Phase 2 Results of the ZUMA-3 Study Evaluating KTE-X19, an Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy, in Adult Patients With Relapsed/Refractory B-Cell Acute Lymphoblastic Leukemia

Bijal D. Shah, MD[1]; Armin Ghobadi, MD[2]; Olalekan O. Oluwole, MD, MPH, MBBS[3]; Aaron C. Logan, MD, PhD[4]; Nicolas Boissel, MD, PhD[5]; Ryan D. Cassaday, MD[6]; Edouard Forcade, MD, PhD[7]; Michael R. Bishop, MD[8]; Max S. Topp, MD[9]; Dimitrios Tzachanis, MD, PhD[10]; Kristen M. O'Dwyer, MD[11]; Martha L. Arellano, MD[12]; Yi Lin, MD, PhD[13]; Maria R. Baer, MD[14]; Gary J. Schiller, MD[15]; Jinghui Dong, PhD[16]; Tong Shen, PhD[16]; Francesca Milletti, PhD[16]; Behzad Kharabi Masouleh, MD[16]; Roch Houot, MD, PhD[17]

[1]Moffitt Cancer Center, Tampa, FL, USA; [2]Washington University School of Medicine, St. Louis, MO, USA; [3]Vanderbilt-Ingram Cancer Center, Nashville, TN, USA; [4]UCSF Medical Center, San Francisco, CA, USA; [5]Hôpital Saint-Louis, Paris, France; [6]University of Washington School of Medicine, Fred Hutchinson Cancer Research Center and Seattle Cancer Care Alliance, Seattle, WA, USA; [7]Centre Hospitalier Universitaire de Bordeaux, Pessac, France; [8]The University of Chicago Medicine, Chicago, IL, USA; [9]Universitätsklinikum Würzburg, Würzburg, Germany; [10]University of California, San Diego, San Diego, CA, USA; [11]Wilmot Cancer Institute of University of Rochester, Rochester, NY, USA; [12]Emory University School of Medicine, Atlanta, GA, USA; [13]Mayo Clinic, Rochester, MN, USA; [14]University of Maryland Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD, USA; [15]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA; [16]Kite, a Gilead Company, Santa Monica, CA, USA; [17]Centre Hospitalier Universitaire de Rennes, Rennes, France

Placeholder for video recording

Background

- Approximately 40%–50% of adults with B-ALL experience relapse after initial treatment, with an overall poor prognosis[1,2]
  - The 1-year OS rate for patients with R/R B-ALL is 26% after first salvage and decreases with subsequent lines of therapy[2]
  - Although the novel agents blinatumomab and inotuzumab ozogamicin lead to CR/CRi rates of 35.1% and 80.7%, respectively, OS remains <8 months and is largely contingent on alloSCT[2-7]
- KTE-X19 is an autologous anti-CD19 CAR T-cell therapy approved for the treatment of R/R MCL[8,9]
- ZUMA-3 is a Phase 1/2, international, multicenter study evaluating KTE-X19 in adults with R/R B-ALL
  - In Phase 1, KTE-X19 demonstrated a manageable safety profile with an overall CR/CRi rate of 83%, and the recommended Phase 2 dose was established as 1×10^6 CAR T cells/kg[10]
- Here, we report the Phase 2 results from ZUMA-3, the pivotal study of KTE-X19 in the largest adult-only R/R B-ALL population to date

1. Paul S, et al. *Mayo Clin Proc*. 2016. 2. Gökbuget N, et al. *Haematologica*. 2016. 3. Topp MS, et al. *Lancet Oncol*. 2015. 4. Kantarjian H, et al. *N Engl J Med*. 2017. 5. Kantarjian HM, et al. *New Engl J Med*. 2016. 6. Kantarjian HM, et al. *Cancer*. 2019. 7. DeAngelo DJ, et al. *Blood Adv*. 2017. 8. TECARTUS® (brexucabtagene autoleucel) Prescribing information. Kite Pharma, Inc; 2021. 9. TECARTUS® (autologous anti-CD19-transduced CD3+ cells) Summary of product characteristics. Kite Pharma EU B.V.; 2021. 10. Shah BD, et al. *Blood.* 2021.

