# A Phase 1 Study of KITE-363 Anti-CD19/CD20 Chimeric Antigen Receptor T-Cell Therapy in Patients With Relapsed/Refractory B-Cell Lymphoma

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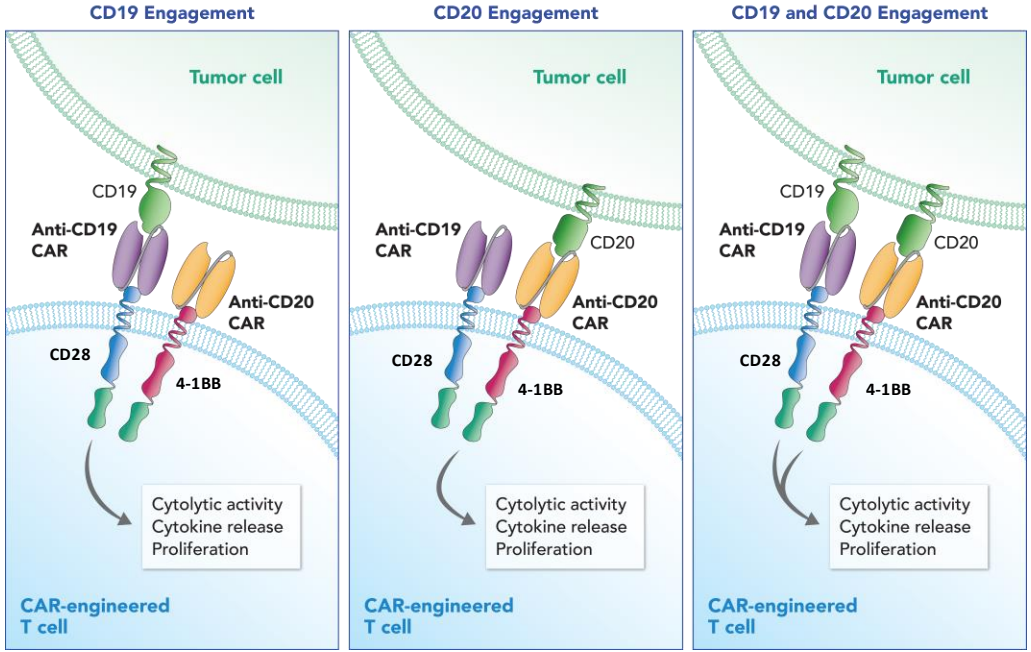
# Key Takeaways

- Results from this trial demonstrate that KITE-363 is a promising therapeutic approach for patients with R/R B-cell lymphoma, including those with highly refractory LBCL
  - **The safety profile was manageable**, with no Grade ≥3 CRS events in patients with LBCL and 2 cases of Grade 3 ICANS with short durations at the highest dose level (none occurring in patients with primary refractory LBCL)
  - **High rates of responses at the highest dose level** were demonstrated in a refractory, CAR-naive LBCL population
  - **CAR T-cell expansion was dose dependent, with markedly robust expansion observed at the highest dose level**

CAR, chimeric antigen receptor; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

# Background

## KITE-363 Structure and Mechanism of Action




- KITE-363 is a bicistronic, lentiviral-encoded, dual-targeting autologous CAR T-cell therapy where the anti-CD19 CAR contains a CD28 co-stimulatory domain and the anti-CD20 CAR contains a 4-1BB co-stimulatory domain[1]
- Dual targeting has the potential to address tumor heterogeneity, and improve the durability of responses by preventing CD19-negative relapses
- Here we present the safety and preliminary efficacy results from a Phase 1, first-in-human, open-label, multicenter study of KITE-363 in patients with R/R B-cell lymphomas

1. Murakami J, et al. ASH 2024. Abstract 3481.
CAR, chimeric antigen receptor; LBCL, large B-cell lymphoma; R/R, relapsed/refractory.

# Study Design

**Phase 1a**

**Dose Escalation**
- 3+3 study design

→

**Phase 1b**

**Dose Expansion**

## Key Inclusion Criteria

- **Phase 1a: Histologically confirmed R/R B-cell lymphoma** (per WHO criteria[1]) after >2 lines of therapy or 2L primary refractory disease[a]
- **Phase 1b: R/R LBCL only (including 2L primary refractory disease)**
- Aged ≥18 years
- ECOG PS 0 or 1

## Key Exclusion Criteria

- Richter transformation
- CNS involvement of lymphoma
- Active infection
- Clinically significant CNS disorder, autoimmune disease, or cardiac disease

## Primary Endpoint

- Phase 1a: Incidence of DLTs
- Phase 1b: ORR (investigator assessed per Lugano 2014 classification)[2]

