Outcomes of Patients with Relapsed/Refractory Mantle Cell Lymphoma Treated with Brexucabtagene Autoleucel in ZUMA-2 and ZUMA-18, an Expanded Access Study

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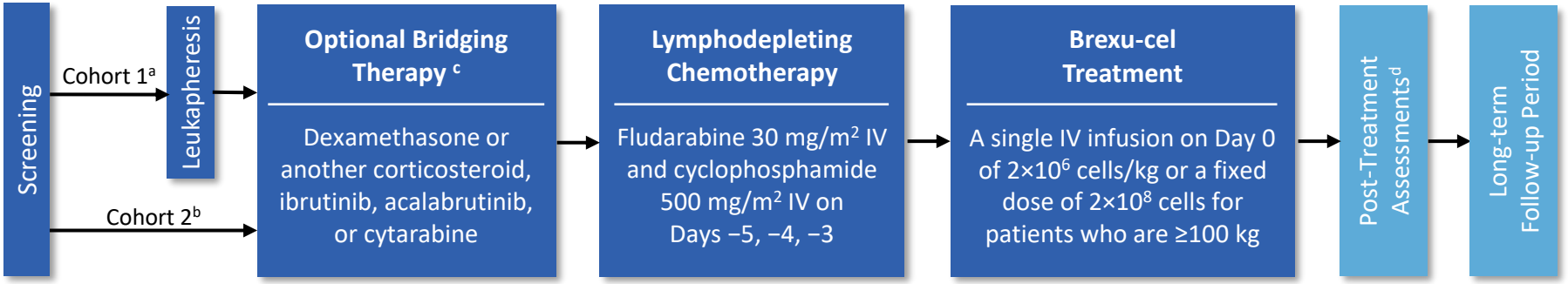
Background

- Brexu-cel is an autologous anti-CD19 CAR T-cell therapy approved in adults with R/R MCL in the US and the EU (following ≥2 prior therapies including a BTKi in EU) based on ZUMA-2 results[1,2]
- After 3 years in ZUMA-2, brexu-cel demonstrated an ORR of 91%, a CR rate of 68%, and a median DOR and OS of 28.2 and 46.6 months, respectively, in patients with R/R MCL (N=68)[3]
- ZUMA-18 is a multicenter, open-label, expanded access study of brexu-cel in the US for the treatment of patients with R/R MCL including BTKi-naive patients who received ≥ 1 prior therapy following ZUMA-2 enrollment completion and prior to FDA approval
- Here we report the primary analysis of ZUMA-18 and the 4-year follow-up of ZUMA-2

1. TECARTUS® (brexucabtagene autoleucel) Prescribing information. Kite Pharma, Inc; 2021. 2. TECARTUS® (brexucabtagene autoleucel) [summary of product characteristics]. Amsterdam, the Netherlands: Kite Pharma EU B.V.; 2023. 3. Wang M, et al. *J Clin Oncol*. 2023;41:555-567.
Brexu-cel, brexucabtagene autoleucel; BTKi, Bruton tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CR, complete response; DOR, duration of response; EU, European Union; ORR, objective response rate; OS, overall survival; R/R MCL, relapsed/refractory mantle cell lymphoma; US, United States.

ZUMA-18: A US Expanded Access Study

ZUMA-18 Study Enrollment: July 2019 to July 2020



Key ZUMA-18 Cohort 1 Eligibility Criteria

- Age ≥18 years with R/R MCL
- At least 1 prior regimen including anthracycline- or bendamustine-containing chemotherapy, or anti-CD20 monoclonal antibody, or BTKi therapy
- Prior alloSCT was allowed if performed ≥6 months prior to enrollment
- CNS involvement was not allowed

Study Objectives

- **Cohort 1**: To provide access to brexu-cel in the US for patients with R/R MCL until it was commercially available
- **Cohort 2**: To provide access to brexu-cel in the US for patients with R/R MCL whose manufactured product did not meet commercial release specifications for cell viability

