Poster
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ZUMA-24 Preliminary Analysis: A Phase 2 Study of Axicabtagene Ciloleucel in the Outpatient Setting With Prophylactic Corticosteroids in Patients With Relapsed/Refractory Large B-Cell Lymphoma

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BACKGROUND

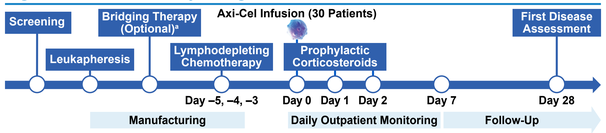
- Axicabtagene ciloleucel (axi-cel) is an autologous chimeric antigen receptor (CAR) T-cell therapy approved for adults with relapsed/refractory (R/R) large B-cell lymphoma (LBCL), based on significant clinical benefit demonstrated in second line (ZUMA-7) and third or later lines (ZUMA-1) of therapy[1-4]
- Second-line axi-cel in ZUMA-7 demonstrated superior overall survival over standard-of-care therapy at a median follow-up of 47.2 months (hazard ratio, 0.726; 95% CI, 0.540-0.977; one-sided *P*=.0168), with no new safety concerns in the second line over later lines[5]
  - The incidence of any-grade cytokine release syndrome (CRS) with axi-cel was 92% (Grade ≥3, 6%)[5]
  - Any-grade neurologic events occurred in 61% of patients (Grade ≥3, 21%)[5]
  - Median duration of hospitalization was 16 days; 25% of patients were admitted to the intensive care unit (ICU)[3]
  - Objective responses were observed in 83% of patients[5]
- In a safety management cohort of ZUMA-1 (Cohort 6),[6] prophylactic corticosteroids and early corticosteroid and/or tocilizumab use post–axi-cel in the inpatient setting were associated with:
  - No Grade ≥3 CRS (any-grade in 80% of patients) and delayed median onset of CRS (5 days)
  - Neurologic events in 58% of patients (Grade ≥3, 18%), with median time to onset of 6 days
  - Efficacy consistent with the pivotal cohorts of ZUMA-1 (Cohort 1+2)
- In a real-world assessment presented at this congress from Mayo Clinic, Rochester, early patient management in the outpatient setting showed improved safety outcomes with axi-cel among patients with R/R non-Hodgkin lymphoma[7]

OBJECTIVE

- To evaluate the safety and efficacy of outpatient dosing of axi-cel with prophylactic corticosteroid use and early adverse event (AE) intervention in patients with R/R LBCL after ≥1 prior line of therapy

METHODS

Figure 1. ZUMA-24 Study Design



Key Eligibility Criteria
- Histologically confirmed LBCL (DLBCL, HGBL, PMBCL, primary cutaneous DLBCL [leg type], TFL)
- R/R disease after ≥1 line of therapy (including anti-CD20 monoclonal antibody and anthracycline-containing regimen)
- ECOG PS 0 or 1

Lymphodepleting Chemotherapy
- Cyclophosphamide 500 mg/m^2 and fludarabine 30 mg/m^2 for 3 days

Axi-Cel
- 2×10^6 CAR T cells/kg

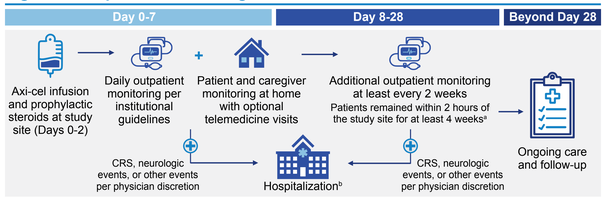
Prophylactic Corticosteroids
- Dexamethasone 10 mg on Days 0 (prior to axi-cel), 1, and 2

Primary Endpoint
- Incidence and severity of CRS and NEs

Key Additional Endpoints
- Time to onset and duration of CRS and NEs, rate and time to/duration of hospitalization[b]
- ORR, CR rate, DOR, PFS, EFS, OS
- CAR T-cell expansion

[a] Bridging therapy was administered per investigator discretion after leukapheresis and no later than 7 days before initiating lymphodepleting chemotherapy.
[b] Time to hospitalization was measured in days as the date of hospitalization – infusion date +1.
Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance score; EFS, event-free survival; HGBL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; NE, neurologic event; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PMBCL, primary mediastinal (thymic) large B-cell lymphoma; R/R, relapsed/refractory; TFL, transformed follicular lymphoma.

Figure 2. Outpatient Monitoring After Axi-Cel Infusion

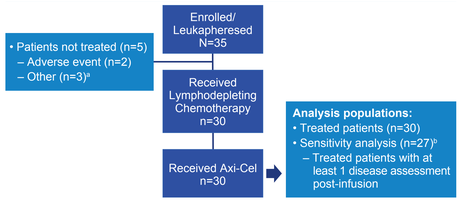


[a] An electronic wearable device was available for continuous temperature monitoring, worn up to 4 weeks per investigator discretion.
[b] For Grade 1-2 CRS and Grade 1 neurologic events, patients may have been admitted for outpatient observation per physician discretion. If symptoms persisted or recurred, patients were to be admitted to the inpatient setting.
Axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome.

