Poster
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Long-Term (5-Year) Overall Survival in ZUMA-1, the Pivotal Study of Axicabtagene Ciloleucel in Patients With Refractory Large B-Cell Lymphoma

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BACKGROUND

- Axicabtagene ciloleucel (axi-cel) is an autologous anti-CD19 chimeric antigen receptor (CAR) T-cell therapy approved for the treatment of patients with relapsed/refractory large B-cell lymphoma (LBCL) after ≥2 prior therapies[1,2]
- ZUMA-1 (NCT02348216) is the multicenter, single-arm, registrational Phase 1/2 study of axi-cel in patients with refractory LBCL[3,4]
- In the 2-year analysis of ZUMA-1 (n=101; median follow-up from axi-cel dosing to data cutoff, 27.1 months), the objective response rate in the pivotal Cohorts 1 and 2 was 83% (including 58% with complete response [CR]) with a 2-year overall survival (OS) rate of 50.5%[4]
- After ≥4 years of follow-up (median follow-up, 51.1 months), median OS was 25.8 months, with a 4-year OS rate of 44%[5]
- Here, we report updated survival results from Phase 2 of ZUMA-1 after 5 years of follow-up, including an exploratory analysis of OS by event-free survival (EFS) status at 12 and 24 months

OBJECTIVE

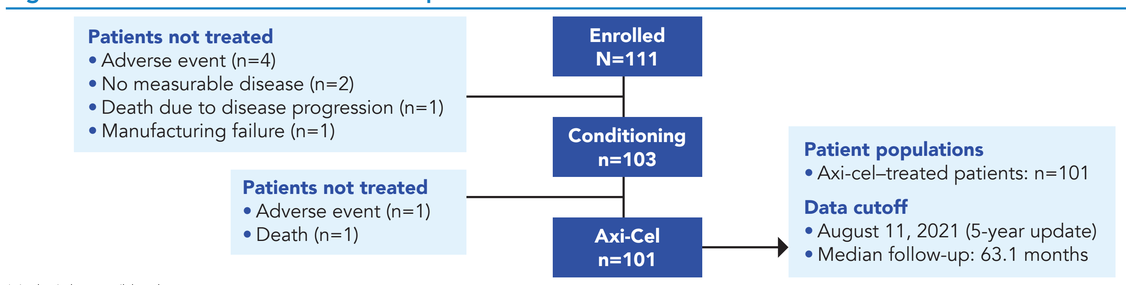
- To present the 5-year updated analysis of Cohorts 1 and 2 from Phase 2 of ZUMA-1
- To explore the potential role of EFS at 12 and 24 months as a surrogate endpoint for OS

METHODS

- The study protocol for Phase 2 Cohorts 1 and 2 of ZUMA-1 was previously described[3]
- Median OS, 5-year survival rates, and time to next therapy were estimated using Kaplan-Meier methodology
- Time to next therapy was defined as time from axi-cel infusion to initiation of new anticancer therapy, including CAR T-cell retreatment and excluding stem cell transplantation (SCT), or death from any cause
- Blood levels of CAR T cells were quantified using a validated polymerase chain reaction assay
- Exploratory analysis of OS by EFS at 12 and 24 months
  - EFS was defined as time from axi-cel infusion until disease progression, initiation of new anticancer therapy (excluding SCT), or any-cause death
  - Kaplan-Meier methodology was used to estimate median OS, 5-year OS rates, median EFS, EFS rates, and comparisons of OS by EFS outcomes

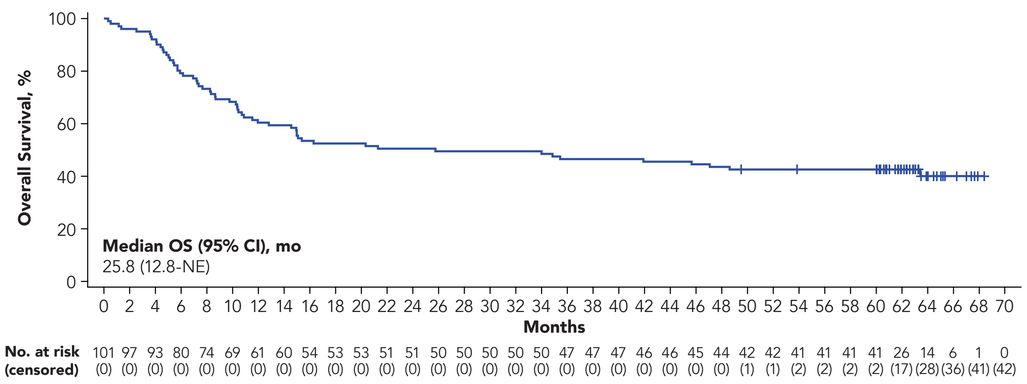
RESULTS

Figure 1. ZUMA-1 Phase 2 Patient Disposition



Axi-cel, axicabtagene ciloleucel.