## Secondary Endpoints

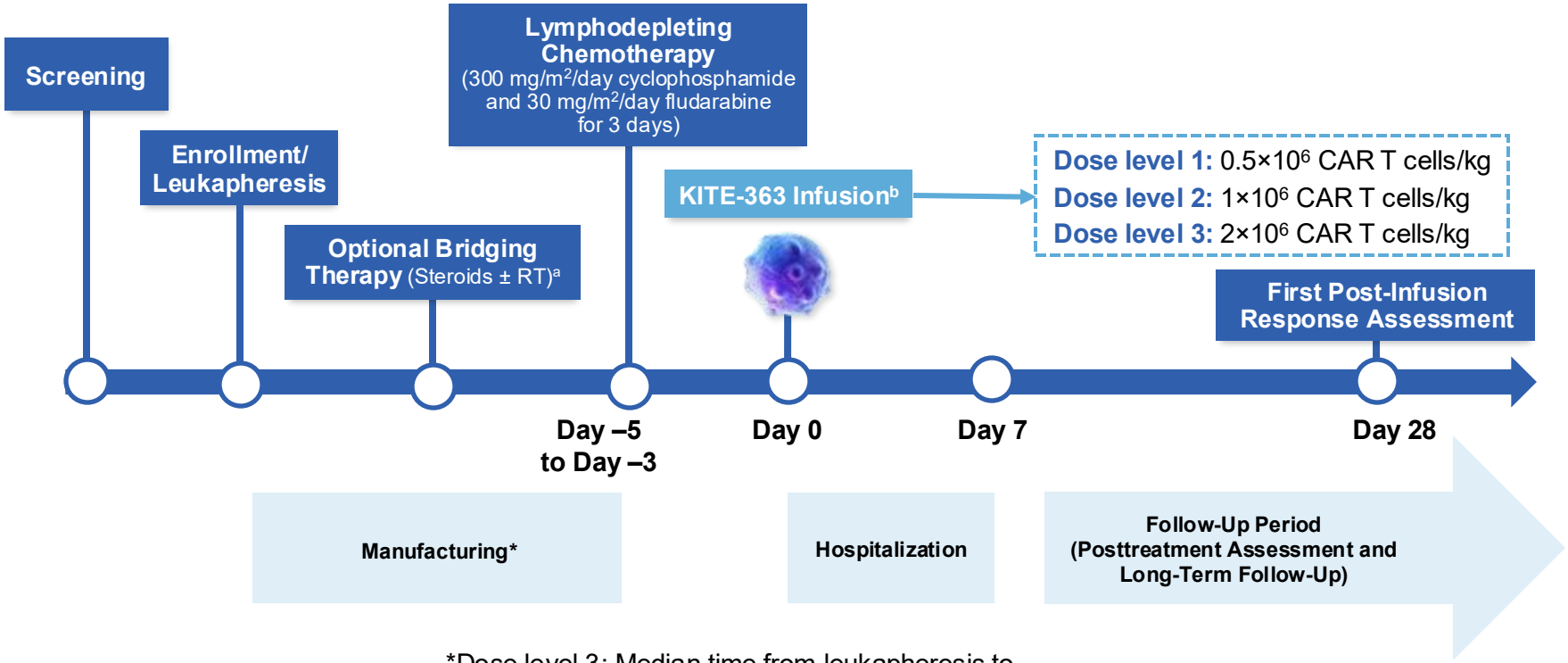
- CR rate
- DOR
- PFS
- TTNT
- OS
- Safety
- Levels of CAR T cells and cytokines in blood

[a] B-cell lymphoma included LBCL (including primary refractory disease and transformed iNHL), iNHL (Grades 1-3a FL; nodal, extranodal, or splenic MZL), NLPHL, and MGZL.

1. Cheson BD, et al. *J Clin Oncol*. 2014;32:3059-3068. 2. Swerdlow SH, et al. *Blood*. 2016;127:2375-2390.

2L, second line; CAR, chimeric antigen receptor; CNS, central nervous system; CR, complete response; DLT, dose-limiting toxicity; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; FL, follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; LBCL, large B-cell lymphoma; MGZL, mediastinal gray zone lymphoma; MZL, marginal zone lymphoma; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; R/R, relapsed/refractory; TTNT, time to next treatment; WHO, World Health Organization.