- Patients were monitored daily at a healthcare facility for at least 7 days after the axi-cel infusion, according to institutional outpatient monitoring guidelines (**Figure 2**)
  - Guidelines for hospitalization included CRS, neurologic events, and other criteria at the discretion of the covering physician

RESULTS

Figure 3. Patient Disposition



[a] Procedure to a single patient IND due to declining status. [b] Among the 3 patients with no disease assessment, 2 did not have ≥1 month follow-up, and 1 had no disease assessment at Week 4 due to hospitalization.
Axi-cel, axicabtagene ciloleucel; IND, investigational new drug.

- As of April 5, 2024, the median follow-up in all treated patients was 7 months (range, 1-18; **Figure 3**)

Table 1. Baseline Patient Characteristics

Characteristic	Treated Patients (N=30)
Median age, years (range)	62 (24-76)
≥65 years, n (%)	11 (37)
Male, n (%)	20 (67)
Ethnicity, n (%)	
Hispanic or Latino	2 (7)
Not Hispanic or Latino	23 (77)
Not reported	5 (17)
Race, n (%)	
Asian	3 (10)
Black or African American	2 (7)
White	22 (73)
Other or missing	3 (10)
ECOG performance status 1, n (%)	10 (33)
Disease type, n (%)	
DLBCL not otherwise specified	24 (80)
HGBL with or without *MYC* and *BCL2* and/or *BCL6* rearrangement	1 (3)
PMBCL	2 (7)
TFL	3 (10)
Disease stage at study entry, n (%)	
I/II	11 (37)
III	5 (17)
IV	14 (47)
IPI score, n (%)[a]	
0-1	25 (83)
2	2 (7)
4	1 (3)
Number of prior chemotherapy regimens, n (%)	
1	28 (93)
2	2 (7)
Median LDH at baseline, U/L (range)[b]	198 (102-1136)
Median SPD at baseline, mm^2 (range)	2348 (221-17,843)

[a] IPI score was missing for 2 patients. [b] The upper limit of normal was 190 U/L.
DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; HGBL, high-grade B-cell lymphoma; IPI, International Prognostic Index; LDH, lactate dehydrogenase; PMBCL, primary mediastinal B-cell lymphoma; SPD, sum of product diameters; TFL, transformed follicular lymphoma.

Table 2. Incidence and Severity of Cytokine Release Syndrome and Neurologic Events

Parameter	Treated Patients (N=30) CRS	Neurologic Events
Any grade, n (%)[a]	27 (90)	23 (77)
Grade 1	11 (37)	8 (27)
Grade 2	16 (53)	8 (27)
Grade 3	0	6 (20)
Grade 4	0	1 (3)
Grade 5	0	0
Median time to onset, days (95% CI)	4 (NE-NE)	7 (6-14)
Median duration of event, days (95% CI)	5 (3-6)	6 (3-13)
Steroids used for treatment of AE, n (%)[b]	9 (30)	13 (43)
Tocilizumab used for treatment of AE, n (%)	26 (87)	0

Medians of time-dependent outcomes were measured using Kaplan-Meier estimates. Time to onset of CRS or neurologic events was defined as the earliest start date of the event – the infusion date +1. For patients who withdrew consent, it was censored at end of study date. [a] CRS was graded per Lee et al 2014.[8] Neurologic events were graded per CTCAE 5.0.
AE, adverse event; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; NE, not estimable.

- No Grade ≥3 CRS events occurred (**Table 2**)
- One patient experienced Grade 4 neurologic events (agitation and depressed level of consciousness); no Grade 5 events occurred (**Table 2**)
  - The most common Grade ≥3 events were confusional state (n=4), and aphasia (n=3)
  - At data cutoff, 3 patients had ongoing neurologic events

Table 3. Common Adverse Events

AEs, n (%)[a]	Treated Patients (N=30) Any Grade	Grade ≥3
Any	30 (100)	24 (80)
Pyrexia	26 (87)	1 (3)
Hypotension	17 (57)	3 (10)
Chills	13 (43)	0
Confusional state	12 (40)	4 (13)
Neutrophil count decreased	12 (40)	12 (40)
Fatigue	11 (37)	0
Headache	11 (37)	0
Platelet count decreased	11 (37)	5 (17)
White blood cell count decreased	10 (33)	9 (30)
Cough	9 (30)	0
Anemia	8 (27)	3 (10)
Constipation	8 (27)	0

AEs were coded using MedDRA Version 26.1 and graded per CTCAE 5.0.
[a] AEs shown are those of any grade that occurred in ≥25% of patients.
AE, adverse event; CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities.

