Poster
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The Comparison of KTE-X19 to Current Standards of Care: A Prespecified Synthetic Control Study Utilizing Individual Patient-Level Data from Historic Clinical Trials (SCHOLAR-3)

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BACKGROUND

- Approximately 40%–50% of adults with B-cell precursor acute lymphoblastic leukemia (B-ALL) experience relapse after initial treatment, with an overall poor prognosis[1,2]
- Novel immunotherapeutic agents blinatumomab and inotuzumab ozogamicin have improved outcomes in relapsed/refractory (R/R) B-ALL, yet the median overall survival (OS) with these agents is <8 months, highlighting the need for more effective therapies[3-8]
- ZUMA-3 is a Phase 1/2, international, multicenter study evaluating KTE-X19 in adults with R/R B-ALL[3]
- SCHOLAR-3 is a synthetic control study using individual patient-level data sampled from historical clinical trials to provide comparator data and contextualize ZUMA-3 results

OBJECTIVES

- To compare the overall complete remission rate at week 24 of the ZUMA-3 pivotal study to an external control arm derived from historical patient-level clinical trial data
- To compare the OS results of the ZUMA-3 pivotal study to an external control arm derived from historical patient-level clinical trial data

METHODS

PATIENT IDENTIFICATION

- A systematic search was conducted to identify all previously completed clinical trials with congruent inclusion and exclusion criteria to the ZUMA-3 investigational trial (**Figure 1** and **Figure 2**)
- The trials that were identified and available in the Medidata Enterprise Data Store (MEDS) were then used to build an external control arm

EXTERNAL CONTROL ARMS FOR PRIMARY ANALYSIS

- Synthetic control arm (SCA)-1: External arm 1 consisted of matched patients who had previously been naive to blinatumomab and inotuzumab therapy
- SCA-2: External arm 2 consisted of matched patients who had previously failed treatment with blinatumomab and/or inotuzumab therapy

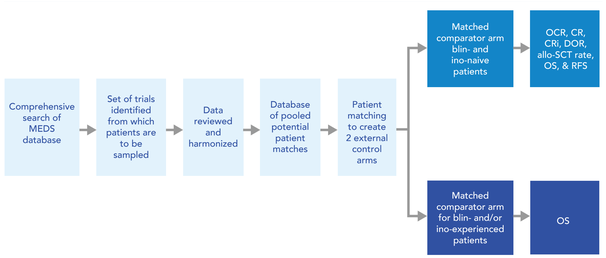
EXTERNAL CONTROL ARM FOR SENSITIVITY ANALYSIS

- SCA-3: External arm 3 consisted of patients who had previously been naive to blinatumomab and inotuzumab therapy matched to all ZUMA-3 patients (irrespective of whether patients were pretreated with blinatumomab or inotuzumab)
- The rationale for this analysis was to compare ZUMA-3 patients to a less heavily pretreated population

PROPENSITY SCORE MATCHING

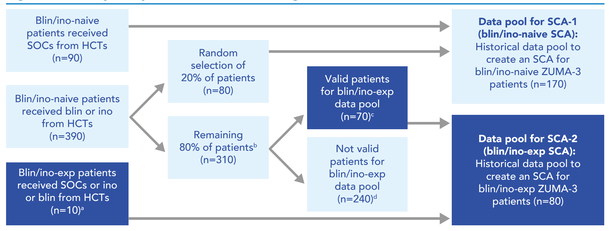
- In order to appropriately build 3 matched external control arms and reduce heterogeneity between cohorts, propensity score matching was used
- The variables used to derive the propensity score included
  - Age, sex, line of therapy, previous stem cell transplantation status, Philadelphia chromosome status, percentage of bone marrow blasts at baseline, primary refractory status, Eastern Cooperative Oncology Group performance status, and presence of extramedullary disease at baseline

Figure 1. Study Schema for Primary Analysis



Allo-SCT, allogeneic stem cell transplantation; blin, blinatumomab; CR, complete response; CRi, complete response without hematologic response; DOR, duration of response; ino, inotuzumab; MEDS, Medidata Enterprise Data Store; OCR, overall complete remission; OS, overall survival; RFS, relapse-free survival.

Figure 2. Primary Analyses Conduct of Matching



[a]Blin/ino-exp patients had previously failed on blin/ino in a previous line of therapy.
[b]The 80% of patients are the remainders of the patients after the 20% random selection of the SCA-1 historical data pool.
[c]Patients had on-study treatment switch from blin or ino to other treatments, and the reassessment dates of key prognostic factors were ≤60 days prior to treatment switch date.
[d]Patients did not have on-study treatment switch from blin or ino to other treatment; or patients had on-study treatment switch from blin or ino to other treatments, but the reassessment dates of key prognostic factors were >60 days prior to treatment switch date.
Allo-SCT, allogeneic stem cell transplantation; blin, blinatumomab; exp, experienced; HCT, historical clinical trial; ino, inotuzumab; SCA, synthetic control arm; SOC, standard of care.