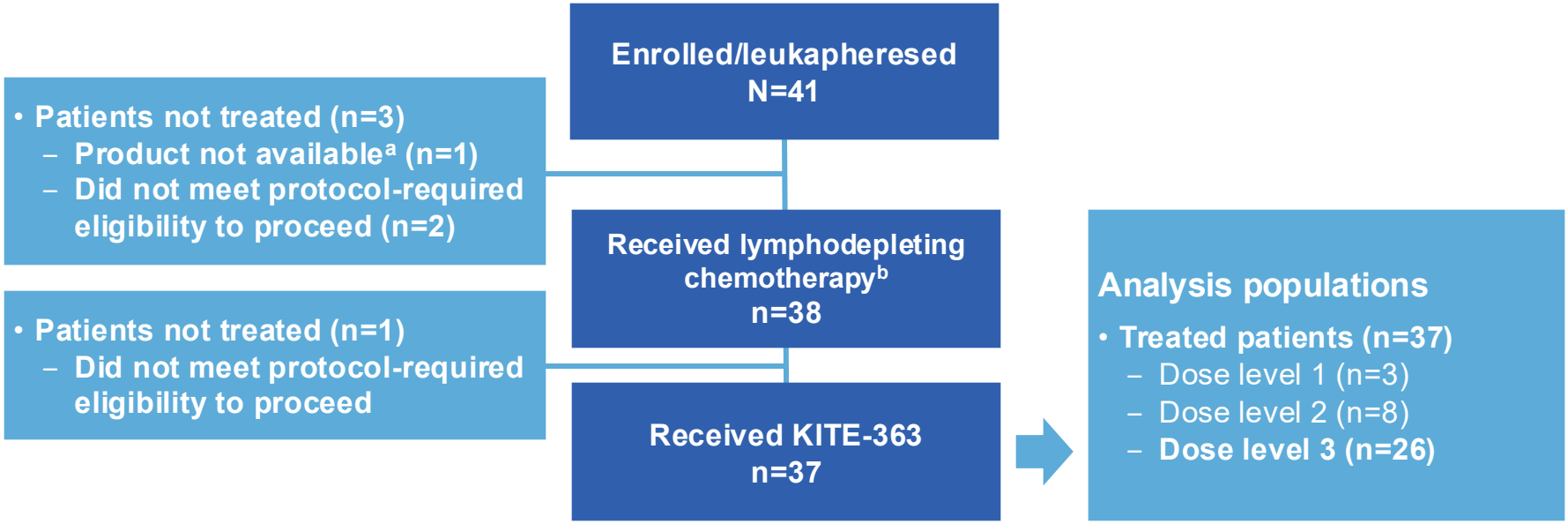
# Treatment Schema




*Dose level 3: Median time from leukapheresis to CAR T-cell infusion was 27 days (range, 21-56)

[a] Corticosteroid bridging therapy ± local radiation therapy was administered at the discretion of the investigator. [b] Dose levels 2 and 3 were explored in Phase 1b.
CAR, chimeric antigen receptor; RT, radiation therapy.

# Patient Disposition




- As of March 18, 2025, median follow-up was
  - **12.4 months (range, 6.0-39.2) in all treated patients**
  - 11.1 months (range, 6.0-22.0) in dose level 3

[a] Product was out of specification due to low potency and the patient had rapidly progressing disease. [b] All eligibility criteria, including presence of measurable disease, must have remain confirmed prior to initiation of lymphodepleting chemotherapy.

# Baseline Patient Characteristics

| Characteristic | All Treated Patients (N=37) | Dose Level 3 (N=26) |
|---|---|---|
| **Median age (range), years** | 62 (25-83) | 60.5 (25-82) |
| ≥65 years, n (%) | 17 (46) | 11 (42) |
| ≥75 years, n (%) | 4 (11) | 3 (12) |
| **Male, n (%)** | 24 (65) | 15 (58) |
| **Ethnicity,[a] n (%)** | | |
| Hispanic or Latino | 4 (11) | 3 (12) |
| Not Hispanic or Latino | 32 (86) | 22 (85) |
| **Race, n (%)** | | |
| Asian | 5 (14) | 4 (15) |
| White | 29 (78) | 19 (73) |
| Other or missing | 3 (8) | 3 (12) |
| **ECOG performance status 1, n (%)** | 22 (60) | 15 (58) |
| **Stage III/IV disease at study entry, n (%)** | 27 (73) | 17 (65) |
| **Histological subtypes, n (%)** | | |
| LBCL[b] | 34 (92) | 25 (96) |
| iNHL | 2 (5) | 0 |
| NLPHL | 1 (3) | 1 (4) |
| **Bulky disease (≥7.5 cm), n (%)** | 7 (19) | 4 (15) |
| **Mean SPD[c] (SD), mm²** | 3552.5 (5987.0) | 3442.1 (6807.7) |
| **Double-/triple-hit status (LBCL only), n/N (%)** | 8/34 (24) | 7/25 (28) |
| **IPI score 3-4 (LBCL only), n/N (%)** | 15/34 (44) | 9/25 (36) |

- All patients had tumors positive for CD19 and/or CD20
  - 78% of patients had tumors that were positive for both
  - 13% were positive for one antigen

[a] The ethnicity of 1 patient was not reported. [b] 2 patients had tMZL and 3 had tFL, all in dose level 3. [c] As measured by the sum of product of diameters of all target lesions at baseline.
ECOG, Eastern Cooperative Oncology Group; tFL, transformed follicular lymphoma; iNHL, indolent non-Hodgkin lymphoma; IPI, International Prognostic Index; LBCL, large B-cell lymphoma; tMZL, transformed marginal zone lymphoma; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma; SPD, sum of the products of the longest perpendicular diameters.

