Poster
7547

Outcomes With KTE-X19 in Patients With Relapsed/Refractory Mantle Cell Lymphoma in ZUMA-2 Who Had Progression of Disease Within 24 Months of Diagnosis (POD24)

Michael L. Wang, MD[1]; Javier Munoz, MD, MS, FACP[2]; Andre Goy, MD[3]; Frederick L. Locke, MD[4]; Caron A. Jacobson, MD, MMSc[5]; Brian T. Hill, MD, PhD[6]; John M. Timmerman, MD[7]; Houston Holmes, MD, MBA, FACP[8]; Samantha Jaglowski, MD[9]; Ian W. Flinn, MD, PhD[10]; Peter A. McSweeney, MB, ChB[11]; David B. Miklos, MD, PhD[12]; Marie José Kersten, MD, PhD[13]; Krimo Bouabdallah, MD[14]; Max S. Topp, MD[15]; Rhine Shen, PhD[16]; Ioana Kloos, MD[16]; Weimin Peng, PhD[16]; Xiang Fang, PhD[16]; Patrick M. Reagan, MD[17]

[1]The University of Texas MD Anderson Cancer Center, Houston, TX, USA; [2]Banner MD Anderson Cancer Center, Gilbert, AZ, USA; [3]John Theurer Cancer Center, Hackensack, NJ, USA; [4]Moffitt Cancer Center, Tampa, FL, USA; [5]Dana-Farber Cancer Institute, Boston, MA, USA; [6]Cleveland Clinic Foundation, Cleveland, OH, USA; [7]UCLA David Geffen School of Medicine, Los Angeles, CA, USA; [8]Texas Oncology, Dallas, TX, USA; [9]The Ohio State University Comprehensive Cancer Center, Columbus, OH, USA; [10]Sarah Cannon Research Institute and Tennessee Oncology, Nashville, TN, USA; [11]Colorado Blood Cancer Institute, Denver, CO, USA; [12]Stanford University School of Medicine, Stanford, CA, USA; [13]Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands, on behalf of HOVON/LLPC; [14]CHU Bordeaux, Service d'Hématologie et thérapie Cellulaire, Bordeaux, France; [15]Medizinische Klinik und Poliklinik II, Universitätsklinikum Würzburg, Würzburg, Germany; [16]Kite, a Gilead Company, Santa Monica, CA, USA; [17]University of Rochester Medical Center, Rochester, NY, USA

BACKGROUND

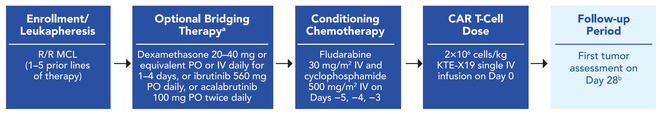
- Progression of disease within 24 months after initial diagnosis (POD24) is an indicator of poor outcomes for patients with mantle cell lymphoma (MCL)[1]
  - In a retrospective analysis of patients with MCL and a median follow-up of 30 months from time of progression, the median overall survival (OS) from time of progression was 12 months for those with POD24, compared with not reached for those without POD24
- KTE-X19, an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, is approved in the United States and European Union for the treatment of relapsed/refractory (R/R) MCL[2,3]
- The pivotal Phase 2 ZUMA-2 study evaluated KTE-X19 in patients with MCL who were R/R to 1–5 prior therapies, including a Bruton tyrosine kinase inhibitor[4]
  - After a median follow-up of 17.5 months in ZUMA-2 (N=60), the objective response rate (ORR) was 92%, with a complete response (CR) rate of 67%[5]

OBJECTIVE

- To report safety and efficacy outcomes and the pharmacokinetic profile among patients in ZUMA-2 with and without POD24

METHODS

Figure 1. ZUMA-2 Study Design



Of 60 efficacy-evaluable patients in ZUMA-2 with MCL treated with KTE-X19 with a median follow-up of 17.5 months[5]
- 92% ORR
- 67% CR rate
- 48% of all patients and 70% of patients in CR in ongoing response at data cutoff