Placeholder for video recording

ZUMA-3: Phase 2 Study Design

Phase 2

R/R B-ALL	Enrolled N=71 Adult Patients

Key Eligibility Criteria

- ≥18 years of age with R/R B-ALL[a] and BM blasts >5%
- Patients could have received prior blinatumomab

Conditioning Chemotherapy

- Fludarabine 25 mg/m^2 IV on Days −4, −3, −2 and cyclophosphamide 900 mg/m^2 IV on Day −2

KTE-X19

- 1×10^6 anti-CD19 CAR T cells/kg on Day 0

Primary Endpoint

- CR/CRi rate by central assessment

Key Secondary Endpoints

- MRD-negativity rate (10^{-4} sensitivity)
- DOR
- RFS
- OS
- Safety
- CAR T-cell levels in blood and cytokine levels in serum

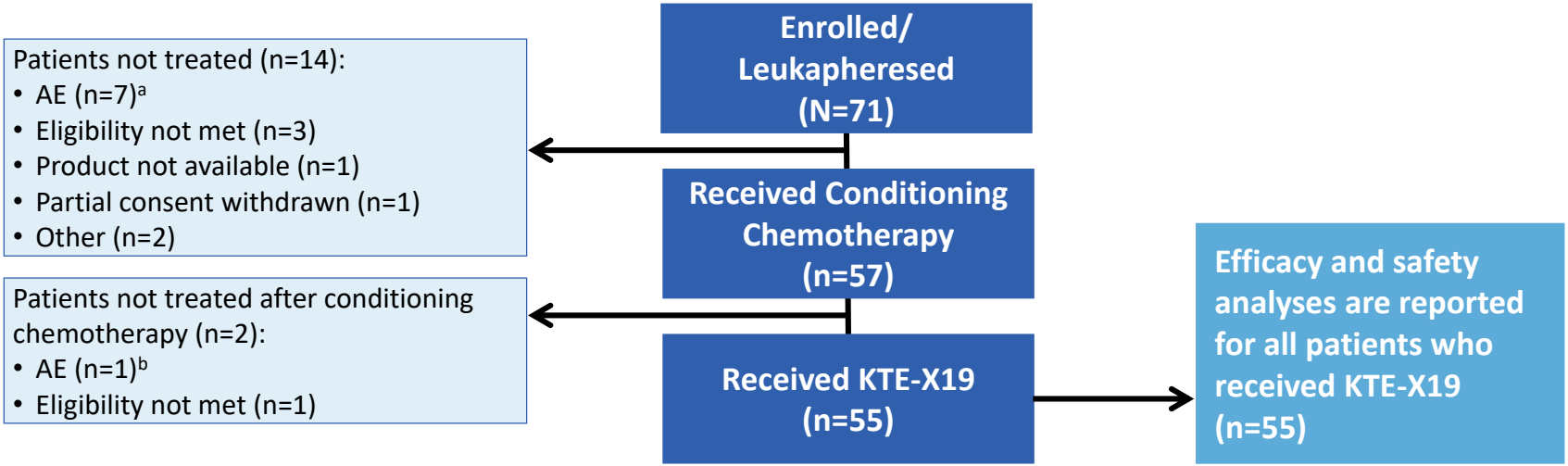
Placeholder for video recording

[a] R/R disease was defined as primary refractory, first relapse with remission ≤12 months, R/R after ≥2 prior lines of systemic therapy, or relapsed after alloSCT.

alloSCT, allogeneic stem-cell transplant; B-ALL, B-precursor acute lymphoblastic leukemia; BM, bone marrow; CAR, chimeric antigen receptor; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; DOR, duration of remission; MRD, minimal residual disease; OS, overall survival; RFS, relapse-free survival; R/R, relapsed/refractory.

