TECARTUS®(brexucabtagene autoleucel): Retreatment in the ZUMA-3 Study

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Relevant TECARTUS Prescribing Information[1]

TECARTUS is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of:

- Adult patients with relapsed or refractory mantle cell lymphoma (MCL).
  This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).

Recommended Dosage for MCL

The target dose is 2×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 2×10^8 CAR-positive viable T cells.

Recommended Dosage for ALL

The target dose is 1×10^6 CAR-positive viable T cells per kg body weight, with a maximum of 1×10^8 CAR-positive viable T cells.

ZUMA-3 Clinical Study (NCT02614066)

Study Design

ZUMA-3 was a multicenter, single arm, phase 1/2 study to evaluate the efficacy and safety of TECARTUS (brexucabtagene autoleucel/KTE-X19) in adult patients with relapsed/refractory B-precursor acute lymphoblastic leukemia (ALL).[2] Key eligibility criteria included patients aged 18 years or older, had Eastern Cooperative Oncology Group (ECOG) performance status of 0–1, and had relapsed or refractory B-precursor ALL with morphological disease in the bone marrow (>5% blasts) at study entry. Relapsed or refractory disease was defined as primary refractory, first relapse with remission of 12 months or less, relapsed or refractory after at least two previous lines of systemic therapy, or relapsed or refractory after allo-SCT. Patients could have received previous blinatumomab. In the study patients must have had an adequate hematologic (absolute neutrophil count [ANC] ≥500/µL, a platelet count ≥50,000/µL, unless in the opinion of the investigator cytopenia is due to underlying leukemia and is potentially reversible with leukemia therapy, and an absolute lymphocyte count [ALC] ≥100/µL), renal, hepatic, and cardiac function.[3] If patients showed signs and symptoms of a serious active infection, they were not allowed to receive treatment until the infection resolved.[3] Patients who had achieved remission of leukemia (CR, CRh, or CRi) after the initial TECARTUS infusion at ≥ Month 3 disease assessment and subsequently progressed could be retreated if they met certain criteria outlined in the protocol.[3]

Treatment Process

Patients underwent leukapheresis to obtain cells for TECARTUS manufacturing before receiving conditioning chemotherapy (intravenous fludarabine 25 mg/m² on days −4, −3, and −2; and intravenous cyclophosphamide 900 mg/m² on day −2).[2] A single TECARTUS infusion was administered at a target dose of 1 × 10^6 CAR T cells/kg on day 0.[2] Patients with a bodyweight greater than 100 kg received a flat dose of 1 × 10^8 CAR T cells.

Retreatment Eligibility in the ZUMA-3 Study

Patients were permitted to receive 1 additional TECARTUS infusion provided the patient achieved remission of leukemia (CR, CRh, or CRi) after the initial TECARTUS infusion at ≥ Month 3 disease assessment and subsequently progressed (>5% bone marrow blasts or progression of extramedullary disease per local assessment).[3]

In addition, the patient must have met all of the following criteria:[3]

- All inclusion criteria
    - Note: inclusion criteria on ALC count ≥ 100/μL only applied if patient must undergo another leukapheresis in order to manufacture another dose of TECARTUS
- All exclusion criteria except for prior TECARTUS used in this study
- Patient must not have had a Grade ≥ 2 TECARTUS-related immediate hypersensitivity reaction
- CD19 tumor expression in bone marrow or peripheral blood must have been documented after progression. If CD19 expression was quantified, then there must have been ≥ 90% CD19 positive blasts.
- Patient did not experience Grade 4 CRS, Grade 4 neurologic events, or any grade of edema in the brain with the first TECARTUS infusion
- Any CRS and neurologic events had fully resolved prior to the retreatment
- Any toxicity related to fludarabine or cyclophosphamide should be resolved to ≤ Grade 1 or return to baseline, prior to retreatment, with the exception of clinically insignificant toxicities (e.g., alopecia)
- The patient had not received subsequent therapy for the treatment of leukemia
- The patient did not have known anti-TECARTUS antibodies
- In consultation with the Kite Medical Monitor, there was agreement to give the additional TECARTUS infusion

Retreatment Results

In phase 2 of the ZUMA-3 study, there were 2 patients retreated with TECARTUS. Both patients had no response to retreatment, and 1 of the patients died as of the data cutoff date on September 9th, 2020.[4]

Table 1. ZUMA-3 Study Retreated Patients: Response to Retreatment

Response to Initial Treatment	Best Response to Retreatment	Transplant After Retreatment
CRi	No Response	No
CR	Relapse	No

CR=Complete Remission. CRi=Complete remission with incomplete hematological recovery.

It is at the discretion of the treating physician to retreat adult patients with relapsed or refractory B-cell precursor ALL with TECARTUS.

The full indication, important safety information, and boxed warnings are available at:

https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf

References

1. TECARTUS® (brexucabtagene autoleucel) [US Prescribing Information]. Santa Monica, CA. Kite Pharma, Inc. 2021
2. Shah BD, Ghobadi A, Oluwole OO, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. Lancet. 2021;S0140-6736(21)01222-8. https://doi.org/10.1016/S0140-6736(21)01222-8.
3. [Supplementary Appendix] Shah BD, Ghobadi A, Oluwole OO, et al. KTE-X19 for relapsed or refractory adult B-cell acute lymphoblastic leukaemia: phase 2 results of the single-arm, open-label, multicentre ZUMA-3 study. Lancet. 2021;S0140-6736(21)01222-8. https://doi.org/10.1016/S0140-6736(21)01222-8.
4. Data on File, Kite Pharma.

Abbreviations

ALC=absolute lymphocyte count
ALL=acute lymphoblastic leukemia
Allo-SCT=allogeneic stem cell transplant
ANC=absolute neutrophil count
CAR=chimeric antigen receptor
CR=complete remission
CRh=complete remission with partial hematologic recovery
CRi=complete remission with incomplete hematologic recovery
CRS=cytokine release syndrome
ECOG= Eastern Cooperative Oncology Group
MCL=mantle cell lymphoma

Product label

For the full indication, important safety information, and Boxed Warning(s), please refer to the TECARTUS® (brexucabtagene autoleucel) US Prescribing Information available at:

https://www.gilead.com/-/media/files/pdfs/medicines/oncology/tecartus/tecartus-pi.pdf

Follow up

For any additional questions, please contact Kite at:

☎1-844-454-KITE (1-844-454-5483) or ✉ medinfo@kitepharma.com

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Kite ☎ 1-844-454-KITE (1-844-454-5483)

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🌐 www.accessdata.fda.gov/scripts/medwatch

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