RESULTS

TRIAL SELECTION

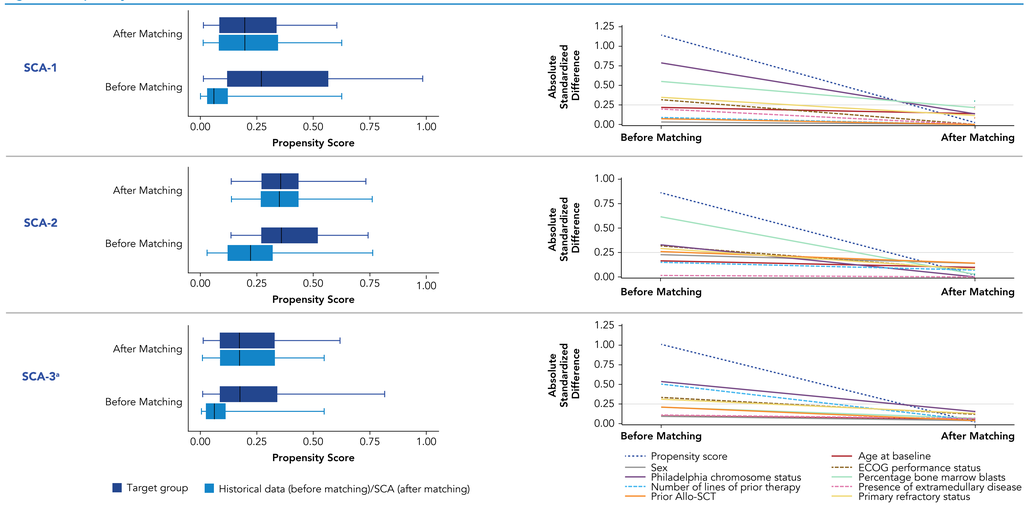
- In total, 135 Phase 1/2, 2, and 3 trials in adult patients with R/R acute lymphoblastic leukemia (ALL) that included regimens containing blinatumomab, inotuzumab ozogamicin, or standard of care therapies were included in the search set
  - 13 trials were included in the R/R ALL superset
- 490 patients met eligibility criteria for inclusion in a SCA

Table 1. Baseline Characteristics Were Well-Balanced Between ZUMA-3 Target Cohorts and SCAs

	SCA-1: Blin/Ino-Naive			SCA-2: Blin/Ino-Exp			SCA-3: Blin/Ino-Naive (ZUMA-3)[a]		
Characteristics	**Target Group 1 (n=20)**	**SCA-1 (n=20)**	**Standardized Difference**	**Target Group 2 (n=29)**	**SCA-2 (n=29)**	**Standardized Difference**	**Target Group 3 (n=53)**	**SCA-3 (n=53)**	**Standardized Difference**
Age at baseline, y			-0.138			-0.098			-0.056
Mean (SD)	42.5 (15.3)	44.8 (16.9)		40.9 (16.9)	42.4 (15.9)		41.5 (15.7)	42.4 (16.4)	
Median	42.5	44.5		40.0	41.0		40.0	39.0	
Min, max	21.0, 68.0	20.0, 72.0		19.0, 84.0	19.0, 70.0		19.0, 84.0	18.0, 78.0	
Sex, n (%)			0.000			0.140			-0.038
Male	12 (60.0)	12 (60.0)		19 (65.5)	17 (58.6)		32 (60.4)	33 (62.3)	
Female	8 (40.0)	8 (40.0)		10 (34.5)	12 (41.4)		21 (39.6)	20 (37.7)	
ECOG, n (%)			0.000			-0.072			-0.119
0	7 (35.0)	7 (35.0)		9 (31.0)	10 (34.5)		16 (30.2)	19 (35.8)	
1	13 (65.0)	13 (65.0)		20 (69.0)	19 (65.5)		37 (69.8)	34 (64.2)	
Philadelphia chromosome status, n (%)			0.135			0.000			-0.154
Positive	4 (20.0)	3 (15.0)		6 (20.7)	6 (20.7)		13 (24.5)	16 (30.2)	
Negative/unknown	16 (80.0)	17 (85.0)		23 (79.3)	23 (79.3)		40 (75.5)	37 (69.8)	
Percentage bone marrow blasts			0.215			-0.027			0.068
Mean (SD)	48.2 (31.6)	41.6 (30.2)		59.3 (32.2)	60.2 (34.6)		55.7 (32.5)	53.6 (28.3)	
Median	50.0	37.5		70.0	70.4		65.0	60.0	
Min, max	2.0, 96.0	0.3, 100.0		2.0, 98.0	0.0, 95.0		0.0, 98.0	0.3, 95.0	
Number of lines of prior therapy, n (%)			0.000			0.070			-0.040
≤2	16 (80.0)	16 (80.0)		11 (37.9)	10 (34.5)		29 (54.7)	30 (56.6)	
>2	4 (20.0)	4 (20.0)		18 (62.1)	19 (65.5)		24 (45.3)	23 (43.4)	
Presence of EMD, n (%)			0.000			0.000			-0.065
Yes	1 (5.0)	1 (5.0)		5 (17.2)	5 (17.2)		6 (11.3)	7 (13.2)	
No/unknown	19 (95.0)	19 (95.0)		24 (82.8)	24 (82.8)		47 (88.7)	46 (86.8)	
Prior allo-SCT, n (%)			0.000			0.141			0.039
Yes	7 (35.0)	7 (35.0)		13 (44.8)	11 (37.9)		22 (41.5)	21 (39.6)	
No/unknown	13 (65.0)	13 (65.0)		16 (55.2)	18 (62.1)		31 (58.5)	32 (60.4)	
Primary refractory status, n (%)			0.114			-0.079			0.130
Yes	7 (35.0)	6 (30.0)		8 (27.6)	9 (31.0)		18 (34.0)	15 (28.3)	
No/unknown	13 (65.0)	14 (70.0)		21 (72.4)	20 (69.0)		35 (66.0)	38 (71.7)	