Key Study Endpoints

- Safety, investigator-assessed ORR (CR + PR), and OS

[a] Enrollment occurred with the commencement of leukapheresis. [b] Enrollment occurred when the informed consent was signed, and eligibility criteria were met. [c] At the discretion of the investigator and after discussion with the Kite medical monitor bridging therapy was allowed if completed within ≥5 days before initiating lymphodepleting chemotherapy. Cytarabine as bridging therapy was not allowed in ZUMA-2 but was allowed in ZUMA-18. [d] Post-treatment assessments occurred at Week 2, Week 4, and Month 3 following brexu-cel infusion. [e] Patients who had alloSCT were eligible if donor lymphocyte infusion was administered ≥6 months prior to enrollment, they had no GVHD therapies within 4 weeks of enrollment, and no evidence of Grade 2-4 acute GVHD by Glucksberg criteria or severity B to D by International Bone Marrow Transplant Registry index within 4 weeks of enrollment.
alloSCT, allogeneic stem cell transplantation; brexu-cel, brexucabtagene autoleucel; BTKi, Bruton tyrosine kinase inhibitor; CAR, chimeric antigen receptor; CNS, central nervous system; CR, complete response; GVHD, graft-versus-host disease; IV, intravenous; ORR, objective response rate; OS, overall survival; PR, partial response; R/R MCL, relapsed/refractory mantle cell lymphoma.

ZUMA-18 Baseline Patient and Disease Characteristics

- From July 2019 to July 2020, 23 patients received brexu-cel (Cohort 1, n=21; Cohort 2, n=2)
- Data cutoff was February 3, 2023, with a **median follow-up of 33.5 months** (range, 24.5-35.3; N=23)
- Most common prior therapies were anti-CD20 (100%), BTKi (91%), alkylating agents (74%), anthracycline (61%), and bendamustine (57%)

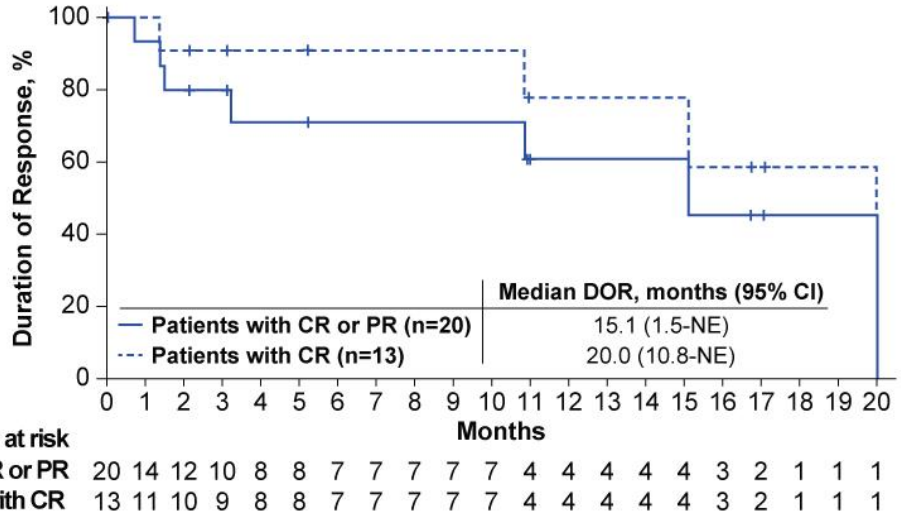
Baseline Characteristic	N=23
Median age (range), years	69.0 (43-79)
Intermediate or high risk Simplified MIPI, n (%)	13 (57)
Blastoid or pleomorphic morphologic characteristics of MCL, n (%)	6 (26)
Extranodal disease, n (%)	9 (39)
Elevated LDH levels (ULN to >1.5 ULN), n (%)	
ULN ≤ LDH <1.5 ULN	4 (17)
1.5 ULN ≥ LDH meant	2 (9)
Median tumor burden (SPD) by central read, mm^2 (range)	874.8 (6-9469)
Received bridging therapy, n (%)	5 (22)
ECOG PS of 1, n (%)	13 (57)
Median no. of prior therapies, n (range)	4 (1-10)
Prior BTKi therapy, n (%)	21 (91)
Ibrutinib	16 (70)
Acalabrutinib	8 (35)
Both	3 (13)
Relapsed or refractory disease, n (%)	
Relapse after autologous SCT	6 (26)
Refractory to last MCL therapy	1 (4)
Relapsed after last MCL	16 (70)

Brexu-cel, brexucabtagene autoleucel; BTKi, Bruton tyrosine kinase inhibitor; ECOG PS, Eastern Cooperative Oncology Group performance status; LDH, lactate dehydrogenase; MCL, mantle cell lymphoma; MIPI, Mantle Cell Lymphoma International Prognostic Index; SCT, stem cell transplant; SPD, sum of the products of diameters; ULN, upper limit of normal.

