Tecartus® (brexucabtagene autoleucel)

Outcomes with or without subsequent allogeneic stem cell transplantation (AlloSCT) in relapsed/refractory B-precursor acute lymphoblastic leukemia (ALL)

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ZUMA-3 Study

Patient Population and Analysis Sets[1,2]

The single-arm, open-label, multicenter, pivotal Phase 2 ZUMA-3 study evaluated the safety and efficacy of Tecartus in adult patients with relapsed or refractory B-precursor ALL. The study included 71 enrolled patients in the intention to treat (ITT) analysis set; 55 patients receiving Tecartus in were included in the modified ITT (mITT) analysis set. The primary endpoint was the rate of overall complete remission (CR) or complete remission with incomplete haematological recovery (CRi) by central assessment: patients who achieved CR or CRi were considered responders.

Of the 55 Tecartus-treated patients in the mITT population, 32 were naïve to alloSCT prior to receiving Tecartus, of which 24 were responders to Tecartus (23 evaluable). Ten alloSCT-naïve patients received alloSCT post-Tecartus infusion, of which 9 achieved CR/CRi with Tecartus and 1 had inconsistent assessments between investigator and central assessment (CRi by investigator assessment vs blast-free hypoplastic/aplastic bone marrow by central assessment).

Post-Hoc Analysis of Overall Survival with or without Censoring at Subsequent AlloSCT

Using the ITT analysis (n=71) and comparing OS (median follow-up time 16.4 months) for all patients without and with censoring at the timepoint of subsequent alloSCT (n=10), the Kaplan-Meier curves for OS converge. Median OS was 19.2 months (95% CI, 10.4–not estimable) for both groups (ITT analysis set).[1,2]

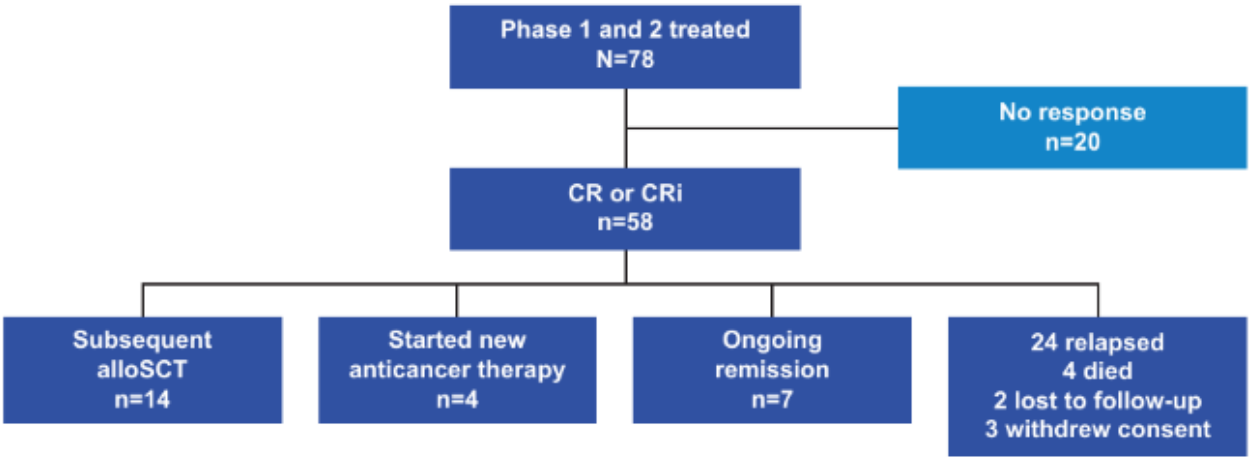
In a combined Phase 1 and 2 analysis at the pivotal 1×10^6 dose level (N=78), the investigator-assessed CR/CRi rate was 74.4% (58 patients; CR rate, 62.8% [49 patients]).[1]

4-year Follow Up Analysis[3]

Oluwole, et al. conducted a pooled analysis that included patients enrolled in ZUMA-3 Phase 1 and 2 (N=99) with a median follow up time for the treated patients (N=78) of 53.6 months (range, 44.7-82.3).

As of data cutoff, 7 patients were in ongoing remission per investigator assessment, 24 relapsed,14 proceeded to subsequent alloSCT, 4 died, 4 started new anticancer therapy, 3 withdrew consent, and 2 were lost to follow-up (Figure 1).

Figure 1. Response status by investigator assessment in ZUMA-3 Phase 1 and 2 treated patients (N=78)[3]



