Rapid Donor Identification Improves Survival in High-Risk First-Remission Patients With Acute Myeloid Leukemia

John M. Pagel, MD, PhD, Megan Othus, PhD, et al. JCO Oncol Pract. 2020 Jun; 16(6): e464-e475

Implications for Community Physicians:

Human leukocyte antigen (HLA) typing along with cytogenetic testing, initiation of donor identification, and referral for hematopoietic cell transplant (HCT) consultation in early disease state produced better health outcomes for patients with newly diagnosed acute myeloid leukemia (AML).

By addressing common barriers to HCT sooner and increasing the likelihood that patients would undergo HCT at the optimal time, it's possible to get more than 60% of adults ≥60 years of age who are in first complete remission (CR1) with high-risk cytogenetics to transplant and improve the overall survival (OS).

In this study, a 65% transplant rate in CR1 was achieved compared to the historical rate of 40% ($p < 0.001$) and a 37% increase in 2-year OS among patients who underwent HCT compared with patients who did not undergo HCT (48% vs 35%, respectively $p = 0.031$).

Objective:

To assess the likelihood that a precise, structured method could increase the number of successful allogeneic HCT to ≥60% of adults with high-risk AML in CR1 compared with historical controls.

Background:

Cytogenetics is the most common and reproducible method of estimating adults' prognosis with AML. Combined with cytogenetics and HLA typing the path towards HCT takes time, effort, and resources to identify potential donors. The process of early risk stratification and HLA typing remains vital to the oncology community at large as typically, only approximately 40% of high-risk patients proceed to HCT.

Design:

N = 738 patients were accrued, morphologically confirmed, newly diagnosed AML patients ages 18-60 (median age of 49).

Cytogenetic risk at enrollment: 159 patients (22%) with high-risk, 457 (63%) with intermediate-risk, and 96 (13%) with favorable-risk; 26 patients (4%) had missing/unknown cytogenetic risk.

Method:

At study entry, each patient's buccal swab was sent to NMDP[SM] to expedite HLA typing while simultaneously performing local, conventional cytogenetic analysis for risk stratification with a 7-10 day turnaround time. Sites that did not submit results within that initial time frame received follow-up from study staff every 7-10 days to ensure timely risk determination.

Among the 70 high-risk CR1 patients who underwent transplantation: 25 (36%) received transplant from matched related donors, 32 (46%) received transplant from matched unrelated donors, 4 (4%) received from mismatched related donors, and 8 (11%) from mismatched unrelated donors.

All high-risk cytogenetic patients received expedited HLA typing in concert with a preliminary search for alternative donors as alternative donors are available for the majority of patients and outcomes are approximate to those seen with matched related donors. The search results, along with donor selection recommendations, were delivered to the referring physician within 5 days of HLA typing completion. This approach was distinct from the characteristic donor search process in which a formal search by the patient's transplant center would be initiated with HLA typing after referral and consultation (see Figure 1). Decisions regarding donor selection and transplantation were at the discretion of the treating

physician, the transplant center, and the patient. Supportive care was provided as per institutional practice.

TRENDS IN AML RECIPIENT AGE

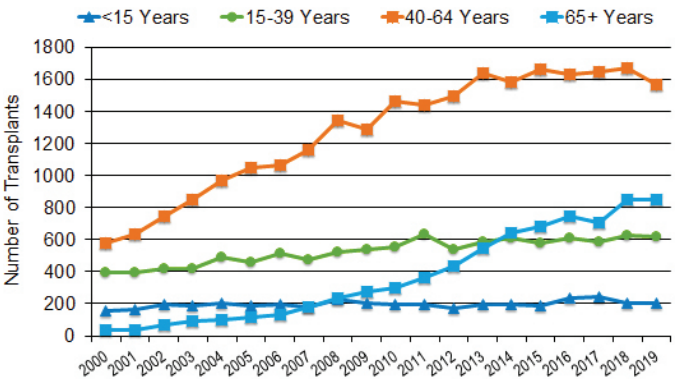

Figure 1. Used with permission from CIBMTR® (Center for International Blood and Marrow Transplant Research®).

Results:

Fifty percent (370) of all patients enrolled received an allogeneic HCT in CR1. Of the 159 high-risk cytogenetic patients, 107 (67%) achieved a CR/CRi between 12 to 88 days with a median of 33 days after random assignment. 70 (65%) of 107 high-risk patients went on to receive a transplant in CR1.

65% transplant rate in CR1 compared to the historical rate of 40% ($p < 0.001$).

37% increase in 2-year OS among patients who underwent HCT compared with patients who did not undergo HCT (48% vs 35%, respectively $p = 0.031$).

Five-year survival after CR1 for transplantation was 52% (allogeneic), 42% (autologous) and 39% for chemotherapy. The advantage of allogeneic transplantation was most apparent for patients with high-risk cytogenetics with a 5-year survival of 44% with allogeneic transplantation versus 15% with chemotherapy alone.

The 2-year OS of the entire cohort was 31%, and the 2-year OS after HCT for those who received HCT in CR1 was 42%.

Conclusions:

The study demonstrates that initiating the donor search process early for newly diagnosed AML patients with high-risk disease increases the likelihood of proceeding to transplant in CR1. Depending on ethnicity, matched unrelated adult donors can be found for 25% to 75% of patients without a matched related donor.

OUTSIDE OF COMPREHENSIVE CANCER CENTERS, PATIENTS ARE OFTEN HLA TYPED AND REFERRED LATE TO TRANSPLANT CENTERS DUE TO A LACK OF ACCESS TO HLA TYPING SERVICES, INSURANCE COVERAGE, AND AWARENESS OF THE BENEFIT OF EARLY HLA TYPING AND TRANSPLANTATION CONSULTATION.