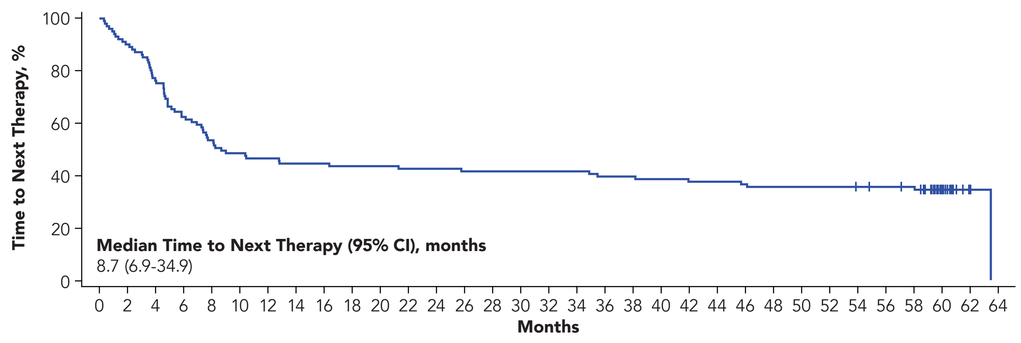
Figure 2. 5-Year Overall Survival



One patient's event time was updated from Month 42 to 39 after data cutoff and is not reflected in this figure.
NE, not estimable; OS, overall survival.

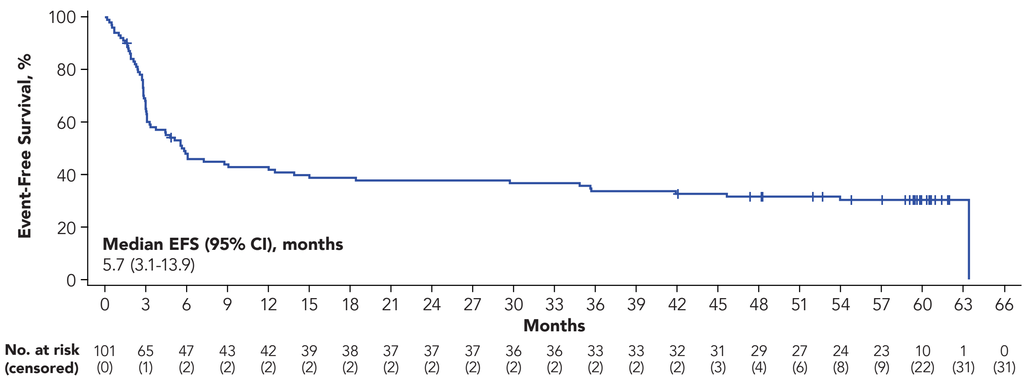
- With ≥5 years of follow-up, the 5-year OS rate was 42.6% (95% CI, 32.8-51.9) among patients treated with axi-cel
- The 5-year OS rate among complete responders was 64.4% (95% CI, 50.8-75.1); the median survival time among complete responders was not reached (95% CI, 63.4-not estimable); 37 of 59 CR patients (63%) are still alive at the 5-year data cutoff
- Since the 4-year data cutoff, 1 death at Month 63 (CR) and 1 progressive disease at Month 54 (partial response) were observed

Figure 3. 5-Year Time to Next Therapy (Exploratory Analysis)



- Median time to next anticancer therapy was 8.7 months (range, 0.3-63.4) after axi-cel infusion, unchanged from previous reports[5]
- By the Year 5 data cutoff, 34 patients (34%) were still alive and received no subsequent therapy (excluding SCT) or retreatment with axi-cel
- Compared with the Year 4 data,[5] 2 patients (2%) who had previously progressed received new anticancer therapy

Figure 4. Event-Free Survival (Exploratory Analysis)

