Poster
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Subgroup Analyses of Brexu-cel, an Anti-CD19 Chimeric Antigen Receptor T-cell Therapy, in Adult Patients With Relapsed or Refractory B-cell Acute Lymphoblastic Leukemia in ZUMA-3

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BACKGROUND

- Adult patients with relapsed or refractory (R/R) B-precursor acute lymphoblastic leukemia (B-ALL) have poor overall survival (OS; 1-year rate, 26%) after salvage therapies, and outcomes worsen with subsequent relapses[1,2]
- Although novel agents such as blinatumomab have improved outcomes in R/R B-ALL, the median OS with blinatumomab is <8 months in adult patients[3,4]
- 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 (based on the positive results of the ZUMA-3 study) and adults with R/R mantle cell lymphoma[5]
- In the pivotal Phase 2 portion of ZUMA-3, brexu-cel demonstrated compelling efficacy and a manageable safety profile in heavily pretreated adults with R/R B-ALL[6]
  - At a median follow-up of 16.4 months (N=55), the overall complete remission (CR) rate (including CR with incomplete hematologic recovery [CRi]) was 71% (95% CI, 57-82) and median OS was 18.2 months
- Here, we report the outcomes of treatment subgroups after >2 years of follow-up in Phase 2 treated patients and in a pooled analysis of Phase 1 and 2 patients who received the pivotal dose of brexu-cel

OBJECTIVE

- To evaluate safety and efficacy outcomes in ZUMA-3 by prior number of therapy lines, prior blinatumomab, prior allogeneic stem cell transplant (alloSCT), and subsequent alloSCT in Phase 2 treated patients and in a larger pooled analysis of Phase 1 and 2 patients treated with the pivotal dose of brexu-cel (1×10^6 CAR T cells/kg)

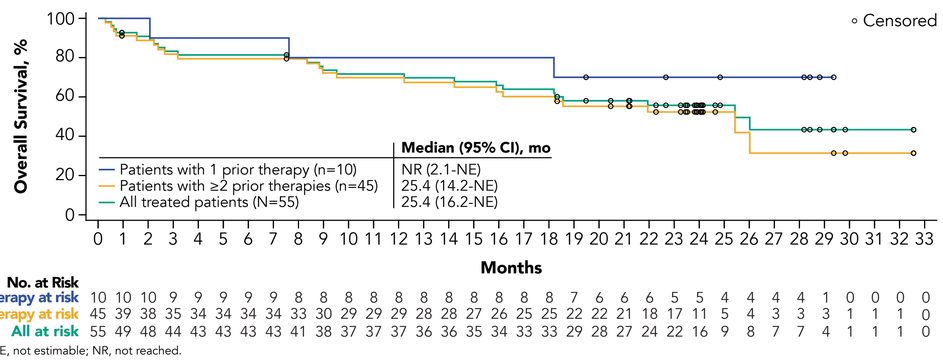
METHODS

- Post hoc efficacy and safety assessments of subgroups in ZUMA-3 are reported in both Phase 2 treated patients (N=55) and in a newly conducted pooled analysis of Phase 1 and 2 patients who were treated with the pivotal dose of brexu-cel (N=78) by
  - Prior number of therapy lines (1 prior line and ≥2 prior lines)
  - Prior blinatumomab therapy (prior blinatumomab and blinatumomab naive)
  - Prior alloSCT (prior alloSCT and no prior alloSCT)
  - Subsequent alloSCT (subsequent alloSCT and no subsequent alloSCT)
- Subsequent alloSCT was allowed per investigator discretion but was not protocol defined
- Statistical analyses
  - Efficacy outcomes were assessed by independent central review
  - Time-to-event endpoints were analyzed using the Kaplan-Meier method
  - Prespecified subgroup analyses were descriptive
- Data cutoff: July 23, 2021

RESULTS

- Median follow-up time was 26.8 months (range, 20.7-32.6) for Phase 2 treated patients (N=55) and 29.7 months (range, 20.7-58.3) for pooled Phase 1 and 2 patients (N=78)
- As previously reported, most Phase 2 patients were heavily pretreated, with a median number of 2 prior therapies and almost half (47%) having received ≥3 prior therapies[6]
- Among Phase 2 treated patients at baseline:
  - 10 patients (18%) had 1 prior line of therapy; 45 patients (82%) had ≥2 prior lines of therapy
  - 25 patients (45%) received prior blinatumomab; 30 patients (55%) were blinatumomab naive
    - 12/25 blinatumomab-exposed patients (48%) had blinatumomab as their last therapy prior to receiving brexu-cel, with a median time from blinatumomab to brexu-cel of 4.9 months (range 2.5-45.7) in these patients
  - 23 patients (42%) received prior alloSCT; 32 patients (58%) did not
    - 5/23 previously transplanted patients (22%) had prior alloSCT as their last therapy prior to receiving brexu-cel, with a median time from alloSCT to brexu-cel of 11.7 months (range, 9.1-45.3) in these patients
- Most baseline patient and disease characteristics were largely similar among subgroups examined