CRS and neurologic events were mostly reversible (N=68 treated patients)[4,5]
- 15% Grade ≥3 CRS; 31% Grade ≥3 neurologic events
- 2 Grade 5 AEs (1 KTE-X19–related)
- No new safety signals observed with longer follow-up

[a]Administered after leukapheresis and completed ≥5 days before initiating conditioning chemotherapy; PET-CT was required postbridging. [b]Bone marrow biopsy was to be done at screening, and if positive, not done, or if indeterminate, a biopsy was needed to confirm CR.
AE, adverse event; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; IV, intravenous; MCL, mantle cell lymphoma; ORR, objective response rate; PO, oral; R/R, relapsed/refractory.

- Product attributes, CAR T-cell levels in blood, and cytokine levels in serum were analyzed using previously described methods[6]
- Safety outcomes, pharmacological profile, and product attributes are reported for all 68 patients treated with KTE-X19 (2×10^6 cells/kg)
- Efficacy outcomes are reported in the 60 treated patients with ≥1 year of follow-up (median 17.5 months)
  - Minimal residual disease (MRD) was assessed in patients with available samples at Week 4 with a sensitivity of 1 in 100,000 cells
- Data are presented with the data cutoff date of December 31, 2019

RESULTS

Table 1. Baseline Characteristics by POD24 Status

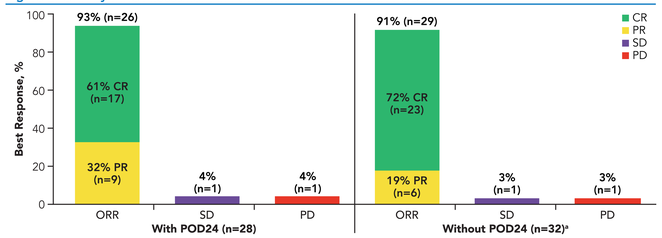
	With POD24 (n=33)	Without POD24 (n=35)
Median age (range), years	65 (38–75)	66 (50–79)
≥65 years, n (%)	18 (55)	21 (60)
Male, n (%)	29 (88)	28 (80)
MCL morphology, n (%)		
Classical	16 (48)	24 (69)
Pleomorphic	2 (6)	2 (6)
Blastoid	11 (33)	6 (17)
Intermediate-/high-risk MIPI, n (%)	14 (48)	22 (63)
Median tumor burden[a] (range), mm²	2255 (260–14,390)	1380 (293–16,878)
Extranodal disease, n (%)	17 (52)	21 (60)
LDH ≥1.5 × ULN, n (%)	8 (24)	3 (9)
Ki-67 proliferation index, n (%)	n=23	n=26
≥30%	19 (83)	21 (81)
≥50%	17 (74)	17 (65)
***TP53* mutated, n/n (%)**	3/20 (15)	3/16 (19)
Median no. prior therapies (range)	3 (2–5)	3 (1–5)
≥3 prior therapies, n (%)	29 (88)	26 (74)
Prior BTKi, n (%)	33 (100)	35 (100)
Ibrutinib	28 (85)	30 (86)
Acalabrutinib	7 (21)	9 (26)
Both	2 (6)	4 (11)
Prior anthracycline, n (%)	22 (67)	27 (77)
Prior cytarabine, n (%)	21 (64)	18 (51)
Prior bendamustine, n (%)	19 (58)	18 (51)
Prior auto-SCT, n (%)	12 (36)	17 (49)
Bone marrow involvement, n (%)	13 (39)	24 (69)

[a]As measured by the sum of product dimensions of all target lesions at baseline. For patients who had bridging therapy, the measurement after bridging therapy is used as baseline.
Auto-SCT, autologous stem cell transplant; BTKi, Bruton tyrosine kinase inhibitor; LDH, lactate dehydrogenase; MCL, mantle cell lymphoma; MIPI, Mantle Cell Lymphoma International Prognostic Index; with POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis; ULN, upper limit of normal.