# Prior Therapies

| Prior Therapy | All Treated Patients (N=37) | Dose Level 3 (N=26) |
|---|---|---|
| **Number of prior regimens, n (%)** | | |
| 1 (primary refractory)[a] | 17 (46) | 15 (58) |
| ≥2 | 20 (54) | 11 (42) |
| **Prior anti-CD19 CAR T-cell therapy, n (%)** | 7 (19) | 3 (12) |
| **Prior autologous stem cell transplant, n (%)** | 5 (14) | 4 (15) |
| **Received bridging therapy (steroids ± RT),[b] n (%)** | 21 (57) | 15 (58) |

- Among patients in dose level 3 who were primary refractory (n=15), 4 had PR as best response to 1L therapy and 11 had PD

[a] Primary refractory disease was defined as chemorefractory disease in which the best response to 1L therapy is PD, SD lasting ≤6 months after ≥4 cycles, or PR following ≤6 cycles. [b] All eligibility criteria, including presence of measurable disease, must have remained confirmed following bridging therapy and prior to initiation of lymphodepleting chemotherapy.
1L, first line; CAR, chimeric antigen receptor; CR, complete response; PD, progressive disease; PR, partial response; RT, radiation therapy; SD, stable disease.

# CRS and ICANS

| Parameter | Dose Levels 1 & 2 (N=11) | | Dose Level 3 (N=26) | |
|---|---|---|---|---|
| | CRS | ICANS | CRS | ICANS |
| **Any grade, n (%)[a]** | 7 (64) | 1 (9) | 24 (92) | 12 (46) |
| Grade 1/2 | 7 (64) | 0 | 23 (88) | 10 (38) |
| Grade 3 | 0 | 1 (9) | 1 (4) | 2 (8) |
| Grade 4 | 0 | 0 | 0 | 0 |
| Grade 5 | 0 | 0 | 0 | 0 |
| **Median time to onset (range), days** | 6 (2-8) | 6 (6-6) | 3.5 (2-9) | 6.0 (2-13) |
| **Median duration of event (range), days** | 3 (1-10) | 6 (6-6) | 5.0 (2-11) | 4.5 (1-13) |
| **AE management, n (%)** | | | | |
| Tocilizumab | 5 (45) | 0 | 23 (88) | 0 |
| Corticosteroids | 3 (27) | 1 (9) | 17 (65) | 10 (38) |
| Anakinra | 0 | 1 (9) | 1 (4) | 4 (15) |

- 1 Gr 3 CRS event occurred (NLPHL; duration of Gr 3, 1 day)
- 3 Gr 3 ICANS events occurred:
  - DL2: 1 (duration of Gr 3, 4 days)
  - DL3: 2 (duration of Gr 3, 1 and 2 days)
- In dose level 3 among patients with primary refractory LBCL (n=15), no Gr ≥3 CRS or ICANS events occurred

[a] Severity of CRS was graded per Lee DW, et al. *Blood.* 2014;124:188-195. Severity of neurologic events was graded per the NCI CTCAE v5.0.
AE, adverse event; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; DL, dose level; Gr, Grade; ICANS, immune effector cell–associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma.

# Summary of Adverse Events

## DLTs: No DLTs occurred in Phase 1a

| AEs,[a] n (%) | Dose Level 3 (N=26) Any Grade | Grade ≥3 |
|---|---|---|
| **Any** | 26 (100) | 21 (81) |
| **Serious** | 14 (54) | 10 (38)[b] |
| **Cardiac disorders** | 9 (35) | 1 (4) |
| **Infections** | 11 (42) | 4 (15) |
| **Heme toxicity** | | |
| Neutropenia | 10 (38) | 8 (31) |
| Thrombocytopenia | 2 (8) | 1 (4) |
| Anemia | 8 (31) | 4 (15) |
| **Hypogammaglobulinemia** | 4 (15) | 0 (0) |

