Tecartus® (brexucabtagene autoleucel)
Primary Analysis of ZUMA-2 Cohort 3

Kite, a Gilead Company is providing this document to US Healthcare Professionals in response to your unsolicited request for medical information. Some of the information contained in this response may be outside of the US FDA-approved Prescribing Information. Kite does not intend to offer an opinion regarding the clinical relevance of these data nor the advisability of administering any drug in a manner inconsistent with its approved labeling. Please refer to the product labeling for complete product information.

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.

Summary

ZUMA-2 Cohort 3

- ZUMA-2 is a Phase 2, single-arm, open-label, registrational, multicenter, global study assessing the safety and efficacy of Tecartus, an anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, in patients with mantle cell lymphoma (MCL) who relapsed or were refractory to ≤5 prior therapies.[1]
- Prior therapy in Cohort 1 included Bruton's tyrosine kinase inhibitor (BTKi) therapy; patients in Cohort 3 were naïve to BTKi therapy.[2]
- The primary analysis of the ZUMA-2 Cohort 3 study was conducted after the patients had received treatment, achieved the first objective response, and been followed for 6 additional months.[2]

Patient Characteristics

- Tecartus was administered to 86 patients enrolled in Cohort 3, who had received a median of 1 prior line of therapy.[2]
- MCL had relapsed after the last MCL regimen in 86% of patients.
- High-risk disease features were common, with 73% having an intermediate or high simplified Mantle Cell Lymphoma International Prognostic Index (sMIPI).

Efficacy Results

- The objective response rate (ORR) as assessed by independent radiology review committee (IRRC) in all treated patients was 91%, with 73% achieving complete response (CR).[2]
- The 12-month duration of response (DOR) rate was 80% for all responders (n=78).
- The 12-month progression-free survival (PFS) rate was 75% for all patients (N=86).
- The 12-month overall survival (OS) rate was 90% for all patients (N=86), with 85% of patients (73/86) still alive at time of analysis.

Safety Results

- The most common Grade ≥3 treatment-emergent adverse events (TEAEs) were neutropenia (43%), decreased neutrophil count (42%), and decreased white blood cell count (WBC; [37%]).[2]
- Grade ≥3 neurologic events occurred in 27%, with 21% experiencing Grade ≥3 immune effector cell-associated neurotoxicity syndrome (ICANS).
- Grade ≥3 cytokine release syndrome (CRS) was reported in 6% of patients. Seven deaths (8%) were attributed to adverse events (AEs), including four related to either Tecartus and/or lymphodepleting treatment.

ZUMA-2 Cohort 3

Background

ZUMA-2 is a Phase 2, single-arm, open-label, registrational, multicenter, global study assessing the safety and efficacy of Tecartus, an anti-CD19 CAR T-cell therapy, in patients with MCL who relapsed or were refractory to ≤5 prior therapies, including BTKi therapy (ibrutinib or acalabrutinib).[1] Patients underwent leukapheresis and optional bridging therapy, followed by conditioning chemotherapy and a single infusion of Tecartus (2×10^6 CAR T-cells/kg).[1]

ZUMA-2 Cohort 3 evaluated the same dose of Tecartus in BTKi-naïve patients with MCL that had relapsed or were refractory to treatment with 1-5 prior therapies, including anthracycline, bendamustine, or high-dose cytarabine, and anti-CD20 monoclonal antibody therapy.[2] Of 95 patients enrolled in Cohort 3, Tecartus was administered to 86 (91%), and the median duration from leukapheresis to delivery of Tecartus to the trial site was 15 days (range, 14-21) in the US and 28 days (range, 20-43) in the EU. The primary endpoint was the ORR (CR+PR) as assessed by IRRC and per the Lugano classification. Secondary endpoints included DOR, best objective response (BOR), PFS, OS, and safety.

The results from the primary analysis of the ZUMA-2 Cohort 3 study, which was conducted after the patients had received treatment, achieved the first objective response, and been followed for 6 additional months, are described below.[2]

Patient Characteristics[2]

The primary analysis (November 26, 2023, data cutoff) reported results for 86 treated patients who had received a median of 1 prior regimen (range, 1-5) for MCL (Table 1). The sMIPI was intermediate or high in 73% of patients. Bridging therapy was administered to 31 (36%) of the 86 patients.