- High-risk disease characteristics were common in patients with and without POD24 (**Table 1**)
  - Patients with POD24 had higher tumor burden and lactate dehydrogenase (LDH) levels, and more had blastoid type MCL, suggesting these patients may be less fit than those without POD24

RESULTS *(continued)*

Figure 2. ORR by IRRC Assessment in Patients With and Without POD24



Assessed by an IRRC according to the Lugano Classification.[7]
[a]One patient was not evaluable.
CR, complete response; IRRC, Independent Radiology Review Committee; ORR, objective response rate; PD, progressive disease; with POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis; PR, partial response; SD, stable disease.

- The ORR was similar among patients with and without POD24, with a slightly higher CR rate in patients without POD24 (**Figure 2**)
- Similar rates of MRD-negativity were also observed among patients with (82%; n=9/11) and without (79%; n=15/19) POD24

Figure 3. Duration of Response, Progression-Free Survival, and Overall Survival by POD24 Status

*Of responding patients.
NE, not estimable; NR, not reached; with POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis.

- Median progression-free survival (PFS) was 11.3 months (95% CI, 6.0–not estimable [NE]) in patients with POD24 and was 29.3 months (95% CI, 14.5–NE) in patients without POD24 (**Figure 3**)
- Medians for duration of response (DOR) and OS were not reached in either group (**Figure 3**)
- Among all enrolled patients (N=74), median OS was not reached in patients with and without POD24; estimated 12-month OS rates were 72% and 81%, respectively

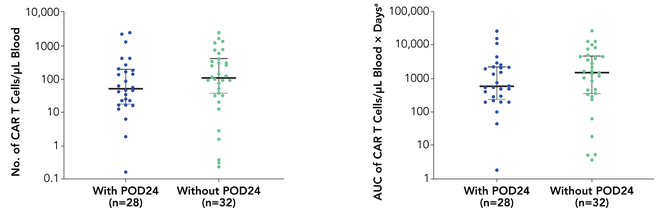
Table 2. Summary of Adverse Events in Patients With and Without POD24

AE[a]	With POD24 (n=33)	Without POD24 (n=35)
Any AE, n (%)	33 (100)	35 (100)
Any Grade ≥3	32 (97)	35 (100)
Grade ≥3 neutropenia	30 (91)	28 (80)
Grade ≥3 thrombocytopenia	20 (61)	16 (46)
Grade ≥3 anemia	18 (55)	18 (51)
Grade ≥3 infection	8 (24)	15 (43)
CRS, n (%)	31 (94)	31 (89)
Grade ≥3	3 (9)	7 (20)
Median time to onset, days	3	2
Median duration, days	8	12
Any neurologic event, n (%)	23 (70)	20 (57)
Grade ≥3	9 (27)	12 (34)
Median time to onset, days	7	7
Median duration, days	10	15

[a]CRS was graded per Lee, et al. 2014.[8] Symptoms of CRS and all other AEs were graded per National Cancer Institute's Common Terminology Criteria for Adverse Events version 4.03.
AE, adverse event; CRS, cytokine release syndrome; with POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis.

- Incidences of Grade ≥3 adverse events were generally similar in patients with and without POD24 (**Table 2**)
  - Incidence of thrombocytopenia and neutropenia appeared higher in patients with POD24 than those without POD24
  - Incidences of infection appeared lower among patients with POD24 than those without POD24
- There were no cases of Grade 5 cytokine release syndrome, KTE-X19–related secondary malignancies, or replication-competent retrovirus in either group

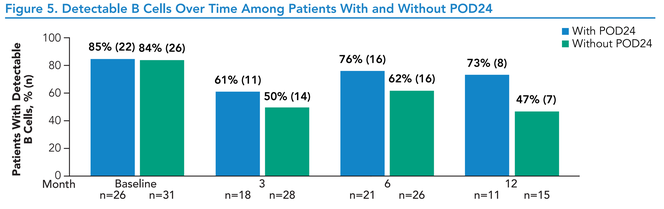
Figure 4. CAR T-Cell Expansion Appeared Lower in Patients With POD24



CAR T-cell levels peaked within 14 days postreatment.
*CAR T-cell levels assessed for Days 0 to 28.
AUC, area under the curve; CAR, chimeric antigen receptor; with POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis.