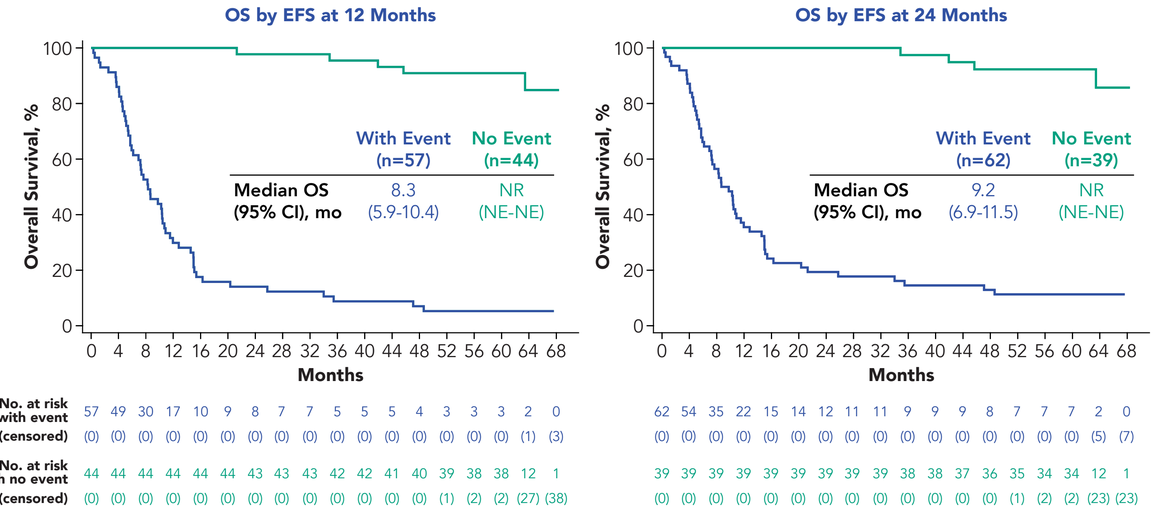


EFS, event-free survival

- Among all treated patients, the 12-month EFS rate was 42.8% (95% CI, 33.0-52.3) and the 24-month EFS rate was 37.7% (95% CI, 28.3-47.2)

RESULTS *(continued)*

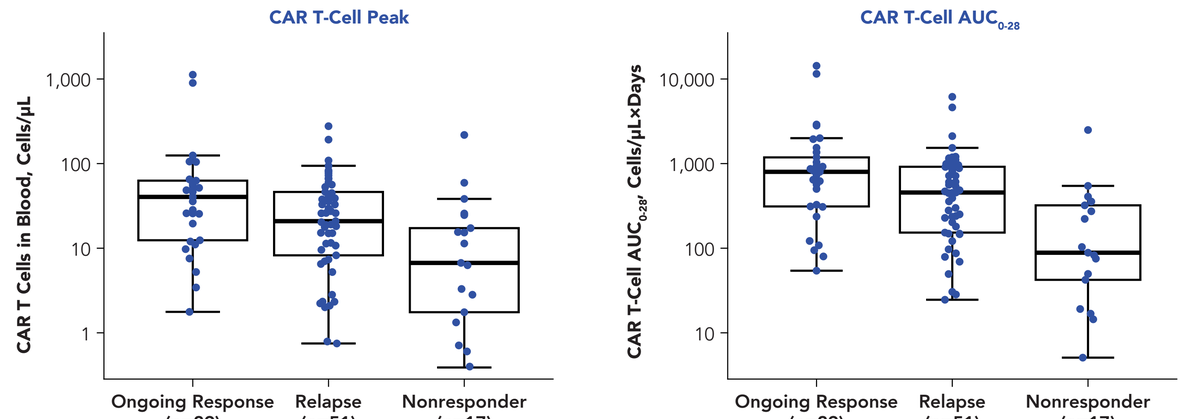
Figure 5. Overall Survival by Event-Free Survival at 12 and 24 Months (Exploratory Analysis)



EFS, event-free survival; NE, not estimable; NR, not reached; OS, overall survival.