### Dose Level 1 and 2

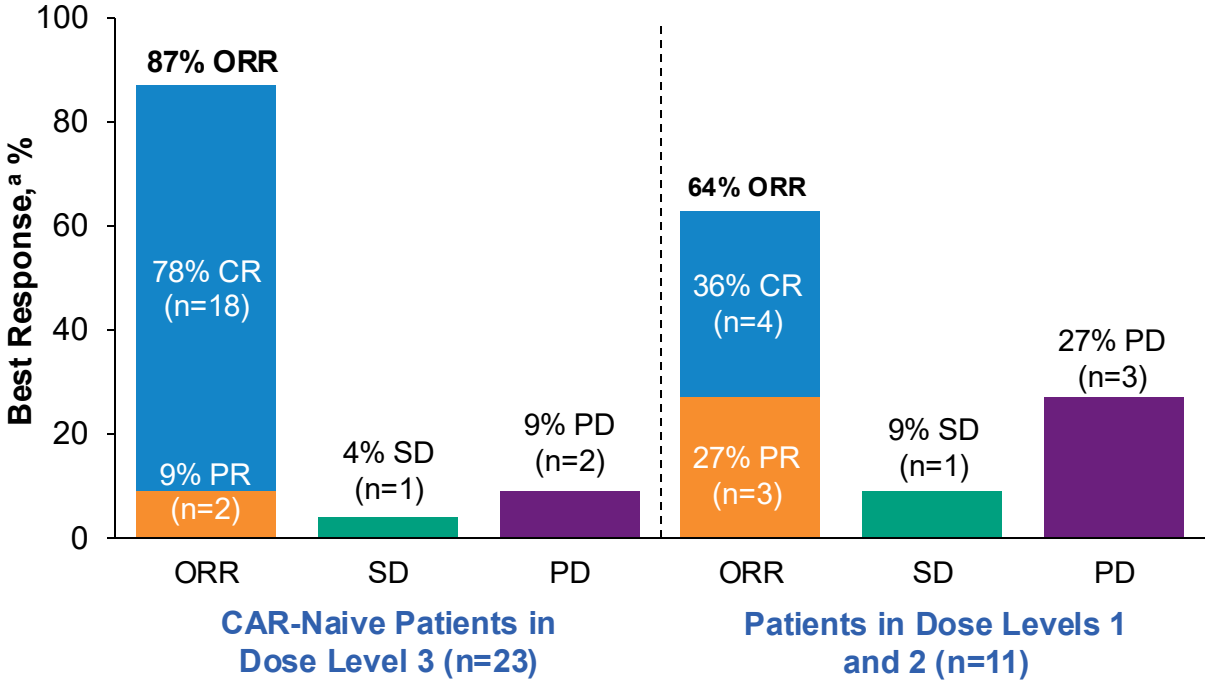
- Grade ≥3 AEs occurred in 2 patients in dose level 1[c]
- Grade ≥3 AEs occurred in 6 patients in dose level 2[d]
  - 1 death considered to be a Grade 5 AE of MDS occurred (subsequent malignancy unrelated to KITE-363)

### Dose Level 3 (See Table)

- The most common Grade ≥3 events among patients in dose level 3 were WBC count decreased (n=11), neutropenia (n=8), and neutrophil count decreased (n=11)

[a] The severity of AEs were graded according to the NCI CTCAE version 5.0. [b] 1 Grade 3 each of febrile neutropenia, tachycardia, lower abdominal pain, COVID-19, sepsis, administration-related reaction, femoral neck fracture, pain in extremity, encephalopathy, hypoxia, and hematoma, and 2 Grade 3 pneumonia.[c] Unrelated to KITE-363 unless specified: 2 Grade 3 cytopenias (1 related); 1 Grade 3 abdominal pain; 2 Grade 3 infections; 2 Grade 3 metabolism and nutrition disorders; 1 Grade 3 syncope; 1 Grade 3 hydronephrosis; 2 Grade 3 respiratory disorders; [d] Unrelated to KITE-363 unless specified: 2 Grade 3 cytopenias (1 related) and 5 Grade 4 cytopenias (4 related); 1 Grade 3 acute cholecystitis; 2 Grade 3 infections (1 related). AE, adverse event; DLT, dose-limiting toxicity; MDS, myelodysplastic syndrome; NCI CTCAE, National Cancer Institute Common Terminology Criteria for Adverse Events; WBC, white blood cell.

