FIVE-YEAR SURVIVAL OUTCOMES OF PATIENTS (PTS) WITH RELAPSED OR REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (R/R B-ALL) TREATED WITH BREXUCABTAGENE AUTOLEUCEL (BREXU-CEL) IN ZUMA-3

Topic: Acute lymphoblastic leukemia - Clinical

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Abstract

Background:

Brexu-cel is an autologous anti-CD19 CAR T-cell therapy approved for pts with R/R B-ALL who are ≥18 y in the United States and ≥26 y in the European Union based on the high complete remission (CR) or CR with incomplete hematologic recovery (CRi) rate observed in the Phase 2 ZUMA-3 study (71% per central review; N=55; Shah et al. Lancet, 2021). The 4-y OS rate among Phase 1 and 2 pts who received the pivotal dose (N=78) was 40% (95% CI, 28-52), with survival benefits observed across key subgroups (Oluwole et al. ASCO 2024. #6531).

Aims:

To report updated 5-y survival, safety, and causes of mortality in ZUMA-3, including outcomes in key subgroups.

Methods:

Eligible pts (≥18 y) with R/R B-ALL underwent leukapheresis, optional bridging therapy, and lymphodepleting chemotherapy, followed by 1 infusion of brexu-cel (1×10^6 CAR T cells/kg). The primary endpoint was overall CR/CRi rate per central review with OS and safety as key secondary endpoints. Post hoc subgroup analyses were exploratory in nature with descriptive statistics reported herein.

Results:

As of July 23, 2024, median follow-up time in Phase 1 and 2 pts ≥18 y (N=78) was 65.7 mo (range, 56.7-94.3). Median OS remained unchanged since the 4-y analysis at 25.6 mo (95% CI, 16.2-60.4) with a 5-y OS rate of 40% (95% CI, 28.4-51.3). Responders, per central review, (CR/CRi; n=57) reached a median OS of 60.4 mo (95% CI, 23.2-not estimable [NE]) and those with a CR (n=47) had not reached a median OS (95% CI, 34.1-NE). The median follow-up time for pts ≥26 y (n=63) was 65.6 mo (range, 56.7-94.3); median OS remained unchanged since the 4-y analysis at 26.0 mo (95% CI, 15.9-NE) with a 5-y OS rate of 42% (95% CI, 28.6-53.9).

The 5-y OS rates (95% CI) for pts with (n=38) and without (n=40) prior blinatumomab were 25% (12.1-40.4) and 54% (36.3-68.5); for pts with (n=17) and without (n=61) prior inotuzumab

were 21% (5.2-43.9) and 45% (31.1-57.4); and for pts with (n=29) and without (n=49) prior allogeneic stem cell transplantation (alloSCT) were 36% (17.1-55.3) and 42% (26.9-55.5), respectively. Median OS (95% CI) was 50.2 mo (10.2-NE) in responders (per investigator review, n=58) who received subsequent alloSCT (n=14) and 60.4 mo (23.2-NE) in responders who did not (n=44). The 5-y OS rates (95% CI) were 42% (16.4-65.4) and 52% (35.8-66.5), respectively.

One new adverse event and death were reported since the 4-y analysis, both in the same patient, cervical cancer and death due to pulmonary failure (both unrelated to brexu-cel). No secondary T-cell malignancies were reported in ZUMA-3. At data cutoff, 44 of 78 pts (56%) had died with 20 pts (26%) alive and 14 pts (18%) who were lost to follow-up or withdrew consent. The estimated 60-mo cumulative incidences of death due to progressive disease (PD) and non-PD reasons were 34% (95% CI, 23.5-45.2) and 26% (95% CI, 16.0-36.7), respectively.

Summary/Conclusion:

Pts in ZUMA-3 continued to experience a survival benefit with a 40% 5-y OS rate. Responders had the greatest benefit with a median OS of >5 y (CR/CRi) and not reached in those with CR. Pts benefitted regardless of age, prior therapy, or subsequent alloSCT status, though small subgroups and unbalanced pt characteristics limit interpretation of post hoc subgroup analyses. No new safety signals were observed. New studies are needed to fully understand how prior therapies and subsequent alloSCT impact long-term outcomes in pts with R/R B-ALL treated with brexu-cel.

Keyword(s):

Relapsed acute lymphoblastic leukemia | CAR-T | Long-term follow-up