Shah et al 2021 Abstract 7002

ZUMA-3: Phase 2 Disposition



- As of September 9, 2020, the median follow-up for all treated patients was 16.4 months (range, 10.3–22.1)
- KTE-X19 was successfully manufactured for 65 of 71 enrolled patients (92%)[c]
- The median time from leukapheresis to KTE-X19 manufacturing release was 13 days for US patients and 14.5 days for European patients

Placeholder for video recording

[a] n=1 each: sepsis, ALL, fungal pneumonia and sepsis (both in the same patient), DVT, encephalopathy and cardiac arrest (both in the same patient), myositis, and hemiparesis due to air embolism. [b] Bacteremia. [c] Of the 14 patients who did not receive conditioning chemotherapy, products were not successfully manufactured for 6 patients: AE (n=1; fungal pneumonia and sepsis [both in same patient]), product not available (n=1), partial consent withdrawn (n=1), eligibility not met (n=1), and other (n=2).

Shah et al 2021 Abstract 7002

ZUMA-3: Baseline Characteristics

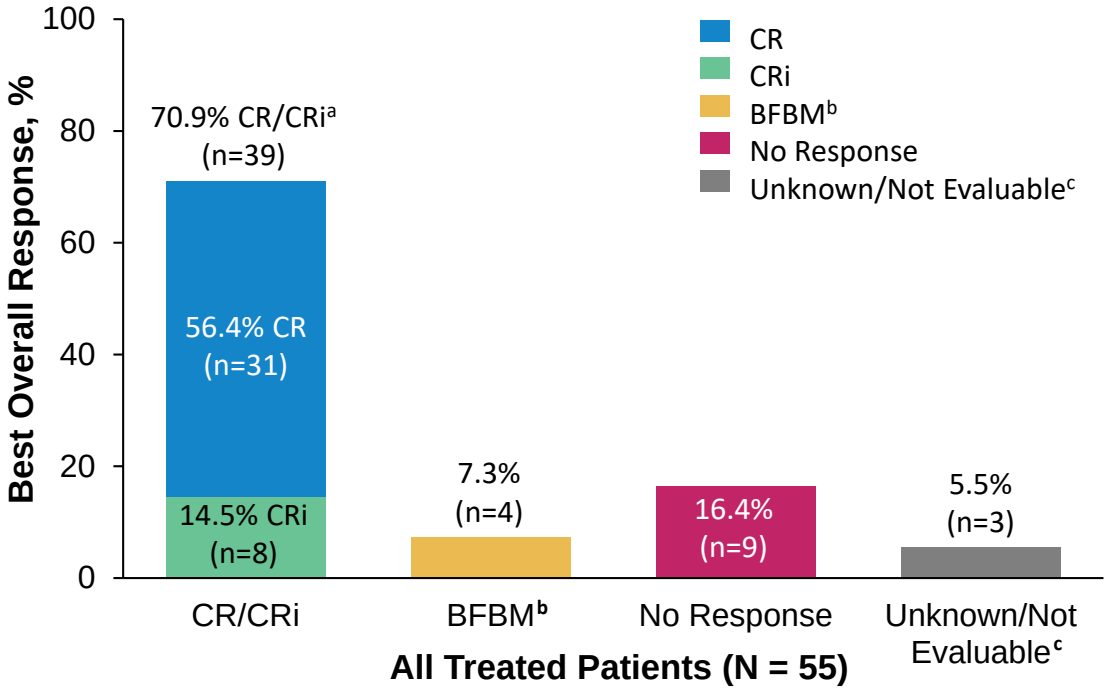
Characteristics	N=55
Age, median (range), years	40 (19–84)
Male, n (%)	33 (60)
ECOG PS of 1, n (%)	39 (71)
Philadelphia chromosome-positive, n (%)	15 (27)
CNS-1 disease at baseline, n (%)[a]	55 (100)
Number of prior therapies, median (range)	2 (1–8)
≥3 prior lines of therapy, n (%)	26 (47)
Prior blinatumomab, n (%)	25 (45)
Prior inotuzumab ozogamicin, n (%)	12 (22)
Prior alloSCT, n (%)	23 (42)
Relapsed/refractory subgroup, n (%)	
Primary refractory	18 (33)
Relapsed/refractory to ≥2 prior systemic therapy lines	43 (78)
First relapse with remission ≤12 months	16 (29)
Relapsed/refractory post-SCT[b]	24 (44)
BM blasts at screening, median (range), %	65.0 (5–100)
BM blasts at preconditioning after bridging chemotherapy, median (range), %[c]	59.0 (0–98)

