Poster
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Updated Outcomes From the Historical Control Study SCHOLAR-3 Contextualizing ZUMA-3 Results of Brexucabtagene Autoleucel (KTE-X19) in Adult Patients With Relapsed or Refractory B-Cell Acute Lymphoblastic Leukemia (R/R B-ALL)

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BACKGROUND

- Despite the availability of new treatments such as blinatumomab and inotuzumab, adults with relapsed or refractory (R/R) B-cell precursor acute lymphoblastic leukemia (B-ALL) have an overall poor prognosis, with median overall survival (OS) of <8 months with these therapies[1,2]
- Brexucabtagene autoleucel (brexu-cel, formerly known as KTE-X19) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved in the United States to treat adults with R/R B-ALL and in the European Union to treat adults ≥26 years of age with R/R B-ALL, based on the results of the pivotal Phase 2 ZUMA-3 study[3]
- After a median follow-up of 26.8 months in ZUMA-3 (N=55), the complete remission rate (CR + complete remission with incomplete hematological recovery [CRi]) with brexu-cel remained high (71%; 95% CI, 57-82), with a median relapse-free survival (RFS) of 11.6 months (95% CI, 2.7-20.5) and a median OS of 25.4 months (95% CI, 16.2-not estimable [NE])[4]
- To better assess the unmet need and the benefit of brexu-cel in adults with R/R B-ALL, the retrospective historical control study SCHOLAR-3 was conducted, comparing ZUMA-3 outcomes with matched individual patient-level data from historical clinical trials[5]
  - Results from the primary analysis demonstrated a significant improvement in outcomes among patients with R/R B-ALL with brexu-cel therapy providing a median OS of 18.2 months (n=49; 95% CI, 12.2-NE) in the ZUMA-3 arm (median follow-up 16.4 months)[6] and standard-of-care therapies providing a median OS of 5.5 months (n=40; 95% CI, 3.3-9.2) in the historical control arm

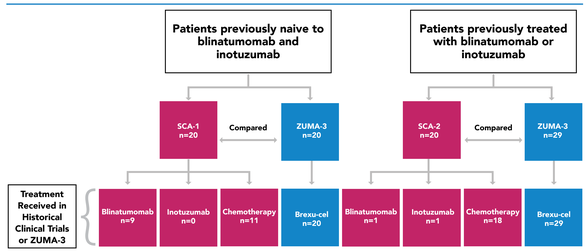
OBJECTIVE

- To contextualize ZUMA-3 efficacy outcomes after 26.8 months median follow-up with patient-matched data from historical clinical trials in the retrospective historical control study SCHOLAR-3

METHODS

- Detailed SCHOLAR-3 methodology was previously reported[5]
  - Briefly, propensity scoring was used to match patients treated with brexu-cel in the Phase 2 portion of ZUMA-3 (NCT02614066), the international, multicenter, single-arm study, with adult patients with R/R B-ALL treated in historical clinical trials (synthetic control arm [SCA]) based on key baseline characteristics and prior therapies[5]
  - In Phase 2 of ZUMA-3, patients (≥18 years) with R/R B-ALL received a single infusion of brexu-cel (1×10^6 CAR T cells/kg) following leukapheresis and conditioning chemotherapy[6]
- Efficacy outcomes are reported for 3 SCA cohorts, which were compared with matched patients in corresponding ZUMA-3 arms (**Figure 1**)
  - SCA-1: patients who were previously naive to blinatumomab and inotuzumab prior to enrollment to the historical clinical trial on which they could have received blinatumomab, inotuzumab, or chemotherapy
  - SCA-2: patients who were previously treated with blinatumomab or inotuzumab prior to enrollment to the historical clinical trial on which they could have received blinatumomab, inotuzumab, or chemotherapy
  - SCA-combined: SCA-1 and SCA-2 combined data set
- The primary endpoint in SCHOLAR-3 was CR/CRi rates for patients previously naive to blinatumomab and inotuzumab (SCA-1)
- Secondary endpoints included OS for all cohorts (SCA-1, SCA-2, and SCA-combined) and RFS for patients previously naive to blinatumomab and inotuzumab (SCA-1)
- Statistical analyses
  - CR/CRi rates were described through crude incidence rates and corresponding 95% CI and odds ratio (95% CI) and 2-sided *P* values were estimated from a logistic regression model[5]
  - Time-to-event endpoints were analyzed using the Kaplan-Meier method and compared using a Cox proportional hazard regression model[5]
- Data cutoff: July 23, 2021

Figure 1. SCHOLAR-3: Summary of Treatment Received in Historical Clinical Trials or ZUMA-3



Brexu-cel, brexucabtagene autoleucel; SCA, synthetic control arm.

