TECARTUS®(brexucabtagene autoleucel): Retreatment in the ZUMA-2 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-2 Clinical Study (NCT02601313)

Study Design

ZUMA-2 was a multicenter, single arm, phase 2 study to evaluate the efficacy and safety of TECARTUS (brexucabtagene autoleucel/KTE-X19) in adult patients with relapsed/refractory mantle cell lymphoma (MCL).[2] Eligible adults (≥18 years of age) had histologically confirmed mantle-cell lymphoma with either cyclin D1 overexpression or presence of the translocation t(11;14) and had disease that was either relapsed or refractory to up to five previous regimens for mantle-cell lymphoma. Previous therapy must have included anthracycline- or bendamustine-containing chemotherapy, an anti-CD20 monoclonal antibody, and BTK inhibitor therapy with ibrutinib or acalabrutinib. In the study, patients must have had an Eastern Cooperative Oncology Group (ECOG) performance status of 0-1 and adequate hematologic (absolute lymphocyte count [ALC] ≥100/µL, absolute neutrophil count [ANC] ≥1000/µL, and a platelet count ≥75,000/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 a partial response (PR) or a complete response (CR) and then had disease progression at least 3 months after the first dose of TECARTUS could be retreated if they met certain criteria outlined in the protocol.[3]

Treatment Process

Patients underwent leukapheresis to obtain cells for TECARTUS manufacturing.[2] Conditioning chemotherapy (fludarabine 30 mg/m^2 and cyclophosphamide 500mg/m^2) was administered on days −5, −4, and −3 before a single intravenous infusion of TECARTUS was administered at a dose of 2×10^6 CAR T cells/kg on day 0.

Retreatment Eligibility in the ZUMA-2 Study

In the pivotal ZUMA-2 study, patients who achieved a PR or CR had an option to receive a second course of conditioning chemotherapy and TECARTUS under the following conditions[3]:

- Patient had a PR or CR at the Month 3 disease assessment.
- Patient's disease subsequently progressed greater than 3 months after TECARTUS infusion.
- CD19 tumor expression confirmed locally by biopsy after disease progression and prior to retreatment. A portion of the biopsy should be sent to the central laboratory.
- Patient met the original study eligibility criteria with exception of prior TECARTUS use in this study. Screening assessments were to be repeated if clinically indicated, as determined by the investigator, to confirm eligibility.
- Patient had not received subsequent therapy for the treatment of lymphoma.
- Patient did not experience a Grade 4 CRS event per Lee 2014 (except for Grade 4 hematology laboratory events, including pancytopenia, anemia, neutropenia, neutropenic fever, leukopenia, and thrombocytopenia) or Grade 4 neurologic toxicity.
- Toxicities related to conditioning chemotherapy (fludarabine and cyclophosphamide), with the exception of alopecia, had resolved to ≤ Grade 1 or returned to baseline prior to re-treatment.
- Patient did not have known neutralizing antibodies (exception: if a non-neutralizing antibody develops, subjects might be retreated if they met the original study eligibility criteria).
- The decision to administer retreatment was made in consultation with the Kite medical monitor.

Retreatment Results

Five patients out of the 68 patients in the ZUMA-2 study were retreated with a second bag of TECARTUS, and a limited number of responses were seen (1 CR and 1 PR as per central review).[4] Due to the limited data and small sample size, no final statement can be made in regard to the efficacy and safety of re-administration of TECARTUS.

It is at the discretion of the treating physician to retreat adult patients with relapsed or refractory MCL 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. Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. *N Engl J Med*. 2020;382:1331-42. DOI:10.1056/NEJMoa1914347
3. Protocol for: Wang M, Munoz J, Goy A, et al. KTE-X19 CAR T-cell therapy in relapsed or refractory mantle-cell lymphoma. *N Engl J Med*. 2020;382:1331-42. DOI:10.1056/NEJMoa1914347
4. Supplement for: Petersohn S, Salles G, Wang M, et al. Cost-effectiveness analysis of KTE-X19 CAR T therapy versus real-world standard of care in patients with relapsed/refractory mantle cell lymphoma post BTKi in England. *J Med Econ*. 2022; 25:1: 730-740. DOI: 10.1080/13696998.2022.2079317

Abbreviations

ALC=absolute lymphocyte count
ALL=acute lymphoblastic leukemia
ANC=absolute neutrophil count
BTK=Bruton's Tyrosine Kinase
CAR=chimeric antigen receptor
CR=complete remission
CRS=cytokine release syndrome
ECOG= Eastern Cooperative Oncology Group
MCL=mantle cell lymphoma
PR=partial response

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

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