Best Overall Responses and Duration of Response in ZUMA-18

Best Overall Response	ZUMA-18 (N=23)
Objective response rate (CR + PR), n (%)	20 (87)
95% CI	66.4-97.2
Complete response, n (%)	13 (57)
95% CI	34.5-76.8
Partial response, n (%)	7 (30)
95% CI	13.2-52.9
Progressive disease, n (%)	2 (9)
95% CI	1.1-28.0
Not done[a], n (%)	1 (4)
95% CI	0.1-21.9

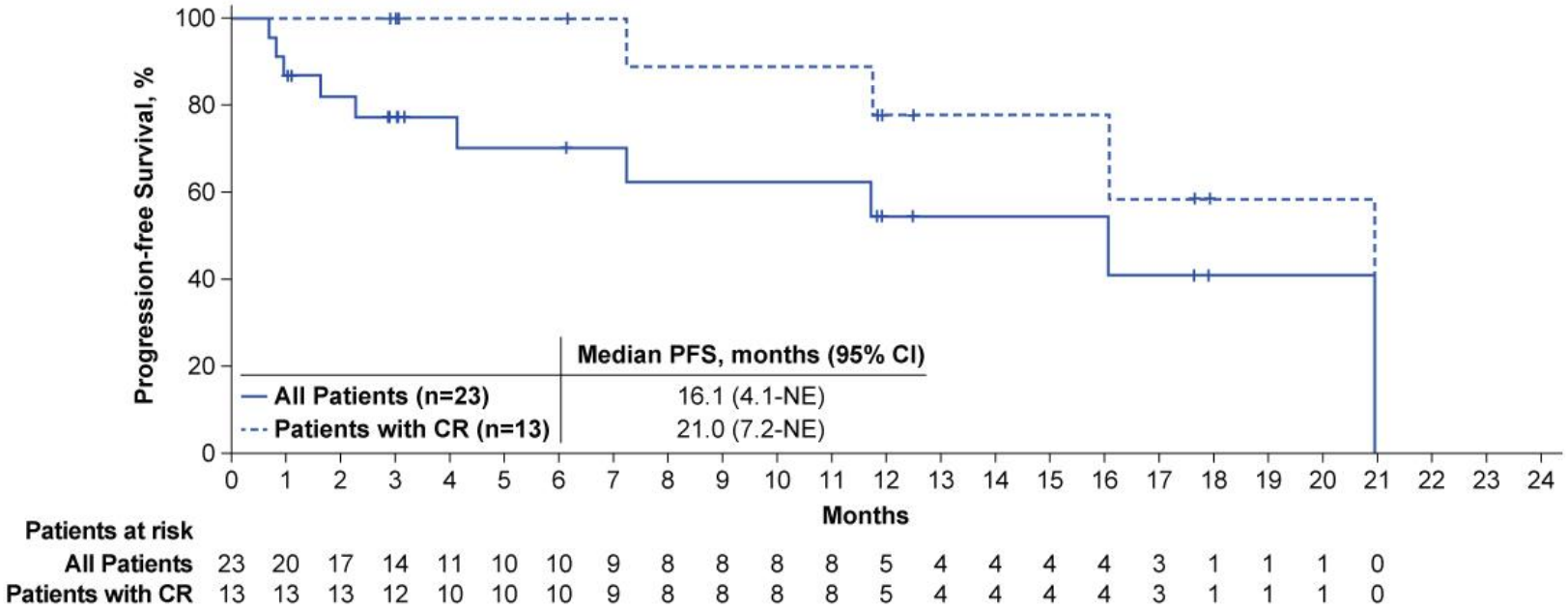
Duration of Response[b]



- At data cutoff, investigator-assessed ORR was 87%, CR rate was 57%, with both Cohort 2 patients having CR
- Median DOR was 15.1 months in responders and 20.0 months in patients with CR
  - 50% (n=10) of the 20 patients with response were still in ongoing response, 20% had disease progression (n=4) , 15% withdrew consent (n=3), and 15% had died (n=3)

[a] One patient not assessed at time of analysis. [b] Data cutoff was February 3, 2023, with a median follow-up of 33.5 months (range, 24.5-35.3; N=23).
CR, complete response; DOR, duration of response; mo, month; NE, not estimable; ORR, objective response rate; PD, progressive disease; PR, partial response.