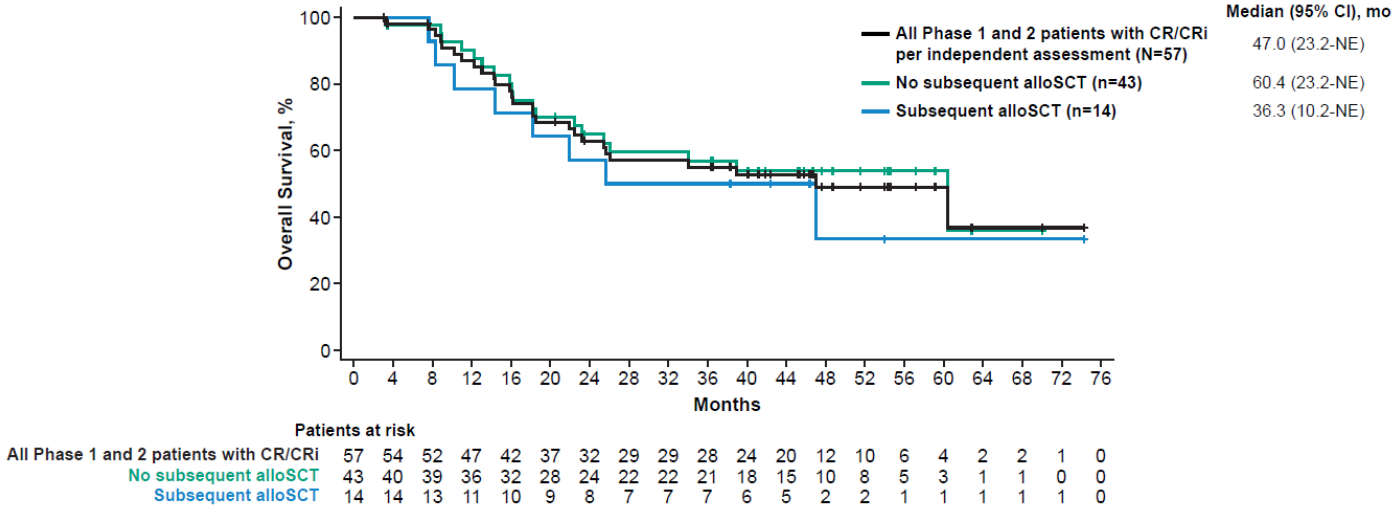
alloSCT=allogeneic stem cell transplantation; CR=complete remission; CRi= complete remission with incomplete hematologic recovery

ZUMA-3 Phase 1 and 2 responders per independent assessment (CR/CRi; n=57) had a median OS of nearly 4 years (47.0 months [95% CI, 23.2-NE]).

Of the 57 responders per independent assessment, 14 patients proceeded to subsequent alloSCT while in CR/CRi.

Median OS was numerically longer among responders who did not proceed to subsequent alloSCT (n=43; 60.4 months [95% CI, 23.2-NE]) than those who did (n=14; 36.3 months [95% CI, 10.2-NE]; Figure 2).

Figure 2. Overall survival (OS) in ZUMA-3 responders per independent assessment by subsequent alloSCT status[3]



alloSCT=allogeneic stem cell transplantation; brexu-cel=brexucabtagene autoleucel; CR=complete remission; CRi=complete remission with incomplete hematologic recovery; NE=not estimable

However, only a small subset of patients received subsequent alloSCT which leads to lack of statistical power to compare between Tecartus with and without subsequent alloSCT. Additionally, ZUMA-3 was neither designed nor powered to detect a difference in outcomes between patients who were treated with Tecartus alone and those receiving subsequent alloSCT. Furthermore, differences in distribution of relevant baseline characteristics introduce additional biases to this analysis.

The small number of patients in the subset precludes statistical comparison and the ability to make inferences from the results, and all analyses should be interpreted with caution and considered as explorative.

Safety

Safety outcomes in relation to subsequent alloSCT are not available. Within the overall mITT population, all treated patients had ≥1 adverse event (AE). The most common Grade ≥3 AEs were anemia (n=27/55 [49%]) and pyrexia (n=20/55 [36%]). Serious AEs were reported in 41 (75%) patients. Cytokine release syndrome (CRS) was reported in 49 (89%) patients, including Grade 3 or 4 events in 13 (24%) patients. Neurologic events (NEs) were reported in 33 (60%) patients, with Grade ≥3 events in 14 (25%) patients. Twenty (36%) treated patients died primarily from progressive disease (13 [24%] patients). Deaths due to Grade 5 AEs unrelated to ALL were reported in 6 (11%) patients, including 2 events (brain herniation and septic shock) considered to be related to Tecartus treatment. Fourteen (25%) patients had infections of Grade ≥3.[1]

The safety profile with extended follow-up was manageable, with no new safety signals and no new AEs of interest (including CRS, NEs, or infections observed since the primary analysis data cutoff).[3]

Ten additional deaths not due to progressive disease (PD) occurred and 3 additional patients died due to Grade 5 adverse events other than ALL, since primary analysis data cutoff. Six of 17 deaths (35%) not due to progressive disease (PD), occurred in patients who had received subsequent alloSCT.[3]

Overall Findings and Limitations[2]

Owing to the small number of patients receiving subsequent alloSCT and differences in distribution of relevant baseline characteristics, interpretation of results in this subgroup of patients is difficult.

References

1. Shah BD, Ghobadi A, Oluwole OO, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. *Lancet*. 2021;398(10299):491-502. DOI: 10.1016/S0140-6736(21)01222-8
2. Data on file, Kite Pharma
3. Oluwole OO, Ghobadi A, Cassaday RD, et al. Long-Term Survival Outcomes of Patients With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia Treated With Brexucabtagene Autoleucel in ZUMA-3. Poster presented at the 2024 American Society of Clinical Oncology (ASCO) Annual Congress; May 31-June 04, 2024; Chicago, IL

Abbreviations

AE=adverse event
ALL=acute lymphoblastic leukaemia
AlloSCT=allogeneic stem cell transplantation
BTK= Bruton's tyrosine kinase
CI=confidence interval
CR=complete remission
CRi=complete remission with incomplete haematological recovery
CRS=cytokine release syndrome
ECOG=Eastern Cooperative Oncology Group
ITT=intention-to-treat
mITT=modified intention-to-treat
NEs=neurologic events
NE=not evaluable
OCR=overall complete remission
OS=overall survival
PD=progressive disease

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