Clinical Decision Making in AML

NEW RESEARCH GUIDES THERAPEUTIC CHOICES

Key Findings

1. Revised risk stratification based on updated molecular markers and cytogenetics research.

2. Therapy decisions should be based on patient health status and disease risk features, not chronological age.

3. Improved outcomes of transplant for AML.
Revised risk stratification

Evolving research is altering how cytogenetic and molecular markers are used to guide therapeutic choices in AML. Table 1 shows risk status based on validated cytogenetics and molecular markers from the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia.

 Emerging data indicate that the presence of c-KIT mutations in patients with t(8;21), and to a lesser extent inv(16), confers a higher risk of relapse; these patients are considered to have intermediate-risk disease. [1]

Table 1. NCCN risk status based on validated cytogenetics and molecular abnormalities for AML. Adapted with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.1.2016. © 2016 National Comprehensive Cancer Network, Inc. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the NCCN Guidelines, go online to NCCN.org. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, NCCN GUIDELINES®, and all other NCCN Content are trademarks owned by the National Comprehensive Cancer Network, Inc.

Recommended timing for transplant consultation for AML

To supplement the NCCN Guidelines®, the National Marrow Donor Program® (NMDP)/Be The Match® and the American Society for Blood and Marrow Transplantation (ASBMT) have jointly developed guidelines for transplant referral timing. [5]

Referral timing guidelines for AML, shown in Table 2, highlight that high-resolution HLA typing should be performed at time of diagnosis for all patients with AML, and identifies those patients who should be referred early after initial diagnosis. This includes all patients with intermediate- and poor-risk cytogenetic/molecular features as well as high-risk disease features.

Table 2. NMDP/Be The Match and ASBMT transplant consultation guidelines for AML in adults. CR1 = first complete remission

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For patients with intermediate- and poor-risk cytogenetics, a meta-analysis demonstrated a survival benefit of allogeneic HCT in first complete remission over chemotherapy. [2] Referral for HCT evaluation for these at-risk patients early in their disease stage can significantly improve survival. [3,4]
New research: HCT eligibility and age

Research has shown that chronological age alone is not a contraindication for HCT in patients with AML. [6-8] Comorbidities and performance status are prognostic factors used to determine eligibility for transplant. [9] This is reflected in a steady increase in the number of unrelated donor transplants for patients older than 64 years with AML from 2007 to 2015 as shown in Figure 1. [10]

Clinical advances improve transplant survival

Overall survival at 1- and 2-years after unrelated donor HCT has improved steadily over time as shown in Table 3. Improvement in survival has occurred even as greater numbers of older patients are undergoing transplant.

Better risk-stratification using AML molecular markers and cytogenetics has contributed to improvements in survival. Other reasons for improved survival rates include the monitoring of minimal residual disease (MRD), which allows for preemptive therapy with persistent or recurrent disease [11], and improved management of post-transplant complications. [12,14]

Disease status at time of transplant can also significantly affect outcomes. Research has shown that transplant in early stage disease can lead to significantly improved survival. [3,4] Figure 2 shows this for adult patients with AML undergoing unrelated donor HCT. [15]

Several studies have shown that unrelated donor and sibling donor HCT outcomes in AML are comparable, including a study of 197 patients ≥50 years with AML in complete remission. [16-17]
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Clinical Action Points

1. Apply cytogenetic and molecular markers for AML risk-stratification to determine prognosis and therapeutic options.

2. Counsel older patients on HCT as a therapeutic choice based on disease risk and health status, not on chronological age.

3. Recommend a transplant consultation early after initial diagnosis for patients with intermediate- or poor-risk molecular/cytogenetics or other high-risk disease features.

SUPPLEMENT TO YOUR TREATMENT GUIDELINES

Our Recommended Timing for Transplant Consultation guidelines provide you with the HCT referral-timing information you need most.

Updated annually, the guidelines provide up-to-date referral timing based on the latest research.

Available free in print, mobile app and online: BeTheMatchClinical.org/guidelines

References:

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5. 2016 NMDP/Be The Match and ASBMT referral timing guidelines – AML.


15. 2015 CIBMTR analysis of NMDP/Be The Match-facilitated transplants.


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