[a] At screening, 47 patients had CNS-1 disease and 5 patients had CNS-2 disease. [b] Includes 1 patient who underwent autologous SCT. [c] n=46 patients with available data.
alloSCT, allogeneic stem-cell transplant; BM, bone marrow; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; SCT, stem cell transplant.

Placeholder for video recording

Shah et al 2021 Abstract 7002

ZUMA-3: A CR/CRi Rate of 70.9% and CR Rate of 56.4% by Central Assessment Was Observed, Meeting Primary Endpoint



- The median time to initial CR/CRi was 1.1 months (range, 0.85–2.99)
- The MRD-negativity rate was 97% in responders, with samples unavailable for 1 patient
- Ten patients (18%), including 9 with CR/CRi and 1 with BFBM, received alloSCT at a median 98 days (range, 60–207) post–KTE-X19 infusion

[a] 95% CI, 57–82 (*P*<.0001). The CR/CRi rate in all enrolled patients (n=71) was 54.9% by central assessment. [b] ≤5% blasts by morphology in BM and any absolute neutrophil count and platelet values not meeting criteria for CR, CRi, or complete remission with partial hematologic recovery. [c] The 3 patients who were unknown/not evaluable died prior to the first disease response assessment.

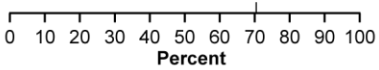
alloSCT, allogeneic stem-cell transplant; BFBM, blast-free hypoplastic or aplastic bone marrow; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; MRD, minimal residual disease.

Placeholder for video recording

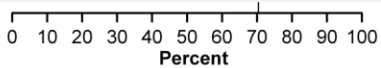
Shah et al 2021 Abstract 7002

ZUMA-3: CR/CRi Rate by Central Assessment Was Generally Consistent Across Subgroups

Covariates		Responding Patients/ Evaluable Patients	Percent of Patients With Response (95% CI)
Overall		39/55	71 (57–82)
Sex	Male	25/33	76 (58–89)
	Female	14/22	64 (41–83)
Age (years)	18-39	16/26	62 (41–80)
	40-64	15/21	71 (48–89)
	≥65	8/8	100 (63–100)
Baseline extramedullary disease	Yes	3/6	50 (12–88)
	No	36/49	73 (59–85)
CNS status at screening	CNS-1	34/47	72 (57–84)
	CNS-2	4/5	80 (28–99)
CD19 % lymphoblast baseline category based on central lab	≥95	29/41	71 (54–84)
	<95	9/12	75 (43–95)
% blasts in bone marrow at baseline	0–5	4/5	80 (28–99)
	>5–25	9/10	90 (55–100)
	>25–50	10/11	91 (59–100)
	>50–75	8/10	80 (44–97)
	>75–100	8/19	42 (20–67)
Philadelphia chromosome	Yes	12/15	80 (52–96)
	No	27/40	68 (51–81)