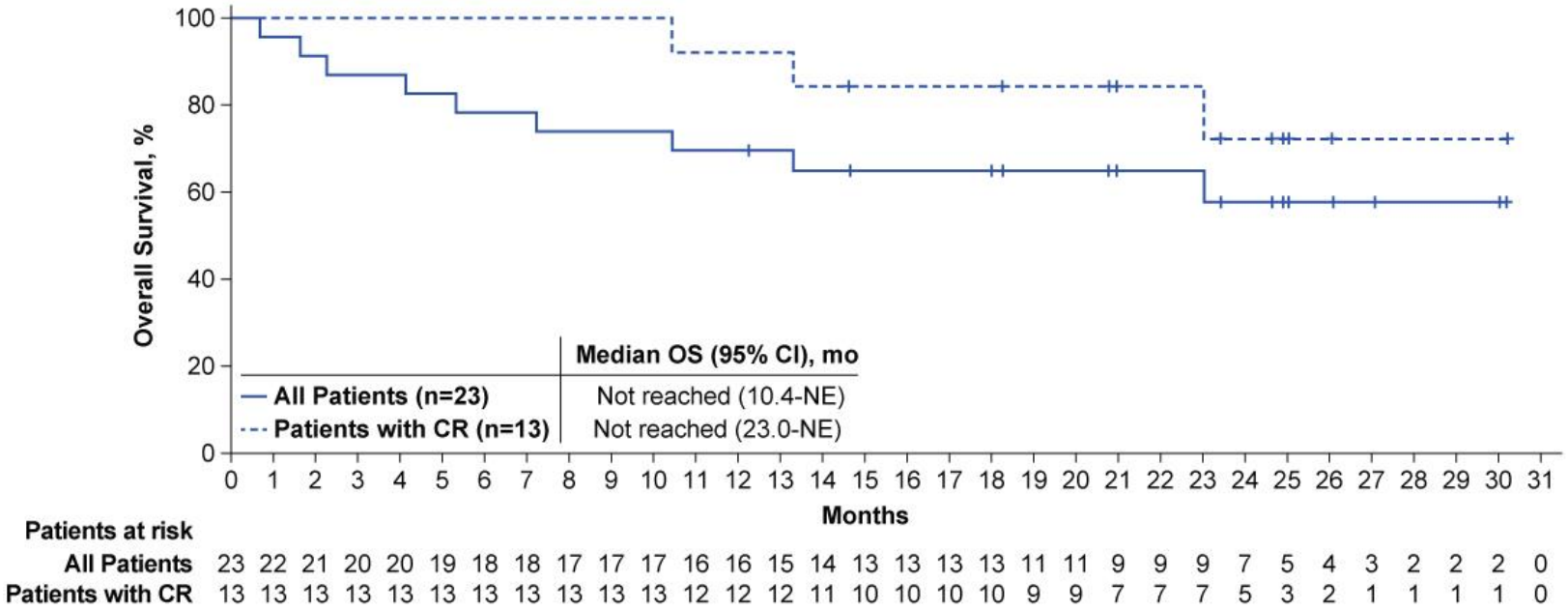
Progression-Free Survival in ZUMA-18



- Median PFS was 16.1 months in all treated patients and 21.0 months in patients with CR

mo, month; NE, not estimable; PFS, progression-free survival.

Overall Survival in ZUMA-18



- The median OS in ZUMA-18 was not reached at data cutoff with a 58% OS rate at 24 months
- At data cutoff, 61% patients were still alive (n=14) and 39% had died (n=9); 5 due to AEs, 2 due to PD, and 2 due to other causes

AE, adverse events; mo, month; NE, not estimable; OS, overall survival; PD, progressive disease.