RESULTS

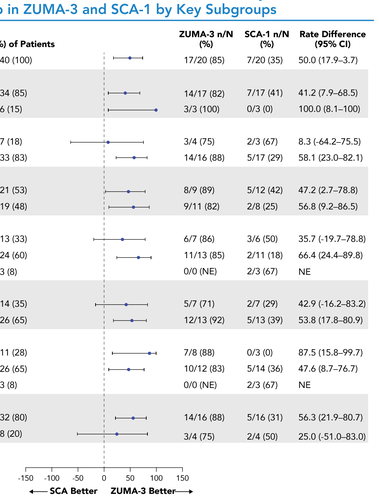
Table 1. Comparison of Efficacy Outcomes in Patients Who Were Previously Naive to Blinatumomab and Inotuzumab in ZUMA-3 and SCA-1

	Blinatumomab and Inotuzumab-Naive Patients	
	ZUMA-3 (n=20)	SCA-1 (n=20)[a]
Overall CR/CRi rate, % (95% CI)[b]	85.0 (62.1-96.8)	35.0 (15.4-59.2)
CR rate, % (95% CI)	75.0 (50.9-91.3)	30.0 (11.9-54.3)
Treatment difference (95% CI)	50.0 (17.9-73.7)	
Odds ratio (95% CI)	10.5 (2.3-48.7)	
P value	0.0031	
AlloSCT rate, % (95% CI)	35.0 (15.4-59.2)	20.0 (5.7-43.7)
Treatment difference (95% CI)	15.0 (–13.7-42.4)	
Odds ratio (95% CI)	2.2 (0.5-9.0)	
P value	0.4801	
Median RFS (95% CI), months	20.5 (2.8-NE)	0.0 (0.0-4.6)
Hazard ratio (95% CI)	0.18 (0.1-0.5)	
P value	0.0004	
Median OS (95% CI), months	NR (18.2-NE)	5.5 (1.9-12.1)
Hazard ratio (95% CI)	0.15 (0.1-0.5)	
P value	0.0001	

[a]SCA-1: SCHOLAR-3 patients who were previously naive to blinatumomab and inotuzumab at enrollment in historical trials in which they may have received blinatumomab or inotuzumab. [b]CR/CRi rates were assessed at 24 weeks. alloSCT, allogeneic stem cell transplant; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; NE, not estimable; NR, not reached; OS, overall survival; RFS, relapse-free survival; SCA, synthetic control arm.

- Propensity-matching scores and baseline patient and disease characteristics were previously reported[5]
- The CR/CRi rate at 24 weeks and medians for RFS and OS for patients previously naive to blinatumomab and inotuzumab in ZUMA-3 were significantly higher compared with SCA-1 (**Table 1**)

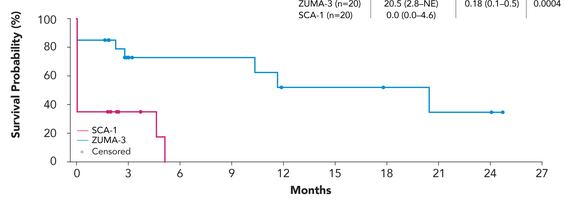
Figure 2. Comparison of CR/CRi Rates in Patients Who Were Previously Naive to Blinatumomab and Inotuzumab in ZUMA-3 and SCA-1 by Key Subgroups



CR, complete remission; CRi, CR with incomplete hematologic recovery; NE, not estimable; SCA, synthetic control arm; SCT, stem cell transplant.