# Response




## Dose Level 3

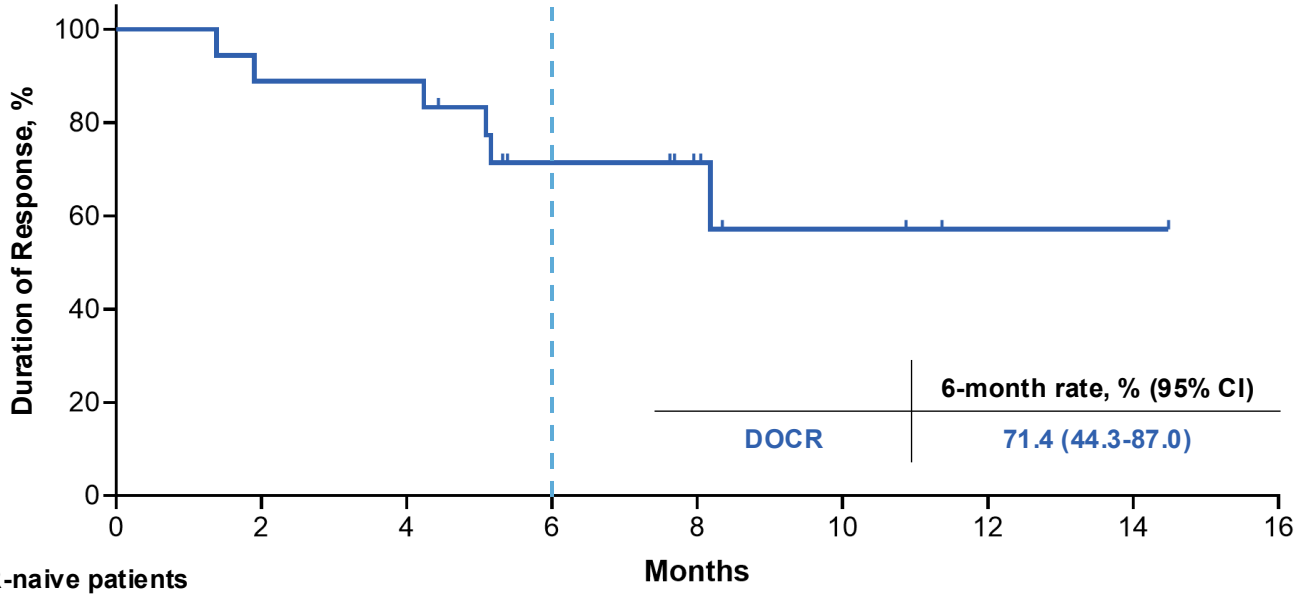
- Among CAR-naive patients (n=23)[b]
  - LBCL with ≥2 prior lines of therapy (n=7): ORR and CR rate of 100%
  - LBCL, primary refractory (n=15): ORR/CR rate of 80%/67%
- In patients with prior CAR exposure (n=3), 1 achieved a response (CR)

[a] Investigator assessed per Lugano 2014 classification.[1] [b] 22 patients had LBCL (including 2 with transformed MZL and 2 with transformed FL) and 1 had NLPHL.

1. Swerdlow SH, et al. *Blood*. 2016;127:2375-2390.

CAR, chimeric antigen receptor; CR, complete response; FL, follicular lymphoma; LBCL, large B-cell lymphoma; MZL, marginal zone lymphoma; NLPHL, nodular lymphocyte-predominant Hodgkin lymphoma; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

# DOCR[a] in CAR-Naive Patients in Dose Level 3



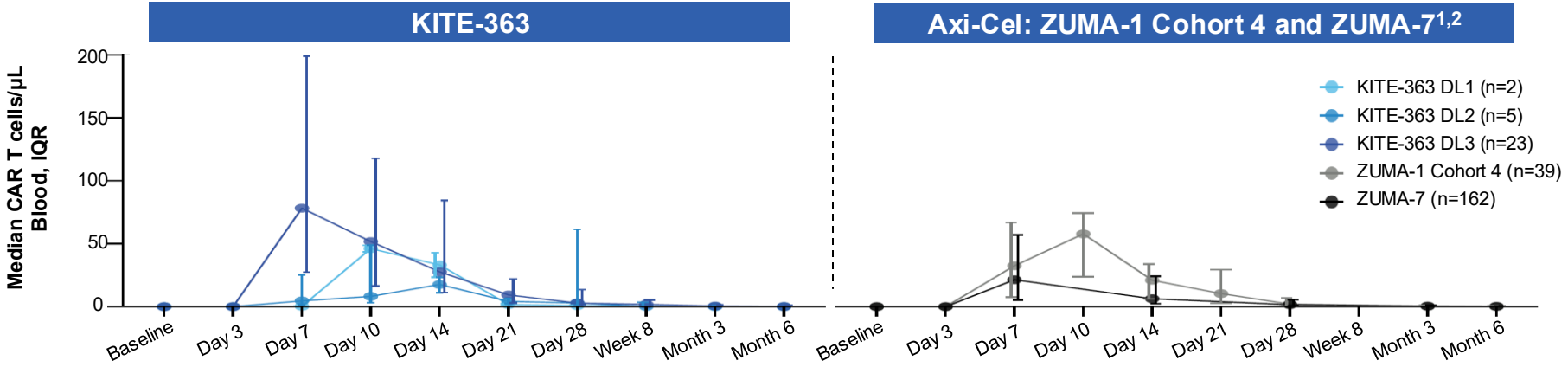

**CAR-naive patients**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **No. at risk** | 18 | 16 | 16 | 10 | 6 | 3 | 1 | 1 | 0 |
| **No. censored** | 0 | 0 | 0 | 3 | 7 | 9 | 11 | 11 | 12 |

- Median DOCR in CAR-naive patients was not reached (95% CI, 5.2-NE)
- 6-month DOCR rate was 71.4%
  - Data beyond 6 months is heavily impacted by censoring. Longer follow-up is needed
- Among all treated patients (N=37), 9 died (8 due to disease progression)

[a] DOCR is defined as DOR of all patients who achieved a best response of CR.
CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; DOCR, duration of complete response; NE, not estimable.

