Patient Selection and Timing of Allogeneic Hematopoietic Stem Cell Transplantation for Relapsed Follicular Lymphoma

Allogeneic hematopoietic stem cell transplantation (allo-HCT) is associated with lower disease relapse rates than autologous hematopoietic stem cell transplantation for the treatment of patients with follicular lymphoma (FL). However, transplantation-related mortality often offsets this advantage. Several recent studies have investigated outcomes of patients with relapsed FL who undergo allo-HCT, with the intent of identifying those most likely to benefit from this procedure.

“Allo-HCT is the only potentially curative approach for FL, with approximately 30% of individuals experiencing long-term remission with reduced-intensity conditioning approaches,” says Christopher R. Flowers, MD, professor of hematology and medical oncology at Emory University School of Medicine in Atlanta, Georgia. “However, it is less commonly used currently due to the aging FL population, other nonchemotherapy (but not curative) approaches, and the toxicity of allo-HCT.” The majority of patients with FL are aged older than 50 years, and transplantation-related mortality is higher among older patients, although approaches to reduce the doses of chemotherapy used prior to allo-HCT make this therapy an option for older patients.

Study Details
One of the new studies examined 1567 patients with relapsed FL who underwent allo-HCT from 2001 through 2011 with a human leukocyte antigen–matched donor. Bone marrow was the source in 154 cases and peripheral blood was the source in 1413 cases (Cancer [published online ahead of print February 9, 2018]. doi: 10.1002/cncr.31264).

Marcelo C. Pasquini, MD, MS, associate professor of medicine in the division of hematology and oncology and senior scientific director of clinical trials support at the Center for International Blood and Marrow Transplant Research (CIBMTR) at the Medical College of Wisconsin in Milwaukee and a coauthor of the new study, says the retrospective analysis is the largest study of allo-HCT for patients with FL ever published. “Since allogeneic transplant is not a very frequent indication, we reached out to European colleagues to contribute to this large study.” As a result, the cohort of patients came from 2 international registries: the European Society for Blood and Marrow Transplantation (EBMT) and CIBMTR.

Dr. Pasquini says the main goals of the study were to understand when to include allogeneic transplantation for patients with FL and to investigate the determinants of a better outcome. “It is really a difficult question because when you look at these large registries, these patients come in for allogeneic transplants at different times, and a lot of times, [the transplants]
are a last resort with many patients undergoing this treatment after exposure to many lines of prior treatment.”

The EBMT is a voluntary organization comprising 640 transplant centers, mainly in Europe. The CIBMTR is research collaboration between the National Marrow Donor Program/Be The Match and the Medical College of Wisconsin. The study was performed through collaboration between the lymphoma disease committees for both organizations.

The researchers compiled data for overall survival, progression-free survival, transplantation-related mortality, and disease relapse/progression. A multivariate analysis was performed to ascertain specific factors associated with outcomes. A prognostic score for treatment failure was developed as a subset analysis. The median follow-up was 55 months. The 5-year probability for overall survival was 61% and that for progression-free survival was 52%.

The researchers found that the 5-year cumulative incidences of disease progression/relapse and transplantation-related mortality were 29% and 19%, respectively. The poorest survival rates occurred in patients with chemoresistant disease, older age, heavy pretreatment, and poor performance status, and those treated with myeloablative protocols.

The prognostic score, which used age, lines of prior therapy, performance status, and whether the disease was refractory to the latest line of therapy, classified patients as being at low, intermediate, and high risk, with 5-year progression-free survival rates of 68%, 53%, and 46%, respectively, and 5-year overall survival rates of 80%, 62%, and 50%, respectively. The researchers concluded that the prognostic score can assist in counseling patients regarding the best times to undergo transplantation.

Clinical Implications
Dr. Pasquini says they still do not have the definitive answer concerning the best time to perform allo-HCT. “But this study demonstrates that it’s better to proceed to allogeneic transplant earlier in the course of therapy,” he says.

“Other important information was related to the actual transplant approach,” says Dr. Pasquini. “We recommend reduced-intensity regimens rather than high-intensity regimens, as patients who received the former did better. And perhaps we can do these transplants a little earlier, before these patients fail multiple lines of therapy.”

Another area the researchers investigated was the outcomes of patients who have a sibling donor versus an unrelated donor. “We wanted to learn if we can use those 2 options interchangeably,” says Dr. Pasquini. “What we found was that the outcomes after HLA-matched unrelated donor allogeneic transplant were similar to the ones from sibling donors, even though it appears that, at least in this series, recipients of unrelated donor transplants were, in general, exposed to a greater number of lines of therapy compared to sibling donor transplant recipients. This is a clue that, in the absence of a sibling donor, physicians are waiting longer to offer an allogeneic transplant to these patients.” He added, “the landscape in allogeneic transplant continues to change with the increasing number of haploidentical donor transplants, which offers yet another option for these patients with readily available donors. Follow-up studies will be needed to further understand who would best benefit from this curative therapeutic strategy.”

Dr. Flowers says the new study is significant because CIBMTR and EBMT are the world’s best resources for information regarding allo-HCT for patients with FL and the study included data from a large international data set. “The study also provides new data on prognostic factors for allogeneic transplantation,” he adds. “For example, it points out that this approach is mostly useful for younger patients with FL who are fit and have a matched related sibling or a matched unrelated donor,” says Dr. Flowers.

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