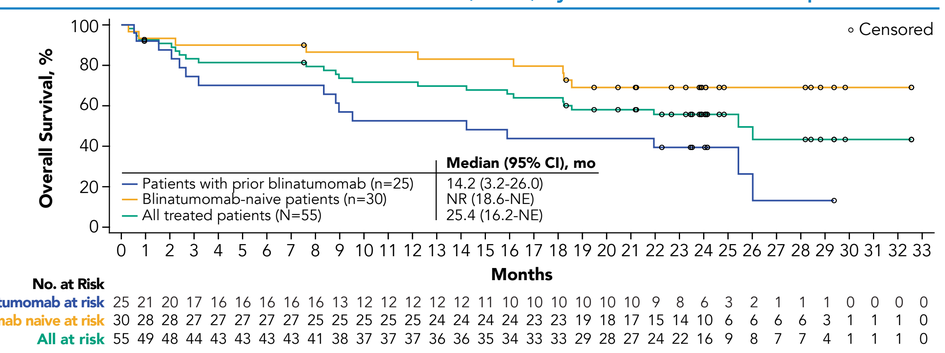
Figure 1. Overall Survival in Phase 2 Treated Patients (N=55) by Prior Number of Therapy Lines



mo, month; NE, not estimable; NR, not reached.

- Median OS was not reached in Phase 2 patients with 1 prior therapy and was 25.4 months in patients with ≥2 prior therapies (**Figure 1**)

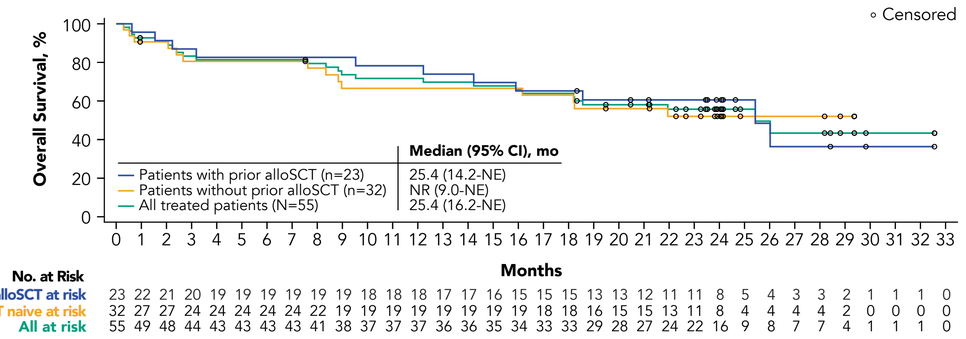
Figure 2. Overall Survival in Phase 2 Treated Patients (N=55) by Prior Blinatumomab Exposure



mo, month; NE, not estimable; NR, not reached.

- In Phase 2 patients who were blinatumomab naive, median OS was not reached vs 14.2 months in those with prior blinatumomab exposure (**Figure 2**)

Figure 3. Overall Survival in Phase 2 Treated Patients (N=55) by Prior AlloSCT Exposure



mo, month; NE, not estimable; NR, not reached.

- After a median follow-up of 26.8 months, the median OS was not reached in Phase 2 patients without prior alloSCT and was 25.4 months for those who had received prior alloSCT (**Figure 3**)