# KITE-363 Showed Pronounced Expansion Across Doses[a]




| Median (Q1-Q3) | KITE-363 DL3 CAR-Naive (n=23) | Axi-Cel ZUMA-1 Cohort 4 (N=39) | Axi-Cel ZUMA-7 (N=162) |
|---|---|---|---|
| **Day 7 CAR T cells/µl** | 78.3 (27.56-199.03) | 32.5 (7.6-66.9) | 21.4 (5.2-57.0) |
| **Peak CAR T cells/µl** | 132.3 (48.29-238.39) | 52.9 (27.3-92.8) | 25.8 (8.2-57.9) |
| **AUC CAR T cells/µl×days** | 819.2 (313.80-2707.46) | 511.2 (216.0-973.5) | 236.2 (76.4-758.0) |
| **Time to peak, days** | 9 (8-14) | 10 (8-13) | 8 (8-9) |

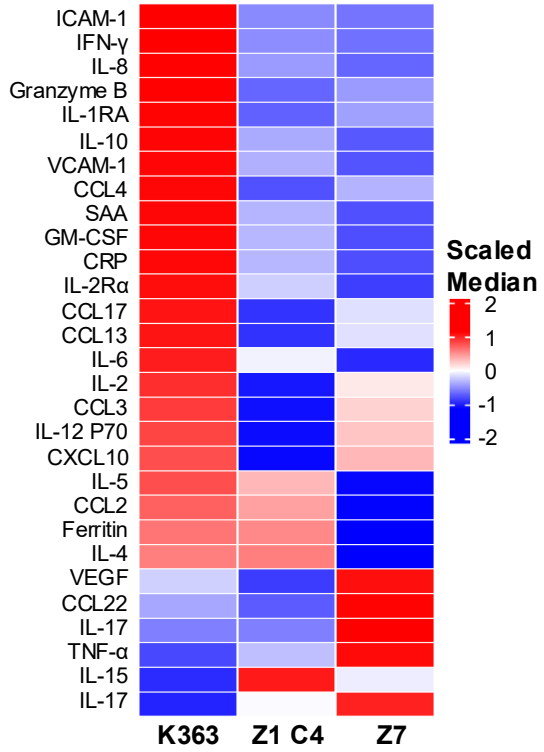
[a] Distinct PK methods were used for KITE-363 and studies of axi-cel (ZUMA-1 Cohort 4 [third-line] and ZUMA-7 [second-line]).

1. Topp MS et al. *Br J Haematol.* 2021;195:388-398. 2. Locke FL, et al. *N Engl J Med*. 2022;386:640-654.

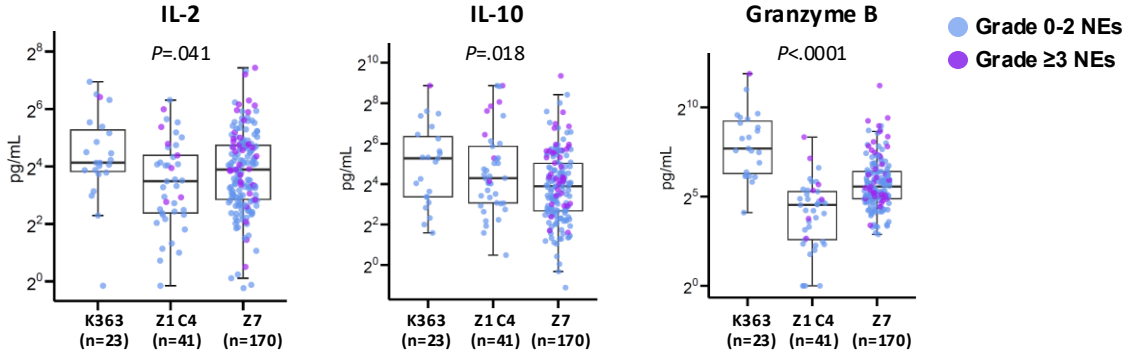
Axi-cel, axicabtagene ciloleucel; AUC, area under the curve; CAR, chimeric antigen receptor; DL, dose level; IQR, interquartile range; PK, pharmacokinetics.