- In patients with POD24, median peak CAR T-cell levels and median area under the curve (AUC) were 53.4 cells/µL (range, 0.2–2566.0) and 583.4 cells/µL × days (range, 1.8–27,743.6; **Figure 4**)
  - Patients without POD24 had median peak CAR T-cell levels and median AUC of 112.4 cells/µL (range, 0.2–2589.0) and 1588.3 cells/µL × days (range, 3.8–27,238.7)

Figure 5. Detectable B Cells Over Time Among Patients With and Without POD24



With POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis.

- Among efficacy-evaluable patients with available data, B cells were detectable by 12 months in 8/11 (73%) patients with POD24 and 7/15 patients (47%) without POD24 (**Figure 5**)

Table 3. KTE-X19 Product Characteristics by POD24 Status

Median characteristic (range)	With POD24 (n=33)	Without POD24 (n=35)
Transduction rate, %	59.0 (34.0–82.4)	57.2 (32.0–77.1)
CD4/CD8 ratio	0.7 (0.04–3.7)	0.7 (0.3–2.7)
CCR7+CD45RA+ T cells, %	26.4 (0.3–80.7)	20.3 (3.2–78.1)
CCR7+ T cells, %	41.3 (2.6–88.5)	37.1 (16.0–88.8)
CCR7− effector + effector memory T cells, %	58.9 (11.4–97.4)	62.9 (11.1–84.1)
(CCR7+ T cells)/(CCR7− effector + effector memory T cells) ratio	0.7 (0.03–7.8)	0.6 (0.2–8.0)
IFN-γ by coculture, pg/mL	6291.0 (492.0–1.8×10⁴)	7120.0 (424.0–2.0×10⁴)

IFN, interferon; with POD24, progression of disease <24 months after initial diagnosis; without POD24, progression of disease ≥24 months after initial diagnosis.

- KTE-X19 product characteristics were similar among patients with and without POD24 (**Table 3**)

CONCLUSIONS

- After a median of 17.5 months of follow-up, KTE-X19 provided a high CR rate in patients with and without POD24, with median DOR and OS not reached in either group
  - Median PFS appeared to be shorter among patients with POD24, compared with those without POD24
- At baseline, patients with POD24 were more likely to have high-risk disease characteristics (high tumor burden, high LDH levels, and blastoid MCL) than those without POD24
- Safety profiles and product characteristics of patients with and without POD24 were generally similar
- Patients with POD24 appeared to have lower CAR T-cell expansion than those without POD24
- Earlier intervention with CD19-directed CAR T-cell therapy may benefit patients with MCL with known high-risk factors[1]

REFERENCES

1. Visco C, et al. *Br J Haematol.* 2019;185:940-944.
2. TECARTUS® (brexucabtagene autoleucel) Prescribing information. Kite Pharma, Inc; 2021.
3. TECARTUS® (autologous anti-CD19-transduced CD3+ cells) Summary of product characteristics. Kite Pharma EU B.V.; 2021.
4. Wang M, et al. *N Engl J Med.* 2020;382:1331-1342.
5. Wang M, et al. *Blood.* 2020; 136(Suppl 1):20-22.
6. Locke FL, et al. *Mol Ther.* 2017;25:285-295.
7. Cheson BD, et al. *J Clin Oncol.* 2014;32:3059-3068.
8. Lee DW, et al. *Blood.* 2014;124:188-195.