Covariates		Responding Patients/ Evaluable Patients	Percent of Patients With Response (95% CI)
Overall		39/55	71 (57–82)
Prior lines of therapy	1	9/10	90 (55–100)
	2	12/19	63 (38–84)
	3	9/14	64 (35–87)
	≥4	9/12	75 (43–95)
Prior alloSCT	Yes	16/23	70 (47–87)
	No	23/32	72 (53–86)
Prior blinatumomab	Yes	15/25	60 (39–79)
	No	24/30	80 (61–92)
Prior inotuzumab ozogamicin	Yes	8/12	67 (35–90)
	No	31/43	72 (56–85)
First relapse ≤12 months	Yes	11/16	69 (41–89)
	No	28/39	72 (55–85)
Primary refractory	Yes	14/18	78 (52–94)
	No	25/37	68 (50–82)
Relapsed/refractory post-SCT[a]	Yes	17/24	71 (49–87)
	No	22/31	71 (52–86)
Relapsed/refractory after ≥2 lines of prior therapy	Yes	28/43	65 (49–79)
	No	11/12	92 (62–100)



Placeholder for video recording

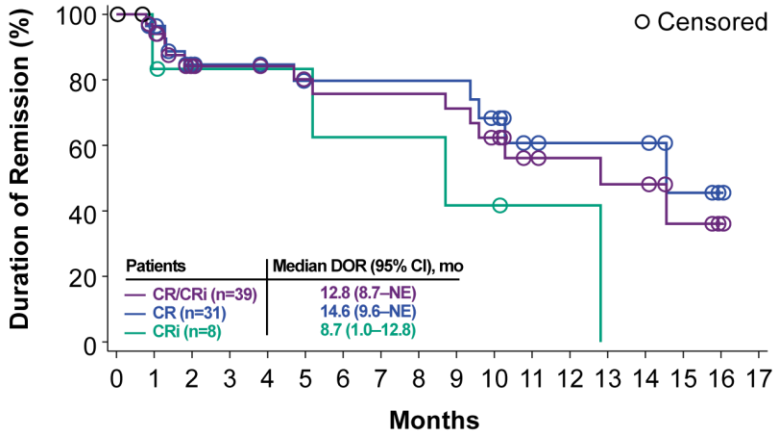
[a] Includes 1 patient who underwent autologous SCT.

alloSCT, allogeneic stem-cell transplant; CR, complete remission; CNS, central nervous system; CRi, complete remission with incomplete hematologic recovery; SCT, stem-cell transplant.

Shah et al 2021 Abstract 7002

ZUMA-3: Median DOR Was 12.8 Months With and Without Censoring Patients at Subsequent AlloSCT

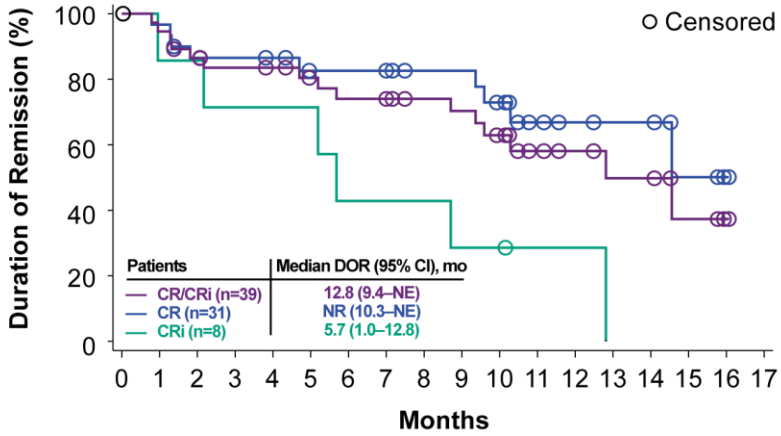
DOR With Censoring at Subsequent AlloSCT



No. at Risk

CR	31	26	19	18	17	14	14	14	14	14	11	7	6	6	6	3	1	0
CRi	8	5	4	4	4	4	3	3	3	2	2	1	1	0	0	0	0	0
CR/CRi	39	31	23	22	21	18	17	17	17	16	13	8	7	6	6	3	1	0

DOR Without Censoring at Subsequent AlloSCT



No. at Risk

CR	31	29	25	24	23	20	20	19	17	17	14	9	7	6	6	3	1	0
CRi	8	6	6	5	5	5	3	3	3	2	2	1	1	0	0	0	0	0
CR/CRi	39	35	31	29	28	25	23	22	20	19	16	10	8	6	6	3	1	0

- As of the data cutoff, 12 of 39 patients who achieved CR/CRi (31%) were in ongoing remission without subsequent alloSCT[a]

[a] Nine of the 39 patients with CR/CRi (23%) proceeded to subsequent alloSCT and 5 (13%) to other anticancer therapies, 12 (31%) relapsed, and 1 (3%) died. Patients undergoing new anticancer therapies (including alloSCT) were censored.

