MEETING NEWS **PERSPECTIVE**

Targeted conditioning improves transplant rate for relapsed, refractory AML

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ORLANDO — Targeted conditioning with anti-CD45 iodine apamistamab enabled older, heavily pretreated patients with relapsed or refractory acute myeloid leukemia to undergo hematopoietic stem cell transplantation with successful engraftment, according to preliminary results of the randomized phase 3 SIERRA trial presented at TCT | Transplantation & Cellular Therapy Meetings.

“After our study reached 50% of the planned enrollment, results showed high rates of allogeneic transplants, which have curative potential, in patients with relapsed or refractory AML,” **Boglarka Gyurkocza, MD,** hematologist and medical oncologist at Memorial Sloan Kettering Cancer Center, said during the presentation. “This is a patient population that is generally not considered candidates for transplant.”

Despite new targeted therapies such as venetoclax (Venclexta; Genentech, AbbVie) and IDH inhibitors, patients with relapsed or refractory AML have very few treatment options outside of allogeneic HSCT. Further, patients aged 55 years and older generally cannot tolerate multiple cycles of intensive therapy to achieve complete remission prior to transplant, nor can they tolerate more intense myeloablative conditioning.

Gyurkocza and colleagues evaluated whether targeted conditioning with radioactive iodine (^{131}I) apamistamab (Actinium Pharmaceuticals) — an anti-CD45 antibody also called Iomab-B — would improve access to HSCT among older patients with active, relapsed or refractory AML.

The preliminary analysis, occurring after 50% of enrollment, included 75 patients randomly assigned to Iomab-B 12 days prior to HSCT followed by fludarabine and total body irradiation (n = 37; median age, 65 years; range, 55-77) or to conventional care (n = 38; median age, 64 years; range, 55-76), which included investigator’s

choice of salvage therapy with newly approved targeted agents. Patients in the conventional care group underwent HSCT if they achieved complete remission, or they could cross over to the Iomab-B group in the absence of complete remission.

All patients were heavily pretreated, with 85% failing two or more therapies and 33% failing targeted therapies. Patients had received a median three (range, 1-5) prior regimens at randomization.

Overall, 84% of patients assigned Iomab-B underwent HSCT compared with 18% of patients assigned conventional care.

In the conventional care group, 82% of patients failed salvage therapy, despite 32% receiving targeted therapy. Seventy-three percent of those who received venetoclax with a hypomethylating agent or low-dose cytarabine did not achieve remission; only three patients (27%) who received this regimen proceeded to HSCT.

Twenty-two patients in the conventional care group were eligible to cross over to the Iomab-B group, 91% (n = 20) of whom received Iomab-B and underwent HSCT despite having a median 35% bone marrow blasts. Researchers noted that nine patients who failed conventional therapy could not cross over to the Iomab-B group, primarily due to disease progression.

Following HSCT, median time to neutrophil engraftment was 15 days (range, 9-22) in the Iomab-B group and 14 days (range, 10-37) in the crossover group, with no incidence of graft failure in either group, compared with 18 days (range, 13-82) in the conventional care group, with one incidence of graft failure.

Rates of 100-day nonrelapse transplant-related mortality were 6% in the Iomab-B group, 29% in the conventional care group, and 10% in the crossover group.

Prior to crossover, a greater proportion of patients assigned conventional care experienced grade 3 or grade 4 febrile neutropenia compared with the Iomab-B group (45.9% vs. 22.9%).

Iomab-B was generally well-tolerated, researchers noted, with no treatment-related deaths and one incidence of grade 3 infusion reaction.

“Iomab-B-based conditioning followed by allogeneic HSCT resulted in 100% neutrophil and platelet engraftment, and there was no graft failure,” Gyurkocza said. “This also has a favorable nonhematologic toxicity profile.” – *by John DeRosier*

Reference:

Gyurkocza B, et al. Abstract 39. Presented at: TCT | Transplantation & Cellular Therapy Meetings; Feb. 19-23, 2020; Orlando.

Disclosures: Gyurkocza reports research funding to his institution from Actinium Pharmaceuticals. Please see the abstract for all other researchers' relevant financial disclosures.

PERSPECTIVE

Richard T. Maziarz

Historically, when we have seen a patient with refractory leukemia who has failed multiple chemotherapy regimens and other interventions, we have told them that they are going to die and that they should go be with their family instead of spending more time in the hospital.

Relapse after transplant is the bane of our existence. People go through so much to get transplanted, and if they relapse after that it feels terrible. But these patients have never, until now, gotten to transplant, and they are surviving.

This is still all preliminary, but this could be a viable option and a change of practice for a patient population that we have nothing else to offer.

I was very excited when I first saw this study and am glad it was selected for presentation.

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