RESULTS *(Continued)*

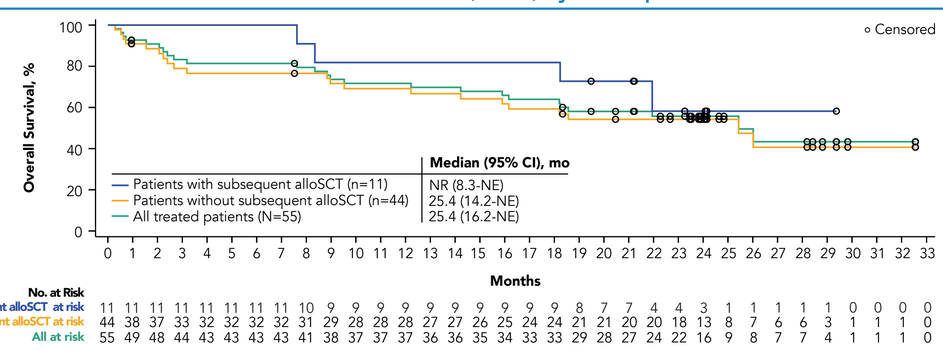
Table 1. Efficacy and Durability Outcomes in All Phase 2 Treated Patients and Pooled Phase 1 and 2 Treated Patients by Prior Therapies

	N	Overall CR rate, n (%)[a]	CR, n (%)[a]	CRi, n (%)[a]	BFBM, n (%)[a]	No response, n (%)[a]	Median DOR, mo (95% CI)[b]	Median RFS, mo (95% CI)[b]	Median OS, mo (95% CI)
Phase 2 treated	**55**	**39 (71)**	**31 (56)**	**8 (15)**	**4 (7)**	**9 (16)**	**14.6 (9.4-NE)**	**11.6 (2.7-20.5)**	**25.4 (16.2-NE)**
Lines of prior therapy									
1	10	9 (90)	8 (80)	1 (10)	1 (10)	0	4.7 (1.8-NE)	5.6 (0.0-NE)	NR (2.1-NE)
≥2	45	30 (67)	23 (51)	7 (16)	3 (7)	9 (20)	14.6 (9.4-NE)	11.0 (1.8-15.5)	25.4 (14.2-NE)
Prior blinatumomab									
Yes	25	15 (60)	10 (40)	5 (20)	2 (8)	6 (24)	19.1 (1.3-NE)	11.6 (0.0-25.4)	14.2 (3.2-26.0)
No	30	24 (80)	21 (70)	3 (10)	2 (7)	3 (10)	10.3 (5.2-NE)	11.7 (2.8-22.1)	NR (18.6-NE)
Prior alloSCT									
Yes	23	16 (70)	13 (57)	3 (13)	2 (9)	4 (17)	14.6 (8.7-23.6)	11.7 (0.0-20.5)	25.4 (14.2-NE)
No	32	23 (72)	18 (56)	5 (16)	2 (6)	5 (16)	NR (4.7-NE)	6.1 (2.2-NE)	NR (9.0-NE)
Pooled Phase 1 and 2 patients[c]	**78**	**57 (73)**	**47 (60)**	**10 (13)**	**6 (8)**	**12 (15)**	**18.6 (9.6-NE)**	**11.7 (6.1-20.5)**	**25.4 (16.2-NE)**
Lines of prior therapy									
1	15	13 (87)	12 (80)	1 (7)	1 (7)	1 (7)	4.9 (1.8-NE)	6.1 (2.8-NE)	NR (7.6-NE)
≥2	63	44 (70)	35 (56)	9 (14)	5 (8)	11 (17)	20.0 (10.3-NE)	11.7 (2.7-20.5)	25.4 (15.9-NE)
Prior blinatumomab									
Yes	38	24 (63)	18 (47)	6 (16)	4 (11)	8 (21)	14.6 (9.6-NE)	7.3 (0.0-15.5)	15.9 (8.3-25.4)
No	40	33 (83)	29 (73)	4 (10)	2 (5)	4 (10)	18.6 (5.2-NE)	11.7 (6.1-NE)	47.0 (18.6-NE)
Prior alloSCT									
Yes	29	22 (76)	17 (59)	5 (17)	2 (7)	4 (14)	14.6 (8.7-23.6)	12.3 (2.7-20.5)	25.4 (14.2-NE)
No	49	35 (71)	30 (61)	5 (10)	4 (8)	8 (16)	NR (5.2-NE)	10.3 (2.7-NE)	47.0 (10.9-NE)

[a] Assessed by independent central review. Overall CR rate includes CR + CRi. [b] Patients censored at subsequent alloSCT. [c] Pooled analysis of Phase 1 and 2 patients who received the pivotal dose of brexu-cel.
alloSCT, allogeneic stem cell transplant; BFBM, blast-free hypoplastic or aplastic bone marrow; brexu-cel, brexucabtagene autoleucel; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; DOR, duration of remission; mo, month; NE, not estimable; NR, not reached; OS, overall survival; RFS, relapse-free survival.