ACKNOWLEDGMENTS

- The patients, families, friends, and caregivers
- The study investigators, coordinators, and health care staff at each study site
- The authors would like to thank Rubina Siddiqi, PhD, of Kite, a Gilead Company, for her expertise and strategic contributions
- Medical writing support was provided by Danielle Luebke, PhD, of Nexus Global Group Science, funded by Kite, a Gilead Company
- This study was funded by Kite, a Gilead Company

DISCLOSURES

MLW: honoraria from Janssen, OMI, DAVA Oncology, and PeerView Institute for Medical Education; consultancy or advisory role for Kite, a Gilead Company, Celgene, Juno, Janssen, Pharmacyclics, AstraZeneca, MORE Health, Pulse Biosciences, InnoCare, Loxo Oncology, CStone, and VelosBio; research funding from Kite, a Gilead Company, Janssen, AstraZeneca, Acerta, Juno, BeiGene, Celgene, Biolinvent, Oncternal, Loxo Oncology, VelosBio, Molecular Templates, InnoCare, and Lilly; and travel support from Kite, a Gilead Company, Janssen, AstraZeneca, DAVA Oncology, OMI, and Pharmacyclics. **JM:** honoraria from Kyowa Kirin and Seattle Genetics; consultancy or advisory role for Pharmacyclics, Bayer, Kite, a Gilead Company, Pfizer, Janssen, Juno/Celgene, Bristol Myers Squibb, Kyowa Kirin, Alexion, Fosun Kite, Innovent, Seattle Genetics, and BeiGene; speakers' bureau participation for Kite, a Gilead Company, Kyowa Kirin, Bayer, Pharmacyclics/Janssen, Seattle Genetics, Acrotech/Aurobindo, BeiGene, Verastem, AstraZeneca, Juno/Celgene/Bristol Myers Squibb, Genentech/Roche, and AbbVie; research funding from Bayer, Kite, a Gilead Company, Celgene, Merck, Portola Pharmaceuticals, Incyte, Genentech, Pharmacyclics, Seattle Genetics, Janssen, and Millennium. **AG:** employment with Regional Cancer Care Associates/OMI; leadership role at COTA (Cancer Outcome Tracking Analysis) and Genomic Testing Cooperative; stock or other ownership in COTA and Genomic Testing Cooperative; honoraria from Celgene, Elsevier PracticeUpdate: Oncology, Kite, a Gilead Company, AstraZeneca, Xcenda, OncLive Peer Exchange, Janssen, Novartis, MorphoSys, Incyte, and Pharmacyclics; consultancy or advisory role for Physcians' Education Resource, Celgene, Elsevier PracticeUpdate: Oncology, Janssen, Kite, a Gilead Company, Medscape, Michael J. Hennessy Associates, Inc., Novartis, and Pharmacyclics; research funding from Acerta, AstraZeneca, Celgene, Genentech, Hoffmann-La Roche, Infinity Pharmaceuticals, Janssen, Karyopharm, and Pharmacyclics; and other relationships with MorphoSys, Incyte Steering Committee, and AstraZeneca MCL Steering Committee. **FLLc** consultancy or advisory role for Kite, a Gilead Company, Novartis, Amgen, Celgene/Bristol Myers Squibb, GammaDelta Therapeutics, Iovance, Bluebird Bio, Wugen Inc., Calibr, Cellular Biomedicine Group Inc., and Allogen; and research support from Kite, a Gilead Company. **CAJ:** honoraria from Kite, a Gilead Company, Bristol Myers Squibb, Celgene, Novartis, Humanigen, Precision BioSciences, Bluebird Bio, Nkarta, Lonza, and AbbVie; consultancy or advisory role for Kite, a Gilead Company, Celgene, Novartis, Bristol Myers Squibb, Precision BioSciences, Nkarta, Lonza, Pfizer, Humanigen, AbbVie, and Bluebird Bio; speakers' bureau participation for Axis and Clinical Care Options; research funding from Kite, a Gilead Company, and Pfizer; and travel support from Kite, a Gilead Company, Celgene, Novartis, Bristol Myers Squibb, Precision Biosciences, Lonza, Pfizer, and Humanigen. **BTH:** honoraria from Kite, a Gilead Company; consulting or advisory role with Kite, a Gilead Company; research funding from Kite, a Gilead