# Post-Infusion Peak Levels of Serum Analytes Associated With KITE-363 PK and Reduced Toxicity

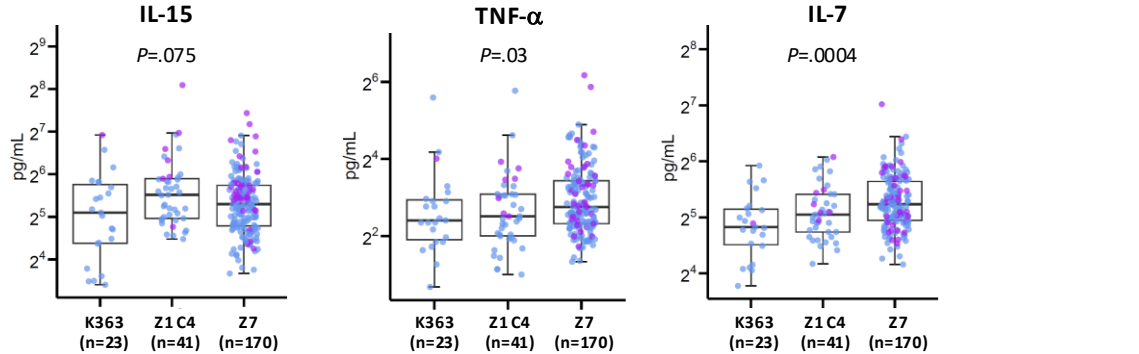
## Post-infusion Serum PD Analytes




## Elevated Cytokines Associated With PK




## Lower Cytokine Levels Associated With Reduced Toxicity




*P* values were calculated using the Kruskal-Wallis test.

C, cohort; IL, interleukin; K363, KITE-363; NE, neurologic events in context of immune effector cell–associated neurotoxicity syndrome; PD, pharmacodynamics; PK, pharmacokinetics; TNF, tumor necrosis factor; Z, ZUMA.

# Conclusions

- The safety profile of KITE-363, a bicistronic, CD19/20–targeting CAR T-cell therapy, was manageable with no DLTs observed in Phase 1a
  - No Grade ≥3 CRS events in patients with LBCL
  - 2 cases of Grade 3 ICANS with short durations
  - No Grade ≥3 ICANS events in patients with primary refractory LBCL in dose level 3
- KITE-363 demonstrated high rates of responses in a highly refractory CAR-naive LBCL population in dose level 3, with an ORR of 87%, a CR rate of 78%, and a median DOCR that is not yet reached
- KITE-363 cell expansion was dose dependent, with markedly robust expansion observed in dose level 3 (appearing >3- to 5- fold higher than with axi-cel)
- Taken together, these results support KITE-363 as a promising therapeutic approach for patients with R/R B-cell lymphoma, including those with highly refractory LBCL
- Given promising early results, specifically robust CAR T-cell expansion and safety profile, KITE-363 is also being developed for the treatment of autoimmune disease

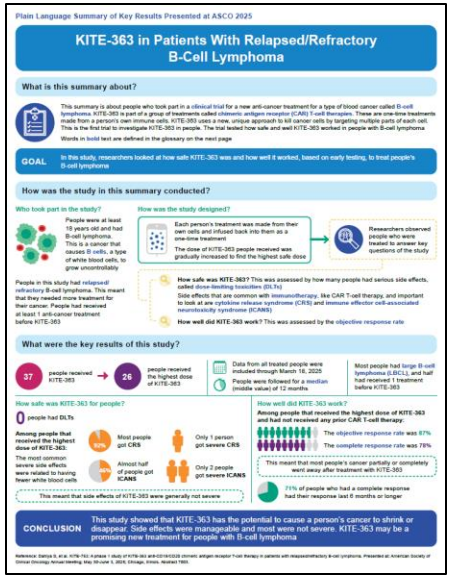
Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLT, dose-limiting toxicity; DOCR, duration of complete response; ICANS, immune effector cell–associated neurotoxicity syndrome; LBCL, large B-cell lymphoma; ORR, objective response rate; R/R, relapsed/refractory.

# Acknowledgments


- We thank the patients, families, friends, and caregivers associated with this study
- We also thank the study investigators, coordinators, and healthcare staff at each study site; and we thank Eric Baehr, Timothy Best, Wende Wu of Kite Global Medical Affairs, and Allen Xue of Kite Biometrics, for their contributions to the analysis and presentation
- Medical writing assistance was provided by Shelley Valle, PhD, of Nexus Global Group Science, LLC, funded by Kite, a Gilead Company
- This study was funded by Kite, a Gilead Company

# Additional Resources

- Full author disclosures are available through the virtual meeting platform
- A plain language summary of the key results from this presentation is available through the Quick Response (QR) code

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