- Response rates in each prior therapy subgroup were largely consistent with the all treated population (**Table 1**)
- Efficacy and durability outcomes in the pooled population of Phase 1 and 2 patients were similar to those observed in Phase 2 patients (**Table 1**)

Figure 4. Overall Survival in Phase 2 Treated Patients (N=55) by Subsequent AlloSCT[a]



[a] This was a single arm study with limited numbers in some subgroups. Subsequent alloSCT was allowed per investigator discretion but was not protocol defined.
alloSCT, allogeneic stem cell transplant; mo, month; NE, not estimable; NR, not reached.

- Eleven of the 55 treated patients (18%; 10 CR/CRi, 1 blast-free hypoplastic or aplastic bone marrow) in Phase 2 proceeded to subsequent alloSCT
- At data cutoff, the median OS was not reached in patients who received subsequent alloSCT and was 25.4 months in patients without subsequent alloSCT (**Figure 4**)

Table 2. Summary of CRS and Neurologic Events in All Phase 2 Treated Patients (N=55) by Prior Therapies

	Prior Lines of Therapy		Prior Blinatumomab		Prior AlloSCT	
	1 (n=10)	≥2 (n=45)	Yes (n=25)	No (n=30)	Yes (n=23)	No (n=32)
CRS, n (%)						
Grade 1	4 (40)	7 (16)	2 (8)	9 (30)	5 (22)	6 (19)
Grade 2	4 (40)	21 (47)	13 (52)	12 (40)	11 (48)	14 (44)
Grade ≥3	1 (10)	12 (27)	6 (24)	7 (23)	4 (17)	9 (28)
Neurologic events, n (%)						
Grade 1	2 (20)	4 (9)	2 (8)	4 (13)	2 (9)	4 (13)
Grade 2	1 (10)	12 (27)	7 (28)	6 (20)	4 (17)	9 (28)
Grade ≥3	3 (30)	11 (24)	5 (20)	9 (30)	6 (26)	8 (25)

alloSCT, allogeneic stem cell transplant; CRS, cytokine release syndrome.

- Incidences of Grade ≥3 cytokine release syndrome and neurologic events were largely similar among prior therapy subgroups (**Table 2**)
- In Phase 2 treated patients, median peak and area under the curve CAR T-cell expansion appeared to trend lower (~3 fold) in patients with prior blinatumomab exposure vs those without; however, the differences were not statistically significant regardless of whether blinatumomab was the last prior therapy before CAR T-cell infusion, potentially due to small sample size (data not shown)

CONCLUSIONS

- With longer follow-up, adult patients with R/R B-ALL continue to benefit from brexu-cel, with manageable safety, regardless of prior lines of therapy or prior exposure to blinatumomab or alloSCT
  - Survival appeared better in patients without these prior therapies and in earlier lines of therapy; however, subgroups were not matched for disease burden prior to brexu-cel infusion and there were limited patient numbers in some subgroups
- The similar results observed in the pooled analysis of Phase 1 and 2 patients further support the subgroup outcomes described in Phase 2 patients
- Patients receiving subsequent alloSCT appeared to have longer OS compared with patients who did not receive subsequent alloSCT; however, patient numbers were limited
- CAR T-cell expansion trended lower in patients with prior blinatumomab exposure than in blinatumomab-naive patients, but the differences were not statistically significant; however, given the small sample size, the interpretation of this result is limited

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ACKNOWLEDGMENTS

- The patients, families, friends, and caregivers
- The study investigators, coordinators, and health care staff at each study site
- We thank Jukka Hartikka, Lisa Thomson, and Kate Wolven, PhD, of Kite for supporting the current analysis and report
- Medical writing support was provided by Ashly Pavlovsky, PhD, of Nexus Global Group Science LLC, funded by Kite
- This study was funded by Kite
- These data were previously presented at the 2022 Annual Meeting of the European Hematology Association[7]

DISCLOSURES

BDS: honoraria from Pharmacyclics, Janssen, Acrotech, Spectrum, BeiGene, and Gilead Sciences; consultancy or advisory role for Adaptive Biotechnologies, Bristol Myers Squibb/Celgene, Novartis, Pfizer, Amgen, Precision Biosciences, and Kite; research funding from Incyte, Jazz Pharmaceuticals, Gilead Sciences, and Kite; and travel support from Celgene, Novartis, Pfizer, Janssen, Seattle Genetics, Stemline Therapeutics, and Kite.

Full author disclosures are available through the Quick Response (QR) code

Presented at the 2023 Annual Meeting of the European Society for Blood and Marrow Transplantation