Table 4. Adverse Events of Interest

AEs, n (%)	Treated Patients (N=30) Any Grade	Grade ≥3
Neutropenia	17 (57)	16 (53)
Thrombocytopenia	13 (43)	6 (20)
Anemia	8 (27)	3 (10)
Cardiac arrhythmias	12 (40)	3 (10)
Infections	8 (27)	3 (10)
Hypogammaglobulinemia	4 (13)	0
Hemophagocytic lymphohistiocytosis	1 (3)	0
Tumor lysis syndrome	0	0

AE, adverse event.

- Overall, Grade ≥3 AEs occurred in 80% of patients (**Table 3**)
  - Serious events of any grade occurred in 80% of patients
  - The most common Grade ≥3 events consisted of cytopenias (neutrophil count decrease [n=12] and white blood cell count decrease [n=9])
- No Grade 5 AEs occurred

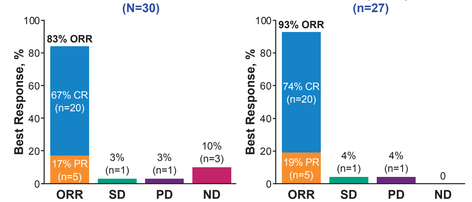
Table 5. Reasons for Hospitalization

Parameter	Treated Patients (N=30)
Outpatients hospitalized after infusion, n (%)	28 (93)
Median time to first hospitalization, days (range)	4 (2-9)
Median duration of first hospitalization, days (range)	8 (2-44)
Reasons for first hospitalization, n (%)[a]	
Grade 1 CRS	17 (57)
Grade 2 CRS	8 (27)
Grade 1 CRS and Grade 1 neurologic event	1 (3)
Grade 2 CRS and Grade 1 neurologic event	1 (3)
Other[b]	1 (3)
Patients admitted to ICU, n (%)[c]	4 (13)

[a] Per Kite medical adjudication. [b] Arrhythmia. [c] ICU admission details are as follows: Patient 1, arrhythmia (Day 1 ICU admission, 2-day stay) and large intestine perforation (Day 12 ICU admission, 8-day stay); Patient 2, other reason (Day 2 ICU admission, 7-day stay); Patient 3, pyrexia (Day 4 ICU admission, 6-day stay); Patient 4, agitation and aphasia (Day 7 ICU admission, 7-day stay) with additional aphasia and depressed level of consciousness developing on Day 8.
CRS, cytokine release syndrome; ICU, intensive care unit.

- After axi-cel infusion, 93% of patients (n=28) were hospitalized (**Table 5**)
  - Among 2 patients who did not have sufficient follow-up for their first disease assessment by data cutoff, both were admitted to the hospital and discharged before data cutoff
- A total of 4 patients (13%) were admitted to the intensive care unit (ICU) after axi-cel (range of length of any stay, 2-8 days; **Table 5**)
- Seven patients (23%) were admitted with Grade 1 CRS that subsequently worsened to Grade 2

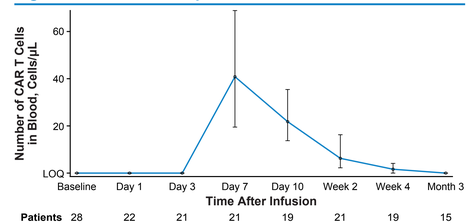
Figure 4. Objective Response Rate



[a] The sensitivity analysis set consisted of treated patients with at least 1 disease assessment after infusion.
CR, complete response; ND, not done; ORR, objective response rate; PD, progressive disease; PR, partial response; SD, stable disease.

- Among all treated patients, the objective response rate was 83% (95% CI, 65-94; **Figure 4**)
  - The complete response rate was 67% (95% CI, 47-83)

Figure 5. CAR T-Cell Expansion Over Time



Graph shows medians and interquartile range. CAR T-cell levels in blood were measured using droplet digital polymerase chain reaction analysis.
CAR, chimeric antigen receptor; LOQ, limit of quantification.

- Among 28 patients with available samples, median peak and area under the curve of CAR T-cell expansion was 40.8 cells/µL (range, 3.9-696.7) and 298.8 cells/µL×days (range, 43.9-4969.4), respectively (**Figure 5**)

CONCLUSIONS

- In this early analysis, prophylactic steroids and early intervention strategies were associated with relatively low rates of severe CRS and neurologic events, and overall safety was consistent with previous clinical experience,[5,6] with the following observations in ZUMA-24:
  - ICU admission rate appeared lower
  - Median duration of hospitalization was numerically shorter
- Outpatient administration of axi-cel demonstrated efficacy and CAR T-cell expansion consistent with those observed in ZUMA-1 and ZUMA-7[3,4,6]
- Results were consistent with those in real-world studies,[7,9] supporting the safety and feasibility of outpatient axi-cel administration in the second line or above for patients with R/R LBCL
- The ZUMA-24 study is ongoing and the primary analysis will be reported at a later date

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DISCLOSURES

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