Company; travel, accommodations, expenses from Kite, a Gilead Company. **JMT:** stock or other ownership in Genmab, Corvus, Marker Therapeutics, and Bluebird Bio; consulting or advisory role with Kite, a Gilead Company, Celgene, Immune Design, and Celldex Therapeutics; research funding from Bristol Myers Squibb, Kite, a Gilead Company, Spectrum Pharmaceuticals, and Merck; travel, accommodations, expenses from Bristol Myers Squibb, and Kite, a Gilead Company. **HH:** consultancy or advisory role for Kite, a Gilead Company, Bayer, Rigel, Johnson & Johnson, and Bristol Myers Squibb; speakers' bureau participation for Kite, a Gilead Company, Seattle Genetics, and Rigel; research funding from Kite, a Gilead Company, Unum, Bristol Myers Squibb, Novartis, Roche, ADC Therapeutics, and Seattle Genetics; patents, royalties, or other intellectual property from a pending patent. **SJ:** consultancy or advisory role for Kite, a Gilead Company, Juno, Novartis, and CRISPR; research funding from Kite, a Gilead Company, and Novartis. **IWF:** employment with Sarah Cannon Research Institute; stock or other ownership in Johnson & Johnson; consultancy or advisory role for AbbVie, AstraZeneca, BeiGene, Gilead, Great Point Partners, Iksuda Therapeutics, Janssen, Juno, Kite, a Gilead Company, MorphoSys, Nurix Therapeutics, Pharmacyclics, Roche, Seattle Genetics, Takeda, Unum Therapeutics (Cogent Biosciences), Verastem, and Yingli Pharmaceuticals; and research funding from AbbVie, Acerta, Agios, AvroBio, AstraZeneca, BeiGene, Calithera Biosciences, Celgene, Constellation Pharmaceuticals, Curis, F. Hoffmann-La Roche, Forma, Forty Seven, Genentech, Gilead, IGM, Incyte, Infinity Pharmaceuticals, Janssen, Juno, Karyopharm, Kite, a Gilead Company, Loxo Oncology, Merck, MorphoSys, Novartis, Pfizer, Pharmacyclics, Portola Pharmaceuticals, Rhizen Pharmaceuticals, Roche, Seattle Genetics, Takeda, Teva, TG Therapeutics, Trillium Therapeutics, Triphase Research & Development Corp., Unum Therapeutics (Cogent Biosciences), and Verastem. **PAM:** employment with Colorado Blood Cancer Institute Medical Group; consulting or advisory role with Kite, a Gilead Company; speakers' bureau with Kite, a Gilead Company; research funding from Kite, a Gilead Company. **DBM:** consultancy or advisory role for Kite, a Gilead Company, Novartis, Juno/Celgene/Bristol Myers Squibb, Adaptive Biotechnologies, Pharmacyclics, Janssen, Allogene, Precision BioSciences, Adicet Bio, Takeda, and Miltenyi; research funding from Kite, a Gilead Company, Novartis, Juno/Celgene/Bristol Myers Squibb, Adaptive Biotechnologies, Pharmacyclics, Allogene, Precision BioSciences, and Adicet; and patents, royalties, or other intellectual property from Pharmacyclics. **MJK:** honoraria from Kite, a Gilead Company, Novartis, and Miltenyi; consultancy or advisory role for Kite, a Gilead Company, Novartis, and Miltenyi; research funding from Roche, Takeda, and Celgene; travel support from Kite, a Gilead Company, Novartis, and Miltenyi. **KB:** honoraria from Kite, a Gilead Company, Takeda, Roche, and Celgene; consultancy or advisory role for Kite, a Gilead Company, Takeda, Roche, and Sandoz; and travel support from Roche. **MST:** consultancy or advisory role for Amgen, Kite, a Gilead Company, Celgene, Roche, and Regeneron; and research funding from Amgen, Kite, a Gilead Company, Roche, MacroGenics, and Regeneron. **XF, IK**, and **RS:** employment with Kite, a Gilead Company; stock or other ownership in Gilead Sciences. **WP:** consultancy or advisory role for Kite, a Gilead Company, and Curis; and research funding from Seattle Genetics and Genentech.