Table 1. Baseline Patient Characteristics in All Treated Patients from ZUMA-2 Cohort 3[2]

Characteristic[a]	Cohort 3 Patients (N=86)
Median age (range), years	64 (40–82)
Male, n (%)	67 (78)
ECOG PS of 1, n (%)	27 (31)
Median tumor burden (SPD)[b] (range), mm^2	1734 (204–31,212)
Median no. of prior regimens (range)	1 (1–5)

Characteristic[a]	Cohort 3 Patients (N=86)
Anti-CD20 mAb, n (%)	86 (100)
Platinum-based, n (%)	11 (13)
Anthracycline, n (%)	68 (79)
Bendamustine, n (%)	23 (27)
Lenalidomide, n (%)	2 (2)
Proteasome inhibitor, n (%)	6 (7)
Prior ASCT, n (%)	41 (48)
High-risk features, n (%)	
Intermediate or high sMIPI	63 (73)
Extranodal disease	45 (52)
Ki-67 ≥50%	18 (21)
TP53 mutation[c]	15 (17)
Relapsed or refractory to last MCL therapy, n (%)	
Refractory	12 (14)
Relapsed	74 (86)
Bridging therapy, n (%)	31 (36)
Systemic	24 (28)
Radiotherapy	4 (5)
Systemic + Radiotherapy	3 (3)

[a]All percentages are calculated out of N.
[b]As measured by the SPD of all target lesions at baseline, by central read. For patients who had bridging therapy, the measurement on or after bridging therapy end date is used as baseline.
[c]TP53 mutation testing was conducted per the discretion of the investigator and was not protocol defined.
ASCT=autologous stem cell transplant; ECOG PS=Eastern Cooperative Oncology Group performance status; mAb=monoclonal antibody; MCL=mantle cell lymphoma; no.=number; sMIPI=simplified Mantle Cell Lymphoma International Prognostic Index; SPD=sum of the products of diameters; *TP53*=tumor protein 53.

Efficacy

Response[2]

At a median follow-up of 15.5 months (range, 5–15), the ORR as assessed by IRRC was 91% (95% CI, 83-96), which represented 63 (73%) patients in CR and 15 (17%) patients in partial response (PR). The ORR ranged from 83% to 100% across subgroups of interest (Table 2). Progressive disease and stable disease were each observed in 3 patients (3%).

Table 2. ORR in Key Subgroups of Interest[2]

Subgroup	Responders (ORR) n (%)
TP53 mutation (n=15)	15 (100)
Baseline tumor burden ≥ median (n=39)	38 (97)
Ki-67 score ≥50% (n=18)	17 (94)
Intermediate or high-risk sMIPI scores (n=63)	56 (89)
Prior bendamustine treatment (n=23)	19 (83)

sMIPI=simplified Mantle Cell Lymphoma International Prognostic Index; ORR=overall response rate; *TP53*=tumor protein 53.

DOR, PFS, and OS[2]

The 12-month DOR rate was 80% for all responders (n=78) with 69% (54/78) of responders in ongoing response at time of analysis. The 12-month DOR rates for patients in CR or PR were 84% and 63%, respectively.

The 12-month PFS rates were 75% for all patients (N=86), 84% for those with CR (n=63), and 65% for those with PR (n=15).

The 12-month OS rate was 90%, with 85% (73/86) of patients still alive at time of analysis.

Kaplan-Meier estimates for DOR (Figure 1), PFS (Figure 2), and OS (Figure 3) are depicted below.

Figure 1. Duration of Response (DOR)[2]

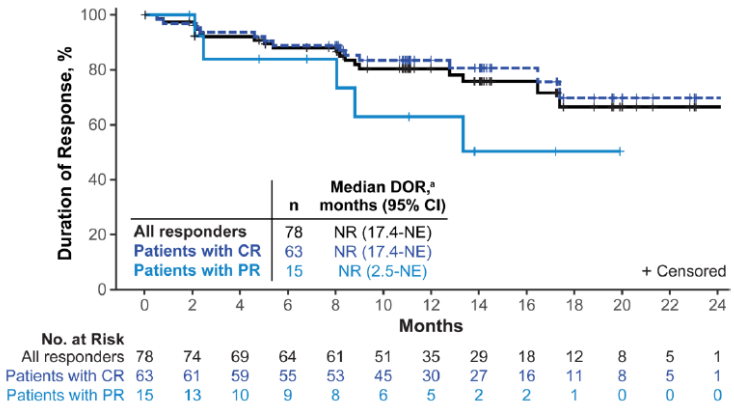


Figure 2. Progression-Free Survival (PFS)[2]

