Conditioning Therapy With Iomab-B Leads to High Transplant Rate in Active AML

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Iodine (131I) apamistamab (Iomab-B) conditioning induced a complete remission (CR) in 84% (31/38) of patients with active acute myeloid leukemia (AML), who were then able to receive allogeneic hematopoietic stem cell transplant (HCT), according to preliminary results from the phase III SIERRA trial.[1]

The data, which were presented at the 2020 Transplant & Cellular Therapies Meeting, also showed that only 18% (7/38) of patients treated with conventional care reached the same result.

"Patients with active relapsed/refractory AML are generally not considered candidates for transplant," Boglarka Gyurkocza, MD, a hematologist and medical oncologist at Memorial Sloan Kettering Cancer Center, said during a presentation of the data. "After 50% enrollment [onto SIERRA], we observed high rates of allogeneic stem cell transplant with curative potential."

Of the 31 patients from the conventional care arm who did not achieve CR, 20 (65%) crossed over to the experiment therapy of Iomab-B. All patients who had Iomab-B conditioning and subsequent HCT had neutrophil and platelet engraftment. The median number of days to neutrophil engraftment was similar in both groups of patients with Iomab-B–based conditioning, at 15 days (range, 9-22) in the patients originally randomized to the experimental arm versus 14 days (range, 10-37) in those who crossed over. No graft failures were observed in either patient set.

In those who received HCT following CR with conventional care, there were a median of 18 days (range, 13-82) to neutrophil engraftment and 1 graft failure was observed.

The median number of days to engraftment following HCT was similar across all patient groups at 20 days in the Iomab-B arm (range, 4-39), 19 days with cross over (range, 13-38), and 22 days for CR after standard care (range, 9-35). Corresponding median time to HCT post randomization was 30 days (range, 23-50), 64 days (range, 44-161), and 67 days (range, 51-86).

Rates of nonrelapse mortality at 100 days following HCT were lower in patients treated in the Iomab-B arm (6%) and in those who crossed over (10%) when compared with patients who received HCT after standard therapy (29%).

Rates of grade 3/4 adverse events were compared to determine if Iomab-B had an unfavorable toxicity profile. Rates of febrile neutropenia (22.9% vs 45.9%) and sepsis/septic shock (2.9% vs 21.6%) were lower with Iomab-B when compared with conventional care. Similar rates of pneumonia (17.1% vs 18.9%), catheter-related infection (8.6% vs 13.5%), and mucositis (11.4% vs 10.8%) were observed in the 2 sets.

“Because the liver was an organ of interest, we looked at rates of sinusoidal obstruction syndrome also known as veno-occlusive disease, or VOD,” said Gyurkocza. “There were 2 patients on the Iomab-B arm who had VOD [of grade 1/2 severity]. Both of these patients recovered fully.”

Grade II to IV acute graft-versus-host disease occurred in 9 of 31 patients receiving Iomab-B and HCT.

Iomab-B is a radioactive iodine (131I)–labeled anti-CD45 antibody that targeted radiation directly to leukemic cells for a targeted antitumor effect. Efficacy and safety of the agent has been tested in 271 patients treated in phase I and I trials.

Patients with active, relapsed or refractory AML are randomized 1:1 to receive either conditioning with Iomab-B followed by allogeneic HCT versus conventional chemotherapy of physician’s choice. Patients achieving CR with conditioning chemotherapy are allowed to receive HCT or physician’s choice of therapy. Patients who do not have a CR with the control are allowed to crossover and receive Iomab-B. The primary end point of the trial is the durable CR rate defined as morphologic CR lasting ≥180 days. The secondary end point is overall survival at 1 year from randomization. The accrual target for the trial is 150 patients.

The control arm involves initial dosimetry using trace amounts of Iomab-B (range, 7-20 mCi)^2 in the outpatient setting to assess radiation exposure to the marrow, spleen, and nontarget organs. Individual patients received a personalized therapeutic dose based on the upper limit of 24 Gy to the liver. After a therapeutic dose, patients are required to have 4 to 5 days of radiation isolation. Patients then undergoing nonmyeloablative condition with fludarabine at 30 mg/m^2 per day followed by total body irradiation and HCT.

To be included on the trial, patients need to have marrow blast count ≥5% of the presence of peripheral blasts, be ≥55 years of age, have a Karnofsky score of ≥70, and have 8/8 allele level unrelated or related hematopoietic stem cell donor matching a human leukocyte antigen (HLA)-A, HLA-B, HLA-C, and DRB-1.

Active, relapsed or refractory AML was defined as disease: with primary induction failure following ≥2 cycles of therapy, which could include either chemotherapy or 2 more cycles of venetoclax (Venclexta) in combination with azacitidine or decitabine; occurring after first early relapse following a CR lasting ≤6 months; relapsed/refractory to salvage combination chemotherapy with high-dose cytarabine; or which is second or subsequent relapse.

Baseline characteristics in the first 75 enrolled patients were well balanced. Patients receiving Iomab-B had an average age of 65 years (range, 56-77) compared with 64 years (range, 56-76) for the control. The majority of

patients in the experimental and control arms had adverse cytogenetic and molecular risk (66% each) and primary induction failure at randomization (57% vs 47%, respectively). The median number of prior therapies was 3 (range, 1-5) for both groups.

Prior to enrollment, 85% of patients had failed ≥2 regimens and 33% had failed targeted therapies such as FLT3 and IDH1,2 inhibitors. Therapies received in the conventional-care arm included targeted therapies, venetoclax plus a hypomethylating agent or low-dose cytarabine, and standard-of-care HCT in patients who received venetoclax and achieved remission.

References

1. Gyurkocza B, Nath R, Stiff PF, et al. Targeted conditioning with ant-cd45 iodine (131I) apamistamab [Iomab-B] leads to high rates of allogeneic transplantation and successful engraftment in older patients with active, relapsed, or refractory AML after failure of chemotherapy and targeted agents: preliminary midpoint results from the prospective, randomized phase 3 SIERRA trial. Presented at: 2020 Transplantation & Cellular Therapy Meetings; February 19-23, 2020. Orlando, FL. Abstract 285. https://bit.ly/3c1TWBs.
2. Nath R, Geoghegan ER, Ulrickson MR, et al. Sierra clinical trial dosimetry results support low dose anti-CD45 Iodine (131I) apamistamab [Iomab-B] for targeted lymphodepletion prior to adoptive cell therapy. *Blood*. 134;(suppl 1;absrt 1958):1958-1958. doi: 10.1182/blood-2019-128838.

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