Adverse Events in ZUMA-18

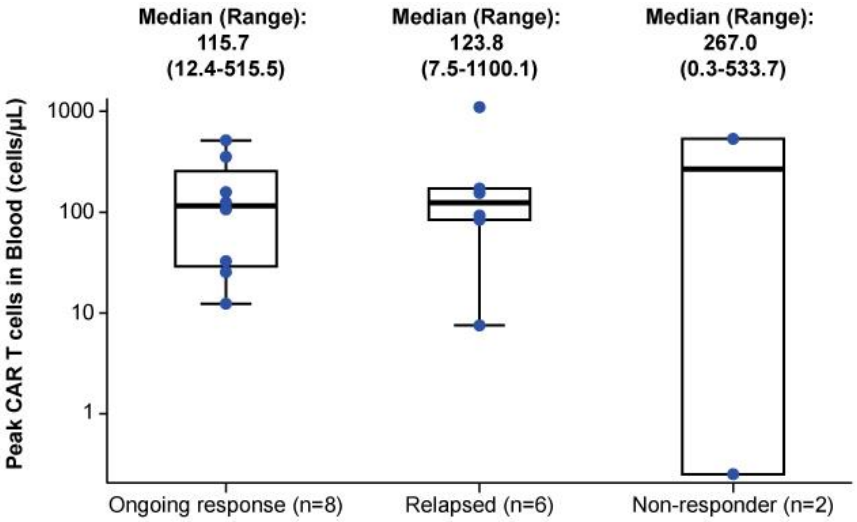
- 18 patients (78%) experienced at least 1 Grade ≥3 brexu-cel–related AE
- Any grade CRS or NEs occurred in 87% and 70% of patients, respectively
  - No Grade 5 CRS or NEs occurred
- 5 Grade 5 AEs occurred
  - 1 deemed related to brexu-cel (multiple organ dysfunction syndrome on Day 20)
  - 4 deemed unrelated to brexu-cel (n=2 sepsis [Days 125 and 219]; n=1 aspiration [Day 49]; and n=1 encephalopathy [Day 68])

MedDRA Preferred Term	Overall (N=23)
Any brexu-cel–related AE, n (%)	23 (100)
Worst Grade ≥3	18 (78)
Grade ≥3 CRS	1 (4)
Grade ≥3 NEs	8 (35)
Grade ≥3 hematologic TEAE occurring in ≥3 patients, n (%)	15 (65)
Anemia	10 (43)
Neutropenia	6 (26)
Leukopenia	4 (17)
Febrile neutropenia	3 (13)
Thrombocytopenia	3 (13)

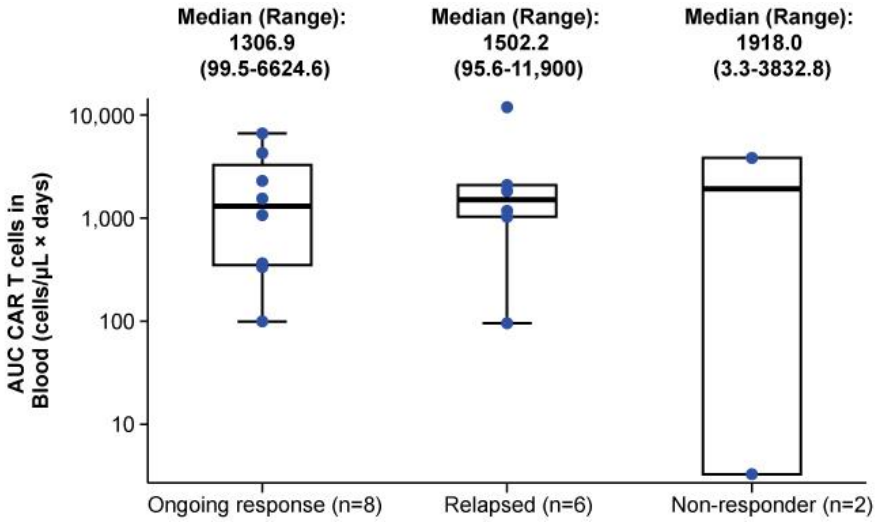
Brexu-cel, brexucabtagene autoleucel; CRS, cytokine release syndrome; MedDRA, Medical Dictionary for Regulatory Activities; NE, neurologic event; TEAE, treatment-emergent adverse events.