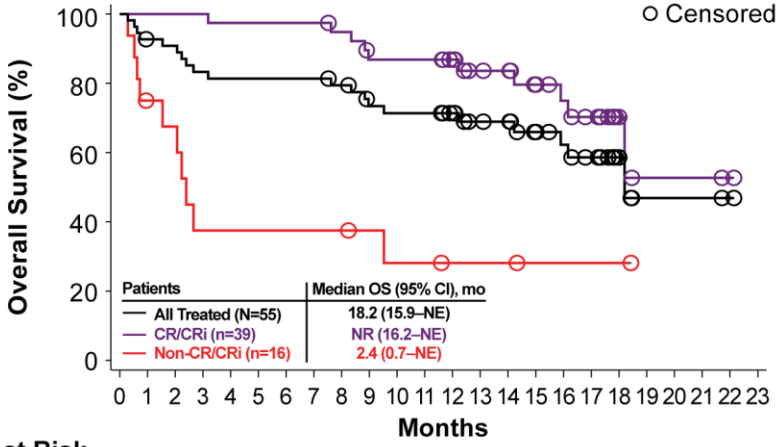
alloSCT, allogeneic stem-cell transplant; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; DOR, duration of remission; NE, not estimable; NR, not reached.

Placeholder for video recording

Shah et al 2021 Abstract 7002

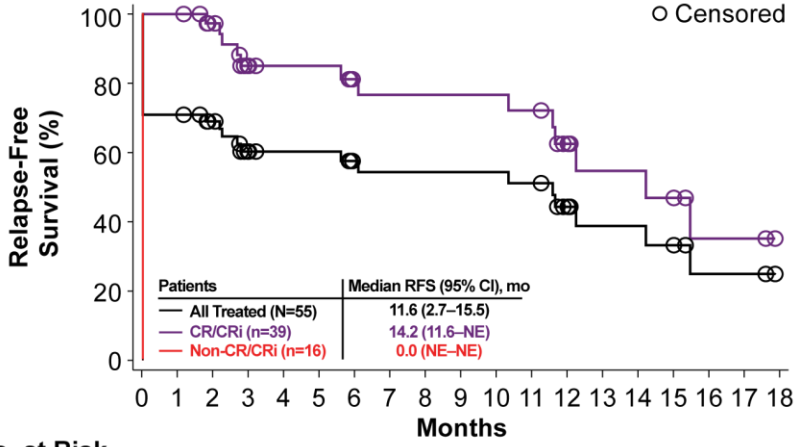
ZUMA-3: Median OS Was 18.2 Months and Median RFS Was 11.6 Months

Overall Survival



No. at Risk																								
CR/CRi	39	39	39	39	38	38	38	38	36	32	32	32	29	24	23	19	16	13	6	2	2	2	1	0
Non-CR/CRi	16	10	9	5	5	5	5	5	5	4	3	3	2	2	2	1	1	1	1	0	0	0	0	0
All Treated	55	49	48	44	43	43	43	43	41	36	35	35	31	26	25	20	17	14	7	2	2	2	1	0

Relapse-Free Survival[a]



No. at Risk																								
CR/CRi	39	39	33	24	22	22	18	17	17	17	17	16	11	7	7	6	3	3	0					
Non-CR/CRi	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0					
All Treated	55	39	33	24	22	22	18	17	17	17	17	16	11	7	7	6	3	3	0					

- Among patients with CR/CRi, median OS was not reached and median RFS[a] was 14.2 months

[a] Patients who underwent subsequent SCT post–KTE-X19 were censored at the last evaluable disease assessment prior to SCT. RFS was defined as the time from KTE-X19 infusion to the date of disease relapse or death from any cause. Patients who did not achieve CR/CRi as of the data cutoff date were evaluated as having an RFS event at Day 0.
CR, complete remission; CRi, complete remission with incomplete hematologic recovery; NE, not estimable; NR, not reached; OS, overall survival; RFS, relapse-free survival; SCT, stem cell transplant.