[a]SCA-3 was an ad-hoc sensitivity analysis.
Allo-SCT, allogeneic stem cell transplantation; blin, blinatumomab; ECOG, Eastern Cooperative Oncology Group performance status; EMD, extramedullary disease; exp, experienced; ino, inotuzumab; SCA, synthetic control arm; SD, standard deviation.

Figure 3. Propensity Scores of SCA-1, SCA-2, and SCA-3 Were Below the Predefined Threshold



[a]SCA-3 was an ad hoc sensitivity analysis.
Allo-SCT, allogeneic stem cell transplantation; ECOG, Eastern Cooperative Oncology Group performance status; SCA, synthetic control arm.

- Patient characteristics between SCA-1, SCA-2, and SCA-3 and their respective target groups from ZUMA-3 were well balanced after matching and fell below the prespecified threshold (**Table 1** and **Figure 3**)

Table 2. Overall Complete Remission Rate at Week 24 for SCA-1 and SCA-3

Primary Analysis SCA-1: Blin/Ino-Naive

Response Category[a]	Target Group 1 (n=20)		SCA-1 (n=20)		Treatment Difference (95% CI)		*P* value
	n	% (95% CI)	n	% (95% CI)	Rate Difference	Odds Ratio	
Overall complete remission rate at week 24[b]	17	85.0 (62.1, 96.8)	7	35.0 (15.4, 59.2)	50.0 (17.9, 73.7)	10.5 (2.3, 48.7)	.0031

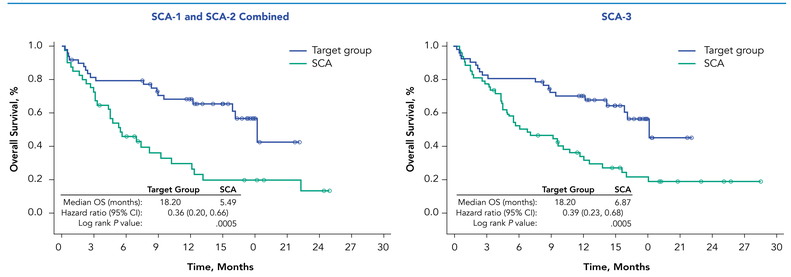
Sensitivity Analysis SCA-3: Blin/Ino-Naive (ZUMA-3)

Response Category	Target Group 3 (n=53)		SCA-3 (n=53)		Treatment Difference (95% CI)		*P* value
	n	%	n	%	Rate	Odds	
Overall complete remission rate at week 24[b]	37	69.8 (55.7, 81.7)	19	35.8 (23.1, 50.2)	34.0 (12.2, 51.3)	4.1 (1.8, 9.3)	.0009

[a]Overall complete remission was not available for SCA-2. [b]Complete response plus complete response with incomplete hematologic recovery.
Allo-SCT, allogeneic stem cell transplantation; blin, blinatumomab; ECOG, Eastern Cooperative Oncology Group performance status; ino, inotuzumab; SCA, synthetic control arm.

- Overall complete remission rate at week 24 was significantly higher in the ZUMA-3 target groups compared to SCA-1 and SCA-3 (**Table 2**)

Figure 4. OS of All Matched Patients of SCA-1 and SCA-2 Combined and SCA-3



OS, overall survival; SCA, synthetic control arm.

- Patients in the ZUMA-3 arm matched to SCA-1 and SCA-2 combined had a median OS of 18.20 months in comparison with 5.49 months in the combined SCA-1 and SCA-2 arm (hazard ratio [95% CI], 0.36 [0.20, 0.66]): **Figure 4**)
- Patients in the ZUMA-3 arm matched to SCA-3 had a median OS of 18.20 months in comparison to 6.87 months in the SCA-3 arm (hazard ratio [95% CI], 0.39 [0.23, 0.68])

CONCLUSIONS

- SCHOLAR-3 is a cohort study of adult patients with R/R B-ALL sampled from historical clinical trials to understand the current unmet medical need of these patients and provide context to the ZUMA-3 study results
- The primary analyses were prespecified and conducted by an independent statistician
- Kite was blinded to all matching and SCA outcomes until the primary analysis was complete
- The results of this study highlight the high unmet need in R/R ALL
- SCHOLAR-3 shows a clinically meaningful treatment effect across all endpoints attributable to KTE-X19 therapy in ZUMA-3 and supports its use in adult patients with R/R B-ALL

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DISCLOSURES

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