemia committee
- CIBMTR scientific directors
- External hematologists with recent experience in assessing MRD data strengths and limitations within the CIBMTR context
- CIBMTR statisticians (MS and PhD level) with extensive experience in multivariable analysis of transplant outcomes
- External cytogeneticist/molecular geneticist with expertise in MRD testing platforms
- Medical informatics specialist
- CIBMTR Data Operation specialist.

The members had 4 meetings so far. Preliminary recommendations were generated. Final recommendations will be forthcoming in January 2026.