Placeholder for video recording

ZUMA-3: Adverse Events

AE, n (%)[a]	N=55					
	Any	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Any AE	55 (100)	0	3 (5)	8 (15)	34 (62)	10 (18)[b]
Pyrexia	52 (95)	8 (15)	24 (44)	17 (31)	3 (5)	0
Hypotension	37 (67)	2 (4)	19 (35)	13 (24)	3 (5)	0
Anemia	29 (53)	0	2 (4)	25 (45)	2 (4)	0
Nausea	21 (38)	12 (22)	9 (16)	0	0	0
Sinus tachycardia	21 (38)	9 (16)	9 (16)	3 (5)	0	0
Headache	20 (36)	12 (22)	8 (15)	0	0	0
Chills	18 (33)	13 (24)	5 (9)	0	0	0
Platelet count decreased	18 (33)	1 (2)	0	3 (5)	14 (25)	0
Hypoxia	16 (29)	1 (2)	4 (7)	7 (13)	4 (7)	0
Fatigue	15 (27)	12 (22)	3 (5)	0	0	0
Hypokalemia	15 (27)	5 (9)	6 (11)	3 (5)	1 (2)	0
Hypophosphatemia	15 (27)	2 (4)	2 (4)	11 (20)	0	0
Neutrophil count decreased	15 (27)	0	0	1 (2)	14 (25)	0
Tremor	15 (27)	14 (25)	0	1 (2)	0	0

- Most common Grade ≥3 AEs were anemia (49%) and pyrexia (36%)
- There were 10 Grade 5 AEs: 4 events were ALL, 2 events were related to KTE-X19 (brain herniation, septic shock), 3 events occurred after initiation of another anticancer therapy (fungal pneumonia, sepsis, respiratory failure), and 1 event of pneumonia was not related to KTE-X19

Placeholder for video recording

[a] AEs shown are those that occurred in >25% of patients. [b] Four patients had ALL reported as a Grade 5 AE.
AE, adverse event; ALL, acute lymphocytic leukemia.

Shah et al 2021 Abstract 7002

ZUMA-3: CRS and Neurologic Events

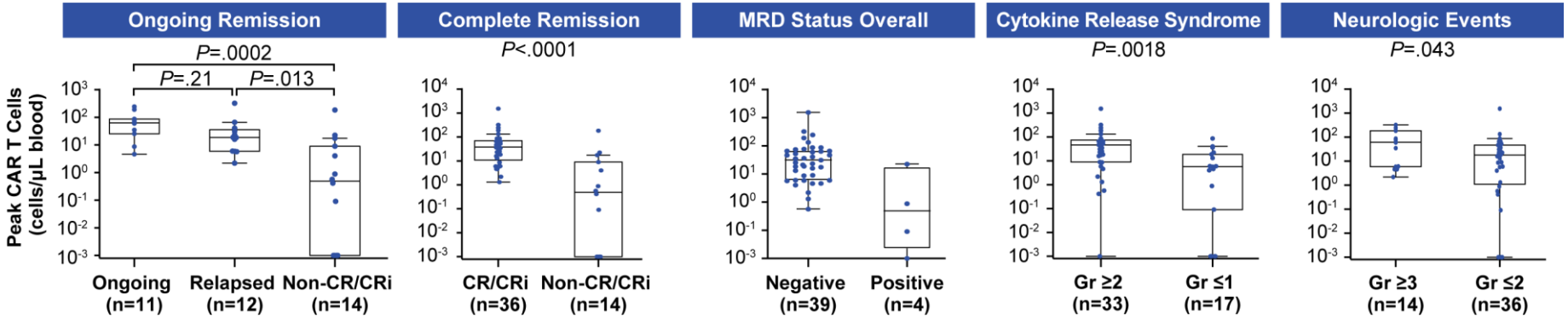
Parameter	N=55
CRS	
Any grade CRS, n (%)[a,b]	49 (89)
Grade ≥3	13 (24)
Most common any grade symptoms, n (%)[c]	
Pyrexia	46 (94)
Hypotension	33 (67)
Median time to onset (range), days	5
Median duration of events, days	7.5
Neurologic Events	
Any grade neurologic event, n (%)[b]	33 (60)
Grade ≥3	14 (25)
Most common any grade symptoms, n (%)	
Tremor	15 (27)
Confusional state	14 (25)
Median time to onset (range), days	9
Median duration of events, days	7