- Among patients with (n=57) and without (n=44) an EFS event by Month 12, respectively, 5-year OS rates were 5.3% (95% CI, 1.4-13.2) and 90.9% (95% CI, 77.6-96.5)
- Among patients with (n=62) and without (n=39) an EFS event by Month 24, respectively, 5-year OS rates were 11.3% (95% CI, 5.0-20.5) and 92.3% (95% CI, 78.0-97.5)

Figure 6. Early CAR T-Cell Expansion Associates With Ongoing Response at Month 60



Ongoing response is defined as responders (CR or PR) who did not have PD or die by the data cutoff. Four patients did not have evaluable post-infusion samples to allow determination of CAR T-cell peak and AUC.
$AUC_{0\text{-}28}$, area under the curve from Day 0 to 28; CAR, chimeric antigen receptor; CR, complete response; PD, progressive disease; PR, partial response.

- Median peak CAR T-cell levels were numerically higher in patients with ongoing response at Month 60 and were considerably lower in patients who relapsed and nonresponders
- A similar trend was observed with CAR T-cell expansion by area under the curve from Day 0 to 28

Table 1. Deaths

n (%)	Total N=101	Year 1	Year 2	Year 3	Year 4	Year 5	Year >5
Patients who died	**59 (58)**	**40 (40)**	**10 (10)**	**4 (4)**	**3 (3)**	**1 (1)**	**1 (1)**
Primary cause of death							
Progressive disease[a]	45 (45)	32 (32)	9 (9)	3 (3)	0	1 (1)	0
Other[b]	9 (9)	5 (5)	0	1 (1)	3 (3)	0	0
Adverse event[c]	4 (4)	3 (3)	1 (1)	0	0	0	0
Secondary malignancy	1 (1)	0	0	0	0	0	1 (1)

[a] During ongoing safety monitoring after the data cutoff, one event of CNS lesion, which was not amenable to biopsy, was reported. Treatment for presumed progressive disease for diffuse large B-cell lymphoma was initiated by the investigator. [b] Events included infection (n=3), cardiac arrest (n=2), pulmonary nocardiosis (n=1), sepsis (n=1), complications of allogeneic transplant for previous treatment-related MDS not related to axi-cel (n=1), and unknown (n=1). [c] Two events had no causal relationship (sepsis, pulmonary embolism) and 2 events were related to axi-cel (brain injury due to cardiac arrest and hemophagocytic lymphohistiocytosis).
Axi-cel, axicabtagene ciloleucel; CNS, central nervous system; MDS, myelodysplastic syndrome.

- Among treated patients, 58% have died as of the data cutoff date (**Table 1**)
- Following the 4-year data cutoff date[5]
  - There has been 1 death which was due to secondary malignancy (prior therapy- and/or conditioning chemotherapy-related myelodysplastic syndrome while in CR for LBCL)
  - No patients received intravenous immunoglobulin
- As of the 5-year data cutoff, no new safety signals have been reported, including
  - No serious adverse events related to axi-cel
  - No secondary malignancies related to axi-cel

CONCLUSIONS

- In this updated, 5-year analysis of the Phase 2 pivotal cohorts of ZUMA-1, axi-cel induced long-term OS with no new safety signals in patients with refractory LBCL
  - In treated patients, the 5-year OS rate was 42.6%
  - Between the 4-year and 5-year analyses, the time to next therapy curve remained stable, and 92% of patients remained alive without need of subsequent therapy, which may be suggestive of a cure for these patients
  - Safety findings were similar to those in previous reports,[3-5] with no new safety signals observed
- Durable responses were strongly associated with peak CAR T-cell expansion
- The exploratory analysis of long-term OS by EFS status appears highly correlative in refractory LBCL
  - These findings can potentially support use of 1-year and 2-year EFS as a surrogate endpoint for long-term OS in R/R LBCL

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- These data were previously presented at the 2021 Annual Meeting of the American Society of Hematology[6]

DISCLOSURES

CAJ: honoraria from Kite, Celgene, Novartis, bluebird bio, Epizyme, Humanigen, Pfizer, Precision BioSciences, Nkarta, Lonza, and AbbVie; consultancy or advisory role for Kite, Celgene, Novartis, Pfizer, Humanigen, Precision BioSciences, Nkarta, bluebird bio, Lonza, Pfizer, Ispen, and AbbVie; speakers' bureau participation for Axis and Clinical Care Options; research funding from Pfizer; and travel support from Kite, Celgene, Novartis, Precision Biosciences, Lonza, Pfizer, and Humanigen.

Full author disclosures are available at the following Quick Response (QR) code:

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