Rapid reduction of peripheral blasts in older patients with refractory acute myeloid leukemia (AML) using reinduction with single agent anti-CD45 targeted iodine (131I) apaminatam (Iomab-B) radioimmunotherapy in the phase III SIERRA trial.

Benjamin Tomlison1, Vijay Reddy2, Mark S. Berger2, Jennifer Spross2, Renee Lichtenstein2, Boglarka Gyurkoza2

1 University Hospitals Case Medical Center, Cleveland, OH, 2 Actinium Pharmaceuticals, New York, NY. 131I SIERRA (NCT02764974). 2019 ASCO Annual Meeting May 31 – June 4, 2019 Chicago, IL

Background & rationale

The SIERRA trial is a prospective, randomized, phase 3, open-label, ongoing multicenter trial for patients aged ≥55 years with active, relapsed/refractory (R/R) AML evaluating allelic hematopoietic cell transplantation (HCT) versus conventional care (CC). Recent preliminary data demonstrated robust donor-engraftment in all patients treated with Iomab-B (Agra et al, Blood 2018 132:1017) despite active disease. Rapid peripheral blast clearance is predictive of CR and RFS after cytotoxic chemotherapy for AML (Elliot et al, Blood 2007 110:4172; Gianfaldoni et al, BJH 2006 134:54). In the present study we characterize the anti-leukemic effect and rate of peripheral disease reduction by single-agent Iomab-B.

We hypothesize that successful engraftment following HCT may be related to myeloablative and anti-leukemic activity by single agent Iomab-B prior to RIC.

Methods

Patients are randomized to receive Iomab-B and HCT or to a CC therapy including approved targeted agents followed by HCT if in remission. Majority of patients (79%) in the CC arm did not achieve CR and the study allowed crossover to receive Iomab-B.

Results

Data were evaluated for the first 25% of patients (N = 38). 29 patients received Iomab-B, either directly (N = 19) or via crossover (N = 10). Median baseline marrow blasts were 30% (4.74%) for Iomab-B and 24% (6.70%) for CC, which increased to 45% (10-70%) at crossover. Peripheral blast data was available in 16 patients (Iomab-B 7, Crossover 9). By day 3 post-Iomab-B, blasts were reduced by 98% with 100% reduction by day 8 (assuming 0% blasts due to lack of differential at WBC 0). All patients engrafted with ANC at a median of 13 days (9-22 days). Patients treated with hydroxyurea versus without were analyzed together as well as separately and showed similar results. One patient received hydroxycure post-Iomab-B therapeutic infusion.

Conclusions

- Targeted radioimmunotherapy with single-agent Iomab-B rapidly decreases peripheral blasts by 98% by day 3 in chemotherapy refractory AML.
- Iomab-B conditioning leads to myeloablative in older patients with active disease (up to a median of 45% blasts in the marrow) as demonstrated by engraftment in all patients.
- Successful engraftment after Iomab-B and HCT benefits patients who had prolonged neutropenia due to active and refractory disease prior to transplant.
- While efficacy data is not yet available for these patients, rapid peripheral blast reduction is encouraging as prior studies utilizing cytotoxic chemotherapy suggest a relationship between the rate of disease reduction and disease response.