TECARTUS®:
(brexucabtagene autoleucel): Incidence of Graft versus Host Disease (GVHD) in the ZUMA-3 Study

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The following information regarding the incidence of GVHD in the ZUMA-3 clinical study is provided below as a professional courtesy in response to your unsolicited request.

Summary

US Prescribing Information[1]

Per US Prescribing Information, the ZUMA-3 study excluded patients with active or serious infections, active graft versus host disease, or taking immunosuppressive medications within 4 weeks prior to enrollment.

GVHD in ZUMA-3[2,3,4]

ZUMA-3 was a Phase 1/2, single-arm, open-label, multicenter study evaluating the safety and efficacy of KTE-X19, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, in adults with relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL). Seventy-one patients were enrolled in the intention to treat (ITT) analysis set of the Phase 2 study, and 55 patients received KTE-X19 in the modified ITT (mITT) analysis set. The median follow-up time was 16.4 months.

The study excluded patients with acute GVHD grade II-IV by Glucksberg criteria or severity B-D by International Bone Marrow Transplant Registry (IBMTR) index. Patients with acute or chronic GVHD requiring systemic treatment within 4 weeks prior to enrollment were also excluded.

In the ZUMA-3 study (N=55), of the 23 patients that were treated previously with allogeneic stem cell transplant (allo-SCT) and received KTE-X19, one patient experienced Grade 2 GVHD. The GVHD event was deemed related to KTE-X19, and started as Grade 1 GVHD on Day 39, worsened to Grade 2 on Day 47. The event was ongoing as of the data cutoff date.

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

Incidence of GVHD in the ZUMA-3 study (NCT02614066)

Study Background[2,3,4]

ZUMA-3 was a Phase 1/2, single-arm, open-label, multicenter study evaluating the safety and efficacy of KTE-X19, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, in adults with relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL).[2,3] Eligible patients were 18 years of age or older and had relapsed/refractory B-ALL with morphologic disease in the bone marrow (greater than 5% blasts) at study entry. After leukapheresis and conditioning chemotherapy, patients received a single KTE-X19 infusion (1×10^6 CAR T cells per kg bodyweight).[2]

The primary endpoint was the rate of overall complete remission (CR) or complete remission with incomplete haematological recovery (CRi) by central assessment. Duration of remission and relapse-free survival, overall survival, minimal residual disease (MRD) negativity rate, and allo-SCT rate were assessed as secondary endpoints.[2] Efficacy and safety analyses were done in the treated population (all patients who received a dose of KTE-X19).

There were 71 patients enrolled in the intention to treat (ITT) analysis set of the Phase 2 study, and 55 patients received KTE-X19 in the modified ITT (mITT) analysis set.[2,3] The median follow-up time was 16.4 months.[2]

In patients who enrolled and received KTE-X19 infusion, adverse events that occurred from enrollment (i.e, commencement of leukapheresis through 3 months after treatment with KTE-X19 infusion were reported.[2,3] After 3 months, only targeted adverse events (AEs) were reported through 24 months after KTE-X19 infusion or disease progression, whichever occurred first.[3] Targeted adverse events included central neurological events, infections, GVHD, autoimmune disorders, and secondary malignancies. Patients who received an allo-SCT were only followed for KTE-X19- related serious adverse events (SAEs); these SAEs were to be reported from the time the SCT preparative regimen commenced through 24 months after the KTE-X19 infusion or disease progression, whichever occurred first.[3,4]

Findings from the ZUMA-3 Pivotal (Phase 2) Study[3,4]

The ZUMA-3 clinical trial excluded patients with acute GVHD grade II-IV by Glucksberg criteria or severity B-D by International Bone Marrow Transplant Registry (IBMTR) index.[3] Patients with acute or chronic GVHD requiring systemic treatment within 4 weeks prior to enrollment were also excluded. As part of the exclusion criteria for ZUMA-3, patients with donor lymphocyte infusion 4 weeks or less prior to enrollment were not eligible. Patients being treated with any drug for GVHD (e.g., calcineurin inhibitors, methotrexate, mycophenolyate, rapamycin, thalidomide, etc.) and any immunosuppressive antibody (e.g., anti-CD20, anti-tumor necrosis factor, anti-interleukin 6 or anti-interleukin 6 receptor, etc.) 4 weeks or less prior to enrollment were similarly excluded from study participation.

In ZUMA-3 (n=55), 42% percent (23/55) of patients underwent a prior allogeneic stem cell transplant (allo-SCT).[2] One KTE-X19 treated patient who received previous allo-SCT had Grade 2 GVHD.[4] This patient had nonserious GVHD that was assessed to be related to KTE-X19. The event started as Grade 1 GVHD on Day 39, worsened to Grade 2 on Day 47, and was ongoing as of the data cutoff date.

GVHD following subsequent allo-SCT after KTE-X19 infusion[2,4]

Of the 55 KTE-X19-treated patients in the mITT population of the Phase 2 study, 32 were naïve to allo-SCT prior to receiving KTE-X19.[2] Ten allo-SCT-naïve patients received subsequent allo-SCT after KTE-X19 infusion. Of these ten patients, 4 patients (7%) experienced GVHD, and 6 patients (11%) did not have GVHD.[4]

Data from the Phase 1 Study[4]

Three patients (7%) in the Phase 1 study had GVHD.[4] Of these three patients, one had Grade 1 nonserious GVHD of the gastrointestinal (GI) tract on Day 176 following a subsequent allo-SCT after KTE-X19 treatment on Day 94. The GVHD event was ongoing as of the data cutoff date. The second patient treated with KTE-X19 who had undergone allo-SCT prior to enrollment experienced Grade 1 nonserious chronic GVHD of the skin and eyes that started on Day 51 and resolved on Day 489. A third patient treated with KTE-X19 who had undergone allo-SCT prior to enrollment experienced Grade 2 serious GVHD of the GI tract that started on Day 209 following a donor lymphocyte infusion on Day 174. The GVHD event decreased in seriousness and severity to a Grade 1 nonserious event on Day 247 and resolved on Day 309. None of the GVHD AEs in the Phase 1 study were assessed as related to KTE-X19.

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;398(10299):491-502. https://pubmed.ncbi.nlm.nih.gov/34097852/
3. Supplement to: 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;398(10299):491-502.
4. Data on file. Kite Pharma.

Abbreviations

AE=adverse events
allo-SCT=allogeneic stem cell transplant
B-ALL=acute B lymphoblastic leukemia
CAR=chimeric antigen receptor
CR=complete remission
CRi=complete remission with incomplete hematological recovery
FDA=Food and Drug Administration
GI=gastrointestinal
GVHD=graft versus host disease
IBMTR=International Bone Marrow Transplant Registry
ITT=intention-to-treat
IV=intravenous
mITT=modified intention-to-treat
MRD=minimal residual disease
SAE=serious adverse event
US=United States

Product label

For the full indication, important safety information, and Boxed Warning(s), please refer to the TECARTUS 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

Adverse event reporting

Please report all adverse events to:

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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