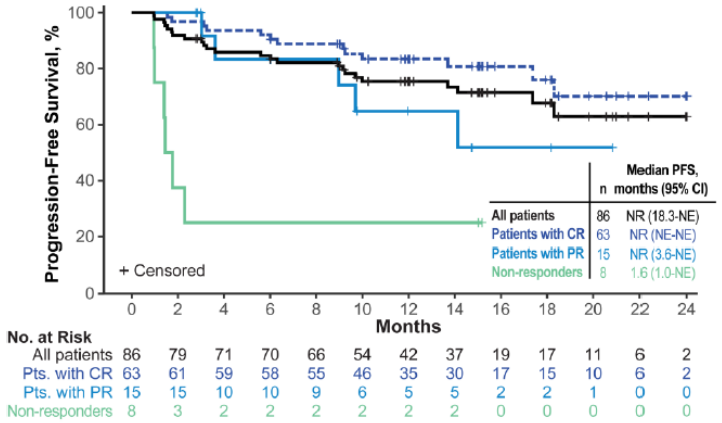
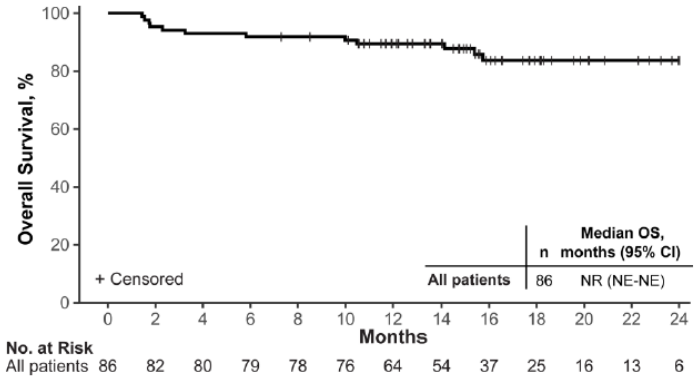


Figure 3. Overall Survival (OS)[2]



[a]Per IRRC assessment.
CR=complete response; DOR=duration of response; IRRC=independent radiology review committee; NE=not estimable; no.=number; NR=not reached; OS=overall survival; PFS=progression-free survival; PR=partial response; pts=patients.
Taken from van Meerten, et al. ASH 2024.

Safety[2]

The most common treatment-emergent adverse events (TEAEs) of any grade were pyrexia (94%), anemia (57%), and hypotension (51%). The most common Grade ≥3 TEAEs were neutropenia (43%), decreased neutrophil count (42%) and decreased WBC (37%). Grade ≥3 neurologic events were reported in 27%, with Grade ≥3 ICANS in 21%; Grade ≥3 CRS was reported in 6%. Rates of serious AEs, most common TEAEs (≥10%), and AEs of special interest are presented in Tables 3 and 4.

Table 3. AEs Among All Treated Patients in ZUMA-2 Cohort 3[2]

AEs[a], n (%)	Cohort 3 Patients (N=86)	
	Any Grade	Grade ≥3
TEAEs	86 (100)	85 (99)
Serious TEAEs	51 (59)	40 (47)
Most Common TEAEs (occurring in ≥25% patients)[b]		
Pyrexia	81 (94)	15 (17)
Anemia	49 (57)	22 (26)
Hypotension	44 (51)	7 (8)
Neutropenia	39 (45)	37 (43)
Neutrophil count decreased	36 (42)	36 (42)
White blood cell count decreased	34 (40)	32 (37)
Nausea	28 (33)	1 (1)
Confusional state	25 (29)	7 (8)
Headache	25 (29)	0
Platelet count decreased	25 (29)	15 (17)
Tremor	25 (29)	2 (2)
Constipation	24 (28)	0
Lymphocyte count decreased	23 (27)	23 (27)

[a]AEs are defined as any AE with onset on or after initiation of Tecartus infusion. AEs that occurred on/after retreatment are not included.
[b]AEs are coded using MedDRA version 27.0 and graded per CTCAE version 4.03. Some preferred terms had similar or overlapping definitions but were coded differently in the reporting system. Multiple incidences of the same AE in 1 patient are counted once at the highest grade for that patient.
AE=adverse event; CTCAE=Common Terminology Criteria for Adverse Events; MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment-emergent adverse event.

