Abstract
P1454

Real-World Outcomes of Brexucabtagene Autoleucel for the Treatment of Relapsed or Refractory Mantle Cell Lymphoma in the United States

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BACKGROUND

- Brexucabtagene autoleucel (brexu-cel), an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, is approved in the United States (US) and European Union for the treatment of adults with relapsed/refractory (R/R) mantle cell lymphoma (MCL) and in the US for adults with R/R B-cell acute lymphoblastic leukemia[1,2]
- In a 3-year follow-up analysis of ZUMA-2, a study of brexu-cel in patients with R/R MCL who received 1-5 prior therapies including a Bruton tyrosine kinase inhibitor (BTKi), the median overall survival (OS) was 46.6 months, with a 30-month OS rate of 60.3%[3]
  - The objective response rate (ORR) with brexu-cel in ZUMA-2 was 91%, with a 68% complete response (CR) rate[3]
- Patients treated with FDA-approved brexu-cel may have had patient and disease characteristics that were broader than the scope of the ZUMA-2 eligibility criteria, including no prior BTKi therapy[4]
- The post-authorization safety study (PASS) of FDA-approved brexu-cel is a long-term noninterventional cohort study using the CIBMTR registry infrastructure

OBJECTIVE

- Assess the real-world efficacy and safety outcomes of brexu-cel in patients with R/R MCL

METHODS

Population in the brexu-cel PASS

- Received FDA-approved brexu-cel for R/R MCL in the US after July 24, 2020
- Provided informed consent
- Not enrolled in any clinical trials

Additional exclusion criteria for this analysis

- No efficacy or safety follow-up

Endpoints of interest

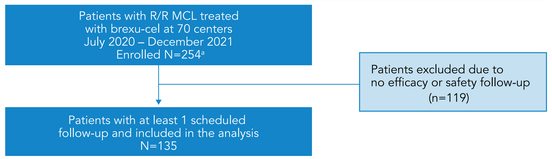
- **Efficacy**: ORR (CR + partial response), CR as best response, duration of response (DOR), progression-free survival (PFS), and OS; outcomes by prior BTKi exposure
- **Safety**: cytokine release syndrome (CRS; per Lee at al 2014 criteria for comparison with ZUMA-2[5]) and immune effector cell-associated neurotoxicity syndrome (ICANS; per American Society for Transplantation and Cellular Therapy consensus grade), prolonged cytopenia, infection, and subsequent neoplasm

Statistical Analyses

- Percentages and 95% Clopper-Pearson exact CIs were calculated for dichotomous outcomes. DOR, PFS and OS were estimated using the Kaplan-Meier estimator. Cumulative incidence functions were used for CRS and ICANS resolution rates

RESULTS

Figure 1. Analysis Population



[a] A total of 500 patients is planned for enrollment.
Brexu-cel, brexucabtagene autoleucel; MCL, mantle cell lymphoma; R/R, relapsed/refractory.