Peak and Area Under the Curve CAR T-Cell Expansion in ZUMA-18

Peak CAR T-Cell Expansion



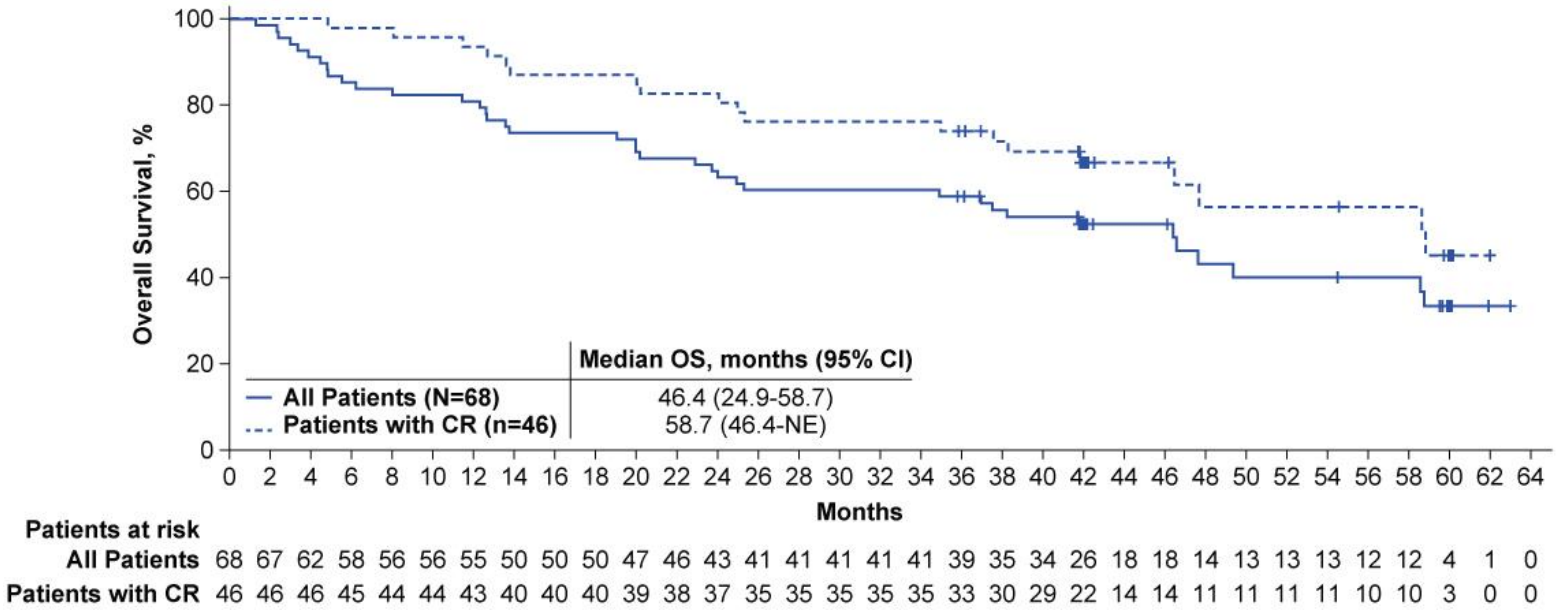
AUC CAR T-Cell Expansion



- Median peak and AUC CAR T-cell levels in responders were similar to those reported in ZUMA-2; however, substantial expansion was also observed in relapsed and non-responding patients, though small patient numbers limit interpretation of these results

1. Wang M, et al. *N Engl J Med*. 2020;382:1331-1342.
AUC, area under the curve; CAR, chimeric antigen receptor.

Overall Survival in ZUMA-2 at 4 years (N=68)



- As of July 23, 2022, median follow-up in ZUMA-2 was 47.5 months (N=68; range, 37.9-68.3)
- Median OS in ZUMA-2 was 58.7 months for patients with a CR (n=46)
- After almost 4 years of median follow-up, 30 patients (45%) were still alive, 27 of which had achieved a CR

CR, complete response; mo, month; NE, not estimable; NR, no response; PR, partial response.

Conclusions

- Consistent with ZUMA-2 findings, brexu-cel demonstrated a high level of efficacy in patients with R/R MCL in the expanded-access ZUMA-18 study, with an ORR of 87% and median OS not yet reached with close to 3 years of follow-up in a heavily pretreated population
- Grade ≥3 CRS was 4% in ZUMA-18 with no new safety signals detected
- Of note, given the small sample size (n=2), no definitive conclusions can be drawn from OOS (cohort 2) patient outcomes alone
- With 4 years of median follow-up in ZUMA-2, patients continued to benefit from brexu-cel with a median OS of almost 5 years in patients with CR
- Together, these results support the continued use of brexu-cel as standard of care in the R/R MCL setting

Brexu-cel, brexucabtagene autoleucel; CR, complete response; OOS, out of specification; ORR, objective response rate; OS, overall survival; R/R MCL, relapsed/refractory mantle cell lymphoma.

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