Table 4. AEs of Special Interest[2]

AEs, n (%)	Cohort 3 Patients (N=86)	
	Any Grade	Grade ≥3
CRS[a]	82 (95)	5 (6)
Neurological Events[b]	67 (78)	23 (27)
ICANS[c]	57 (66)	18 (21)
Thrombocytopenia[d]	45 (52)	29 (34)
Neutropenia[d,e]	74 (86)	73 (85)
Anemia[d]	49 (57)	22 (26)
Serious Infection[d]	21 (24)	20 (23)
Hypogammaglobulinemia[d]	7 (8)	0

[a]CRS events are graded per the revised grading system proposed by Lee et al, *Blood*, 2014;124(2):188-195.
[b]Neurologic events are identified based on Topp, et al. 2015.
[c]ICANS events are graded per the ASTCT ICANS grading *in* Lee DW, et al. *Biol Blood Marrow Transplant*. 2019(4):625-638.
[d]All other events are graded per CTCAE version 4.03.
[e]Includes neutropenia, neutrophil count decreased and febrile neutropenia.
AE=adverse event; ASTCT=American Society for Transplantation and Cellular Therapy; CRS=cytokine release syndrome; CTCAE=Common Terminology Criteria for Adverse Events; ICANS=immune effector cell-associated neurotoxicity syndrome.

The median time to onset and duration of CRS events was 4 days (range, 1-12) and 6 days (1-36), respectively, and the median time to onset and duration of ICANS was 7 days (1-31) and 7 days (1-122), respectively.

Grade ≥3 ICANS events were significantly associated with CAR T-cell expansion (*P*=0.013), but Grade ≥3 CRS events were not (*P*=0.8649). At data cutoff, 13 (15%) patients had died of which 7 (8%) were due to AEs, including 4 that were considered related to Tecartus and/or lymphodepleting treatment (1 event each of progressive multifocal leukoencephalopathy, septic shock, polymicrobial infection, and human herpesvirus 6 encephalitis). No deaths occurred ≤30 days after Tecartus infusion.

References

1. 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(14): 1331-1342. DOI: 10.1056/nejmoa1914347
2. van Meerten T, Kersten MJ, Iacoboni G, et al. Primary analysis of ZUMA-2 Cohort 3: brexucabtagene autoleucel in patients with relapsed/refractory mantle cell lymphoma who are naive to bruton tyrosine kinase inhibitors. Presented at the 66th American Society of Hematology (ASH) Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA.

Abbreviations

AE=adverse event
ASCT=autologous stem cell transplant
ASTCT=American Society for Transplantation and Cellular Therapy
BTKi=Bruton's tyrosine kinase inhibitor
CAR=chimeric antigen receptor
CI=confidence interval
CR=complete response
CRS=cytokine release syndrome
CTCAE=Common Terminology Criteria for Adverse Events
DOR=duration of response

ECOG PS=Eastern Cooperative Oncology Group performance status
ICANS= immune effector cell-associated neurotoxicity syndrome
IRRC=independent radiology review committee
mAb=monoclonal antibody
MCL=mantle cell lymphoma
MedDRA=Medical Dictionary for Regulatory Activities
NE=not estimable
NR=not reached
ORR=overall response rate
OS=overall survival
PFS=progression free survival
PR=partial response
sMIPI=simplified Mantle Cell Lymphoma International Prognostic Index
TEAE=treatment-emergent adverse event

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 Medical Information 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

Data Privacy

The Medical Information service at Kite, a Gilead Company, may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Kite or Gilead colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Kite or Gilead product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Kite's affiliates, business partners, service providers and regulatory authorities located in countries besides your own. Kite has implemented measures to protect the personal information you provide. Please see the Kite Privacy Statement (https://www.kitepharma.com/privacy-policy/) for more information about how Kite handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact privacy@kitepharma.com.

TECARTUS, KITE and the KITE logo are trademarks of Kite Pharma, Inc. GILEAD and the GILEAD logo are trademarks of Gilead Sciences, Inc.
© Kite Pharma, Inc. All rights reserved.