Kite A GILEAD Company | Medical Information

TECARTUS®
(brexucabtagene autoleucel): Minimal Residual Disease (MRD) Outcomes in the ZUMA-3 Study

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The following information regarding MRD outcomes following TECARTUS treatment is provided below as a professional courtesy in response to your unsolicited request.

Summary

ZUMA-3 Pivotal Phase 2 Study

ZUMA-3 is a single-arm, open-label, multicenter Phase 1/2 study that evaluated the safety and efficacy of TECARTUS in adult patients with relapsed or refractory B-precursor acute lymphoblastic leukemia (B-ALL). Eligible patients underwent conditioning chemotherapy prior to receiving a single IV infusion of TECARTUS at a target dose of 1×10^6 CAR T cells/kg.

Data from the pivotal Phase 2 portion of the ZUMA-3 study are reported here. The modified intention-to-treat (mITT) analysis set included 55 patients who received treatment with TECARTUS. Median follow-up was 16.4 months.

MRD Assessment

MRD negativity was defined as MRD $<10^{-4}$ as assessed by a validated flow cytometry method performed by a central laboratory. Subjects were considered MRD negative overall if they achieved an MRD negative response at any postinfusion visit (ie, Day 28, Week 8, or Month 3).

Results

The secondary efficacy endpoint of MRD negativity rate was met, as 42 (76%) of all treated patients were MRD negative ($p<0.0001$). In responding patients (CR or CRi), 38 (97%) of 39 achieved MRD negativity (one patient did not have evaluable samples for MRD assessment). A positive association was also seen between CAR T-cell expansion and MRD negativity.

In ZUMA-3, initial patient enrollment began in March 2016. The MRD assay used in ZUMA-3 was not analytically validated in accordance with the US FDA guidance subsequently issued in 2020. Therefore, MRD outcomes were not included within the approved US label for 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

Approved for Use on 11 Jul 2024

MRD Outcomes Following TECARTUS Treatment

Findings from the ZUMA-3 Pivotal (Phase 2) Study (NCT02614066)

Study Overview[1,2]

The single-arm, open-label, multicenter pivotal Phase 1/2 ZUMA-3 study evaluated the safety and efficacy of TECARTUS in adult patients with relapsed or refractory B-precursor ALL. Data from the pivotal Phase 2 portion are reported here from 55 patients who received TECARTUS in the mITT analysis set. Median follow-up was 16.4 months.

The primary endpoint was the rate of complete remission (CR) or complete remission with incomplete hematological recovery (CRi) by central assessment; patients who achieved CR or CRi were considered responders. Centralized MRD negativity rate, as assessed by a validated flow cytometry method, was among the secondary endpoints. MRD negativity was defined as MRD $<10^{-4}$ (ie, sensitivity of 0.01%).

MRD Assessment[1,2,3]

Bone marrow was evaluated for disease assessment. MRD negativity was defined as MRD $<10^{-4}$ as assessed by a validated flow cytometry method performed by a central laboratory. Subjects were considered MRD-negative overall if they achieved an MRD-negative response at any postinfusion visit (ie, Day 28, Week 8, or Month 3). MRD-negative remission rates were estimated for all dosed patients, patients with a CR, patients with a CRi, and for patients with either a CR or CRi combined.

Detection of MRD in ZUMA-3 was performed in a CAP/CLIA certified central laboratory using a validated test method based on the Children's Oncology Group B-ALL MRD multiparametric flow cytometry assay.

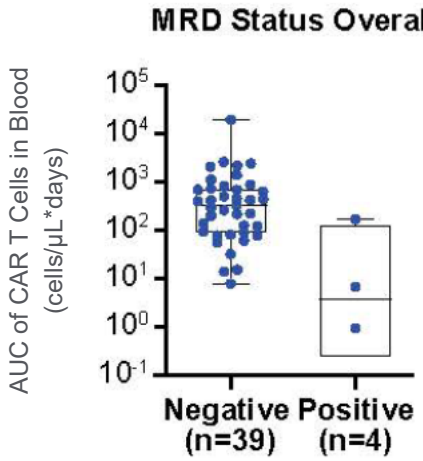
Results[1,2]

The secondary efficacy endpoint of MRD negativity rate was met with 42 (76%) of all treated patients achieving MRD negativity ($p<0.0001$). In patients who were responders (CR or CRi), 38 (97%) of 39 reached MRD negativity (evaluable samples [for MRD assessment] were not available for one patient).

A positive association was also seen between CAR T-cell expansion and MRD negativity (Figure 1); median CAR T-cell levels were more than 60 times higher in patients with MRD-negative versus MRD-positive status after infusion (Table 1).

All MRD-positive patients had morphological disease.

Figure 1. AUC of CAR T-Cell Levels and Associations with Overall MRD Status[2]



Abbreviations: AUC, area under the curve; CAR, chimeric antigen receptor; MRD, minimal residual disease.

Table 1. CAR T-Cell Levels in Blood by Overall MRD Status (mITT Analysis Set).[2]

	MRD Status Overall in Bone Marrow Sample	
	Positive (n=4)	Negative (n=42)
Peak (cells/µL)	n=4	n=39
Median	0.49	31.00
IQR	0.05–11.65	6.04–65.85
AUC_{0-28} (cells/µL•days)	n=4	n=39
Median	3.87	329.81
IQR	0.48–90.05	90.53–731.14

Abbreviations: AUC_{0-28}=area under the curve from Day 0 to Day 28; CAR=chimeric antigen receptor; IQR=interquartile range; MRD=minimal residual disease.

Omission of MRD Data from the FDA-Approved Product Labeling[3,4,5]

In ZUMA-3, initial patient enrollment began in March 2016. The MRD assay used in ZUMA-3 was not analytically validated in accordance with the FDA guidance subsequently issued in 2020. Therefore, MRD outcomes were not included within the approved label for TECARTUS.

References

1. 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/
2. 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.
3. Data on File, Kite Pharma.
4. TECARTUS® (brexucabtagene autoleucel) [US Prescribing Information]. Santa Monica, CA: Kite Pharma, Inc.; 2021.
5. FDA.gov. *Hematologic Malignancies: Regulatory Considerations for use of Minimal Residual Disease in Development of Drug and Biological Products for Treatment*. Updated January 2020. Accessed February 16, 2022.

Abbreviations

AUC_{0-28}=area under the curve from day 0 to day 28
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
IQR=interquartile range
IV=intravenous
mITT=modified intention-to-treat
MRD=minimal residual disease
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

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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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