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Targeted Conditioning with Anti-CD45 Iodine (^{131}I) Apamistamab [Iomab-B] Leads to High Rates of Allogeneic Transplantation and Successful Engraftment in Older Patients with Active, Relapsed or Refractory (rel/ref) AML after Failure of Chemotherapy and Targeted Agents: Preliminary Midpoint Results from the Prospective, Randomized Phase 3 Sierra Trial

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Background

Patients with rel/ref AML have very few options, despite novel targeted therapies (e.g. venetoclax, IDH inhibitors), other than allogeneic hematopoietic cell transplantation (HCT) to achieve a durable CR. In addition, patients ≥55 years of age cannot tolerate multiple cycles of intensive therapy trying to achieve a CR prior to transplant. Older patients are also unable to tolerate more intense myeloablative conditioning. The SIERRA trial is a prospective, randomized, phase 3 trial addressing the unmet need to improve access of older patients with active, rel/ref AML to HCT, the only potentially curative therapy available to them.

Methods

Patients are randomized (1:1) to receive Iomab-B (day-12) followed by FLU/TBI and HCT, or to conventional care (CC). CC patients may receive investigator's choice of salvage therapy, including newly approved targeted agents and may proceed to standard HCT if they achieve CR. If patients do not achieve CR, the study allows cross-over (CO) to Iomab-B/HCT.

Results

Preliminary data are available from 75 (50%) patients (Table 1). Patients (median age 64) were heavily pretreated with 85% failing ≥2 induction therapies and 33% failing targeted therapies. All patients transplanted after Iomab-B engrafted. After randomization, 82% (31/38) patients in the CC arm failed salvage therapy, despite 32% (12/38) receiving targeted therapy. 73% (8/11) of the patients receiving venetoclax with HMA or LDAC did not achieve remission. Of the 31 patients, 9 were not CO transplant candidates. Of the 22 patients that crossed over for transplant, majority (91%, N=20) were able to receive Iomab-B/HCT, despite a median of 35% BM blasts. The most common reason preventing CO to transplant was disease progression. CC patients showed increased incidence of Grade 3 febrile neutropenia, compared to Iomab-B patients prior to CO or HCT (34% vs 8%). Iomab-B administration was generally well-tolerated with 1 Grade 3 and no Grade 4, infusion reaction. There were no Iomab-B-related deaths and 100-day non-relapse TRM was 3% on the Iomab-B arm (Table 1).

Conclusion

Despite advanced age, active disease and heavily pre-treated patients, 100% (31/31) of all patients in the Iomab-B arm who received treatment with Iomab-B were able to undergo HCT and successfully engrafted. In comparison, only 18% (7/38) of the patients on the CC arm achieved remission and underwent conventional HCT despite a high percentage receiving recently approved agents and targeted therapies. Overall, including patients crossing over to receive Iomab-B/HCT after failure of salvage therapy in the CC arm, 68% (51/75) of all patients enrolled in the trial underwent HCT after Iomab-B. These preliminary results represent significant improvements in the current rates of transplantation in this patient population. This SIERRA trial is currently enrolling (www.sierratrial.com or clinicaltrials.gov NCT02665065).

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