- CR/CRi rate differences for ZUMA-3 vs SCA-1 were largely similar among prespecified subgroups though they varied among Philadelphia chromosome status and number of prior lines of therapy subgroups, with some subgroups having limited patient numbers (**Figure 2**)

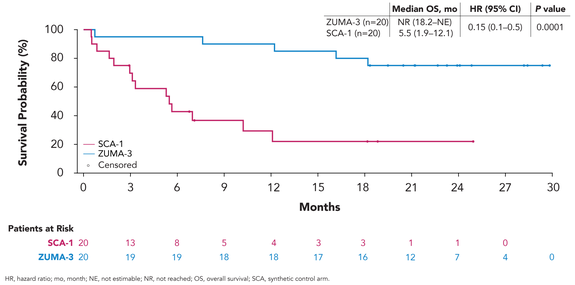
Figure 3. Relapse-Free Survival in Patients Who Were Previously Naive to Blinatumomab and Inotuzumab in ZUMA-3 vs SCA-1



HR, hazard ratio; mo, month; NE, not estimable; RFS, relapse-free survival; SCA, synthetic control arm.

- The median RFS was significantly higher in ZUMA-3 patients who were previously naive to blinatumomab and inotuzumab compared with patients in SCA-1, 20.5 months vs 0.0 months (*P*=0.0004), respectively (**Figure 3**)

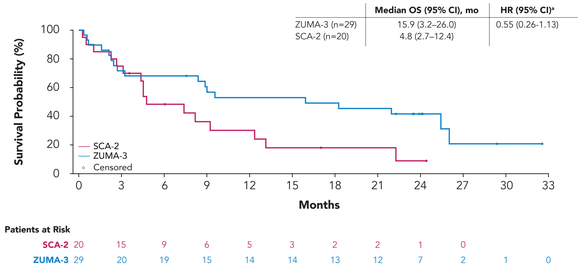
Figure 4. Overall Survival in Patients Who Were Previously Naive to Blinatumomab and Inotuzumab in ZUMA-3 vs SCA-1



HR, hazard ratio; mo, month; NE, not estimable; NR, not reached; OS, overall survival; SCA, synthetic control arm.

- The median OS in ZUMA-3 patients who were previously naive to blinatumomab and inotuzumab was significantly higher than the median OS in SCA-1 patients, not reached vs 5.5 months (*P*=0.0001), respectively (**Figure 4**)

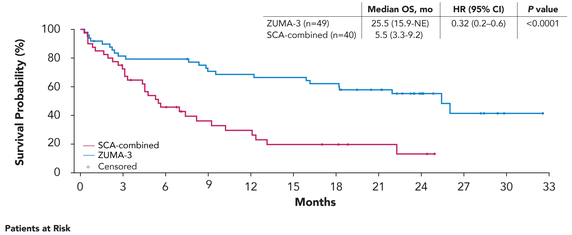
Figure 5. Overall Survival in Patients Who Were Previously Treated With Blinatumomab or Inotuzumab in ZUMA-3 and SCA-2



*Adjusted hazard ratio (95% CI) is based on the Cox proportional hazards model with treatment group, baseline bone marrow blasts (%) and number of prior lines of therapy (≤2 vs. >2) as the covariates. *P* value was not significant.
mo, month; OS, overall survival; SCA, synthetic control arm.

- The median OS in ZUMA-3 patients who were previously treated with blinatumomab and inotuzumab was 15.9 months and 4.8 months in SCA-2 (**Figure 5**)

Figure 6. Overall Survival in All Matched Patients in ZUMA-3 vs SCA Combined



HR, hazard ratio; mo, month; NE, not estimable; OS, overall survival; SCA, synthetic control arm.

- The median OS in all matched ZUMA-3 patients was significantly higher than the median OS in all SCA patients, regardless of prior blinatumomab or inotuzumab therapy, 25.5 months vs 5.5 months (*P*<0.0001), respectively (**Figure 6**)

CONCLUSIONS

- With longer follow-up in the ZUMA-3 study (median 26.8 months), SCHOLAR-3 results demonstrated that outcomes of patients treated in historical standard-of-care trials remained poor regardless of prior therapy status (blinatumomab/inotuzumab-treated or -naive), with a median OS of less than 6 months
- In contrast, matched ZUMA-3 patients achieved a median OS of >25 months, more than 4 times that of SCA patients, highlighting a considerable benefit of brexu-cel over standard-of-care therapies in this patient population
- A limitation to this analysis is that at the time of SCHOLAR-3 initiation, blinatumomab and inotuzumab were newly available treatments and therefore the predominant treatment received by the historical control cohort was chemotherapy, which limits the interpretability of these results and warrants further analyses
- These results suggest that brexu-cel may improve outcomes compared with historical standard-of-care therapies and helps to address an unmet need for patients with R/R B-ALL

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DISCLOSURES

Full author disclosures are available at the following Quick Response (QR) code:

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