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PHASE 2 RESULTS OF THE ZUMA-3 STUDY EVALUATING KTE-X19, AN ANTI-CD19 CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY, IN ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Topic: 02. Acute lymphoblastic leukemia - Clinical

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Background: ZUMA-3 is a Phase 1/2 multicenter study evaluating KTE-X19, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, in adult patients with relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL). Phase 1 efficacy results at the recommended Phase 2 dose (1×10^6 CAR T cells/kg) were encouraging (Shah et al. *J Clin Oncol.* 2019;37[suppl, abstr]:7006).

Aims: To present the pivotal Phase 2 results of ZUMA-3.

Methods: Eligible adults had R/R B-ALL, >5% bone marrow blasts by local evaluation, and Eastern Cooperative Oncology Group performance status of 0–1. Patients received a single infusion of KTE-X19 after conditioning chemotherapy. The primary endpoint was the overall complete remission (CR) rate (CR + CR with incomplete hematologic recovery [CRi]) by central review. Key secondary endpoints were duration of remission, relapse-free survival, overall survival, measurable residual disease negativity rate by flow cytometry, and safety. Data are reported in all treated patients.

Results: As of 9/2020, 55 of 71 enrolled patients received KTE-X19, with a median follow-up of 16.4 months (range, 10.3–22.1). Adverse events (n=8) and ineligibility (n=4) were the most common reasons enrolled patients did not receive KTE-X19 infusion. Median age was 40 years (range, 19–84); median bone marrow blasts at screening were 65% (range, 5–100); and 47% of patients had ≥3 prior therapies, with 45%, 22%, and 42% having previously received blinatumomab, inotuzumab ozogamicin, or allogeneic stem cell transplant, respectively.

The CR + CRi rate was 71% (95% CI, 57–82; 56% CR, 15% CRi); 31% of responders had ongoing responses. Medians (95% CI) for duration of remission, relapse-free survival, and overall survival were 12.8 months (8.7–not estimable), 11.6 months (2.7–15.5), and 18.2 months (15.9–not estimable), respectively. In responders, medians (95% CI) for relapse-free survival and overall survival were 14.2 months (11.6–not estimable) and not reached (16.2–not estimable). The measurable residual disease negativity rate was 97% among patients with CR + CRi. Among 25 patients with prior blinatumomab treatment, the CR + CRi rate was 60%. Ten patients (18%) received subsequent allogeneic stem cell transplant at a median of 98 days post–KTE-X19 infusion. Median duration of remission remained unchanged when not censoring for allogeneic stem cell transplant.

Grade ≥3 adverse events occurred in 95% of patients, most commonly anemia (49%) and neutropenia (49% [febrile 13%]). Grade ≥3 cytokine release syndrome (per Lee et al. [*Blood.* 2014;124:188-195]) and neurologic events occurred in 24% and 25% of patients, respectively, and were generally reversible. Two Grade 5 KTE-X19–related events occurred (brain herniation, n=1; septic shock, n=1). Median times to onset of cytokine release syndrome and neurologic events were 5 days and 9 days, with median durations of 7.5 days and 7 days, respectively. Median peak CAR T-cell levels (cells/μL) were 40.5 (range, 1.3–1533.4) in patients with CR and 0 in nonresponders. CAR T cells were undetectable by 9 months in ongoing responders.

Summary/Conclusion: After a median follow-up of 16.4 months, KTE-X19 demonstrated compelling clinical benefit in heavily pretreated adults with R/R B-ALL, with the median overall survival not yet reached for responding patients and a manageable safety profile.

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