- The data cutoff date for this analysis was December 24, 2021

RESULTS *(Continued)*

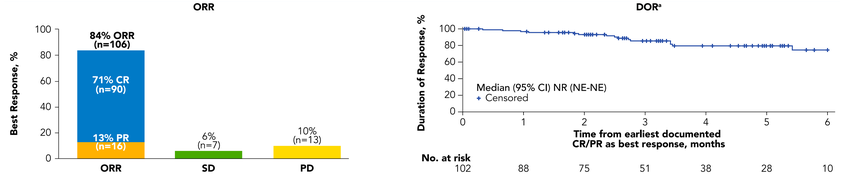
Table 1. Baseline Characteristics

Key Variable of Interest	BTKi-Naive (n=12, 9%)[a]	BTKi-Exposed (n=120, 89%)[a]	All Patients (N=135)
Median age (range), years	68 (54-77)	65 (37-84)	66 (37-84)
Age ≥65 years, n (%)	9 (75)	62 (52)	72 (53)
Male sex, n (%)	9 (75)	94 (78)	106 (79)
ECOG PS ≥2 prior to infusion, n (%)	0	7 (6)	7 (5)
Clinically significant comorbidities / HCT-CI score ≥3[4], n (%)	9 (75) / 4 (33)	87 (73) / 32 (27)	96 (71) / 36 (27)
Disease stage at diagnosis: I-II / III-IV n (%)[b]	2 (17) / 9 (75)	9 (8) / 89 (74)	11 (8) / 99 (73)
***TP53* deletion at diagnosis, n/n (%)**	2/11 (18)	8/57 (14)	10/69 (14)
Ki-67 proliferation index at diagnosis ≥30%, n/n (%)	7/9 (78)	46/65 (71)	53/75 (71)
Extranodal CNS involvement prior to infusion, n (%)	0	5 (4)	5 (4)
Chemo-sensitive/resistant prior to infusion, n (%)[b]	3 (25) / 7 (58)	33 (28) / 73 (61)	36 (27) / 83 (61)
Median no. of prior lines of therapy (range)	3 (2-6)	4 (2-12)	4 (2-12)
Prior SCT: ASCT / alloSCT, n (%)	2 (17) / 1 (8)	38 (32) / 5 (4)	41 (30) / 6 (4)
Bridging therapy: any type / systemic / radiation, n (%)[c]	2 (17) / 2 (17) / 1 (8)	24 (20) / 15 (13) / 12 (10)	26 (19) / 17 (13) / 13 (10)
≥12 Months from initial diagnosis to infusion, n (%)	11 (92)	107 (89)	120 (89)
Median time from leukapheresis to infusion (range), days	27 (22-35)	28 (18-96)	28 (18-96)
Infused in the outpatient setting, n (%)	2 (17)	10 (8)	12 (9)

[a] Three patients did not report the status of prior BTKi exposure. [b] Disease stage was not reported for 25 patients, and sensitivity to chemotherapy was unknown in 16 patients. [c] The incidence of bridging therapy was derived from the number of patients who received a prior therapy after leukapheresis and before conditioning chemotherapy.
AlloSCT, allogeneic stem cell transplantation; ASCT, autologous stem cell transplantation; CNS, central nervous system; ECOG PS, Eastern Cooperative Oncology Group performance status; HCT-CI, hematopoietic cell transplantation-specific comorbidity index; SCT, stem cell transplantation.

- Of 135 patients, 79 (59%) were considered not eligible for ZUMA-2

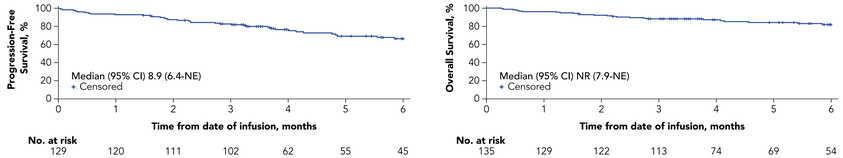
Figure 2. Objective Response and Duration of Response



[a] Among patients who achieved CR/PR as best response.
CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

- Among patients with best response assessed and reported (n=126), 106 (84%; 95% CI, 77-90) had an objective response (**Figure 2**)
- With a median 6 months of follow-up, the median DOR was not yet reached (**Figure 2**); the estimated 3- and 6-month DOR rates were 85% (95% CI, 75-92) and 75% (95% CI, 58-85), respectively

Figure 3. Progression-Free and Overall Survival



[a] PFS is censored at subsequent cell therapy/SCT.
NE, not estimable; NR, not reached; OS, overall survival; PFS, progression-free survival; SCT, stem cell transplantation.