- No Grade 5 CRS occurred
- One patient had Grade 5 brain herniation related to KTE-X19
- Tocilizumab, steroids, and vasopressors were given to 80%, 75%, and 40% of patients, respectively

[a] CRS was graded per Lee DW, et al. *Blood*. 2014;124:188–195. [b] Individual symptoms of CRS and neurologic events were graded per National Cancer Institute's Common Terminology Criteria for Adverse Events version 4.03. [c] Percentages for individual CRS symptoms were calculated out of the 49 patients who experienced CRS.
CRS, cytokine release syndrome.

Placeholder for video recording

ZUMA-3: Associations Between CAR T-Cell Levels and Clinical Outcomes



- Peak CAR T-cell levels were higher in
  - Patients with ongoing CR/CRi, followed by patients who relapsed, and lower in non-CR/CRi patients
  - Patients with CR/CRi vs non-CR/CRi
  - MRD-negative vs MRD-positive patients
- Peak CAR T-cell levels were positively associated with Grade ≥2 CRS and Grade ≥3 neurologic events
- Median time to peak CAR T-cell levels in blood post-KTE-X19 infusion was 15 days (range, 7-32)
  - In the 10 of 12 ongoing responders with evaluable samples at Month 12, all (100%) had recovered peripheral B cells and only 1 (10%) had detectable CAR T cells

Placeholder for video recording

P values were calculated using the Wilcoxon rank sum test for 2-group comparisons and Kruskal-Wallis test with post hoc Dunn test for 3-group comparisons.
CAR, chimeric antigen receptor; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; CRS, cytokine release syndrome; MRD, minimal residual disease.

Shah et al 2021 Abstract 7002

ZUMA-3: Conclusions

- At a median follow-up of 16.4 months, a single infusion of KTE-X19 showed a high and durable response rate in heavily pretreated adults with R/R B-ALL, most of whom had high disease burden
  - The CR/CRi rate was 70.9%, with a CR rate of 56.4%; 31% of responding patients were in ongoing remission at the data cutoff
  - The CR/CRi rate was consistent across subgroups
  - The median OS was 18.2 months in all treated patients and was not yet reached in patients with CR/CRi
- The safety profile was manageable, and AEs were largely reversible
- The efficacy, rapid manufacturing, and manageable safety support the promising potential of KTE-X19 to provide long-term clinical benefit in adults with R/R B-ALL

Placeholder for video recording

AE, adverse event; B-ALL, B-precursor acute lymphoblastic leukemia; CR, complete remission; CRi, complete remission with incomplete hematologic recovery; OS, overall survival; R/R, relapsed/refractory.

Shah et al 2021 Abstract 7002

Acknowledgments

- The patients, families, friends, and caregivers
- The study investigators, coordinators, and health care staff at each study site
- Martha Sensel, PhD, Christine Wang, PhD, Daniela Van Eickels, MD, MPH, Petra Schuberth, PhD, and Daniel Lee, MD of Kite, a Gilead Company, for supporting the development of the presentation
- Medical writing support was provided by Nexus Global Group Science LLC, funded by Kite, a Gilead Company

Placeholder for video recording