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The Bottom Line

Transplant for Acute Myeloid Leukemia in Patients Aged 70 Years and Older: Optimism and Opportunity

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With a median age at diagnosis of 68 years, nearly half of all acute myeloid leukemia (AML) patients are aged 70 or older [1]. Fortunately, the last few years have ushered in an array of new therapeutic options for older adults with AML. Simultaneously, recent advances in the field of allogeneic hematopoietic cell transplantation (HCT), including routine access to a variety of donor types and stem cell sources and new, exciting approaches to graft-versus-host disease (GVHD) prophylaxis and treatment, offer the promise of widely available, safer, and more effective transplants for this same population. One would think (and hope) that the combination of these achievements will result in a greater proportion of older AML patients receiving effective induction therapy and undergoing HCT with subsequent survival benefit.

However, as we look toward the future of HCT for older adult AML, it is instructive to evaluate where we have been. Although the development of reduced-intensity conditioning has provided an opportunity to transplant older and frailer patients, only some older adults with AML undergo HCT. This is evidenced by an analysis performed by the Center for International Blood and Marrow Transplant Research (CIBMTR) demonstrating that as of 2013, a mere 4% of all AML patients 70 years and older in the United States received HCT [2]. Relative to the prior decade when only .1% of all allogeneic HCTs performed in the United States were for patients in their 70s, this actually represents a marked increase in HCT utilization for older adults in the last 5 to 10 years. The CIBMTR data also established that survival for older adults after HCT has improved over time: 2-year overall survival (OS) for patients 70 years and older transplanted for a variety of disease indications between 2008 and 2013 jumped to 39%, a significant increase from the 26% 2-year OS for patients in the same age group transplanted between 2000 and -2007. Progress has been made, but more work is clearly needed because the nonrelapse mortality for these patients has remained unacceptably high at 30% to 35% and too many patients are still succumbing to their initial disease.

In the current issue of *Biology of Blood and Marrow Transplantation*, Ringden et al. [3], from the Acute Leukemia working party of the European Society for Blood and Marrow Transplantation (EBMT), add to this growing literature by drilling down on the population of patients 70 years and older who underwent HCT exclusively for AML and were reported to the EBMT. Similar to the CIBMTR report, the EBMT analysis shows that transplants for AML in this age group are rising (543 patients were transplanted from 2010 to 2014 relative to 170 from 2004 to 2009), 2-year OS is approximately 40%, and 2-year nonrelapse mortality is high at 34%. By focusing solely on AML patients, Ringden et al. were able to provide additional insights. Notably, for patients aged 70 and older with AML in first complete remission, the 2-year OS of 43% is quite promising. As expected, patients with active disease (>5% marrow blasts) did not fare as well, but even 35% of these patients survived 2 years post-HCT. Undergoing HCT beyond first complete remission was also independently associated with increased nonrelapse mortality, higher incidence of relapse, and worse GVHD-relapse-free survival.

Through the work of the EBMT and CIBMTR, we now have ample population-based historical data on key transplant outcomes for older adults undergoing allogeneic HCT. We can estimate the probability of survival after HCT for a 70-year-old AML patient in first complete remission, and we have a general awareness of predictors of favorable and poor HCT outcomes for these patients. What is missing, however, from these registry analyses of older adults is a sense of the quality of survival for these patients. The 2-year cumulative incidence of chronic GVHD in Ringden et al.'s [3] 70 and older cohort was over 40%, similar to the rate of chronic GVHD that occurs in younger patients. Chronic GVHD has been clearly linked to reductions in quality of life and increased late effects after HCT [4,5]. Assessment of quality of life, function, and symptoms in older adult survivors of HCT would greatly enhance the descriptive outcomes data captured by the national and international HCT registries. An attempt to prospectively evaluate geriatric syndromes, function, and quality of life in older adults across

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the allogeneic HCT trajectory is currently underway in the United States through the BMT CTN CHARM protocol (NCT03992352). Reporting of survival in conjunction with quality of life endpoints will also be informative as non-HCT options for AML consolidation and maintenance continue to proliferate and begin to offer viable non-HCT alternatives for older adults seeking longer-term survival.

Nevertheless, the EBMT report by Ringden et al. demonstrating long-term survival for adults 70 and older with AML after HCT should be cause for optimism for AML and for the field of transplantation. We must continue to rigorously advance the science and clinical care so that HCT may not only be offered to more patients well into their eighth decade, but so that more patients can expect to survive well after our therapy.

DECLARATION OF COMPETING INTEREST

There are no conflicts of interest to report.

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