- The median PFS was 8.9 months (95% CI, 6.4-NE; **Figure 3**), and the 6-month PFS rate was 66% (95% CI, 56-75)
- The median OS was not reached, and the 6-month OS rate was 79% (95% CI, 71-86; **Figure 3**)

Table 2. Efficacy Outcomes by Prior BTKi Exposure

	BTKi-Naive (n=12)[a]	BTKi-Exposed (n=120)[a]	All Patients (N=135)
ORR (95% CI), %	91 (59-100)	84 (76-90)	84 (77-90)
CR	82 (48-98)	71 (62-80)	71 (63-79)
PR	9 (<1-41)	13 (7-20)	13 (7-20)
Median DOR (95% CI), months	NR (NE-NE)	NR (NE-NE)	NR (NE-NE)
3-Month estimated DOR (95% CI), %	100	85 (74-92)	85 (75-92)
6-Month estimated DOR (95% CI), %	NE (NE-NE)	73 (56-84)	75 (58-85)
Median PFS (95% CI), months	NR (1.6-NE)	8.9 (6.4-NE)	8.9 (6.4-NE)
6-Month estimated PFS (95% CI), %	74 (39-91)	66 (55-75)	66 (56-75)
Median OS (95% CI), months	NR (2.3-NE)	NR (7.9-NE)	NR (7.9-NE)
6-Month estimated OS (95% CI), %	73 (38-91)	80 (70-87)	79 (71-86)

[a] Three patients did not report prior BTKi exposure.
BTKi, Bruton tyrosine kinase inhibitor; CR, complete response; DOR, duration of response; NE, not estimable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PR, partial response.

- Efficacy outcomes appeared generally consistent among patients with and without prior BTKi therapy, though the sample size of BTKi-naive patients was limited (**Table 2**)

Table 3. CRS and ICANS

Parameter	All Patients (N=135)
Any-grade CRS (95% CI), %	84 (76-89)
Grade ≥3 (95% CI), %	9 (5-15)
Median time to onset (range), days	4 (1-46)
Median duration of events (range), days	5 (1-80)
Patients with resolved events by 21 days since onset (95% CI), %[a]	95 (88-98)
Any-grade ICANS (95% CI), %	57 (48-66)
Grade ≥3 (95% CI), %	29 (22-38)
Median time to onset (range), days	7 (1-31)
Median duration of events (range), days	10 (2-98)
Patients with resolved events by 21 days since onset (95% CI), %[a]	75 (63-83)
AE management, n (%)	
Tocilizumab	93 (69)
Steroids[b]	74 (55)

[a] Data on the outcome of ongoing events is not available. [b] Data on dosing of steroids is not available.
AE, adverse event; CRS, cytokine release syndrome; ICANS, immune effector cell-associated neurotoxicity syndrome.

Table 4. Other Treatment-Emergent Adverse Events of Interest

Parameter	All Patients (N=135)
Prolonged cytopenias[a], n/n (%)	28/129 (22)
Neutropenia	6/129 (5)
Thrombocytopenia	25/129 (19)
Clinically significant infection, n (%)	43 (32)
Bacterial	27 (20)
Fungal	10 (7)
Viral	23 (17)
Subsequent neoplasms[b], n (%)	4 (3)
Deaths, n (%)	27 (20)
Primary disease	15 (11)
New malignancy (after CAR T-cell therapy)[c]	1 (<1)
Chronic graft-versus-host disease	1 (<1)
Infection	5 (4)
Cardiac failure	1 (<1)
Hemorrhage	1 (<1)
Neurotoxicity	2 (1)
Cardiac/pulmonary arrest	1 (<1)

[a] Among patients who survived 30-day post-infusion. [b] During follow-up for this CAR T-cell therapy. Subsequent neoplasms were genitourinary malignancy (n=1), myelodysplasia/myeloproliferative neoplasm + squamous cell skin malignancy (n=1), and sarcoma (n=2). [c] One patient with a subsequent neoplasm of sarcoma died of the new malignancy.
CAR, chimeric antigen receptor

CONCLUSIONS

- This is the first report of the PASS evaluating the real-world experience with brexu-cel in the US and largest real-world brexu-cel report to date
- In patients with R/R MCL, safety and efficacy of brexu-cel was consistent with clinical reports, even though 59% of patients in the PASS would have been ineligible for ZUMA-2
  - Responses appeared to be independent of prior BTKi exposure, although the sample size was small (n=12 BTKi-naive patients)
- Overall, these results support a broad use of brexu-cel in clinical practice

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- * Dr. Shah was an employee of Kite when the analyses reported here were conducted

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DISCLOSURES

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