AXI-CEL DELIVERS SIMILAR OUTCOMES REGARDLESS OF ASCT-ELIGIBILITY IN SECOND LINE R/R LBCL: COMBINED DATA FROM ZUMA-7 AND ALYCANTE

Authors, R. Houot[1], P. Arija[2], E. Bachy[3], G. Cartron[4], F. Gros[5], F. Morschhauser[6], C. Portugues[7], C. Thieblemont[8], M. Ray[9], Y. Yang[9], S. Cundari[9], C. Linot[9], D. Mistry[10], M. Simons[2], A. Gittfried[2], F. Lemonnier[11]

1 Centre Hospitalier Universitaire de Rennes, Rennes, France; 2 OPEN Health HEOR & Market Access, Rotterdam, Netherlands; 3 Hospices Civils de Lyon, Pierre-Bénite, France; 4 Centre Hospitalier Universitaire Montpellier, Montpellier, France; 5 Hematology Department, Centre Hospitalier Universitaire Bordeaux, Bordeaux, France; 6 Centre Hospitalier Universitaire Lille, Lille, France; 7 Lyon-Sud Hospital, Department of Biostatistics, LYSARC, Pierre-Bénite, France; 8 Hôpital Saint Louis, Department of Hemato-oncology, Paris, France; 9 Kite, a Gilead Company, Santa Monica, United States; 10 OPEN Health HEOR & Market Access, London, United Kingdom; 11 Henri Mondor Hospital, Lymphoid Hematology, Créteil, France

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INTRODUCTION

The treatment landscape for relapsed/refractory large B-cell lymphoma (R/R LBCL) is shifting toward chimeric antigen receptor T-cell (CAR-T) therapy, reducing reliance on autologous stem-cell transplant (ASCT) eligibility and broadening access to effective cellular therapies.

ZUMA-7 (NCT03391466) and ALYCANTE (NCT04531046) evaluated axicabtagene ciloleucel (axi-cel), a CAR-T therapy, as second-line (2L) therapy for patients with R/R LBCL, with ZUMA-7 patients being eligible for ASCT, whereas ALYCANTE patients were ineligible for ASCT.[1,2]

AIM

With CAR-T therapy now established as 2L standard of care, this pooled analysis of axi-cel for patients with R/R LBCL from the ZUMA-7 and ALYCANTE trials assessed efficacy, safety, and health-related quality of life (HRQoL) across the full CAR-T–eligible population to explore whether ASCT eligibility impacts outcomes.

METHODS

- Data from axi-cel patients in ZUMA-7 and ALYCANTE were pooled without weighting
- Efficacy endpoints were event-free survival (EFS), overall response rate (complete + partial metabolic response [CMR + PMR]), and CMR defined from leukapheresis; overall survival (OS) and progression-free survival (PFS), defined from axi-cel infusion; and duration of response (DOR). EFS and other time-to-event (TTE) outcomes were analyzed using Kaplan-Meier methods. Subgroup analyses was conducted for ZUMA-7 patients based on age.
- Safety was evaluated based on treatment-emergent adverse events (TEAEs).
- Longitudinal HR-QoL outcomes (EQ-5D-5L and EORTC QLQ-C30) were assessed using mixed models for repeated measures (MMRM).

RESULTS

Baseline characteristics

ZUMA-7 had 4 years of follow-up post-randomization, whereas ALYCANTE had 2 years of follow-up post-infusion. Baseline characteristics are presented in Table 1.

Table 1. Baseline characteristics

Characteristic	Pooled (N = 249)	ZUMA-7 (N = 180)	ALYCANTE (N = 69)
Age			
Median (range)	62 (21 – 81)	58 (21 – 80)	70 (49 – 81)
≥ 70 years	25.70%	14.44%	55.07%
Sex			
• Male	• Male: 161 (64.7%)	• Male: 110 (61.1%)	• Male: 51 (73.9%)
• Female	• Female: 88 (35.3%)	• Female: 70 (38.9%)	• Female: 18 (26.1%)
ECOG status at screening			
• 0	• 0: 125 (50.2%)	• 0: 95 (52.8%)	• 0: 30 (43.5%)
• 1	• 1: 122 (49.0%)	• 1: 85 (47.2%)	• 1: 37 (53.6%)
• 2	• 2: 2 (0.80%)	•	• 2: 2 (2.90%)
Response to first-line therapy	• Primary refractory: 171 (68.67%)	• Primary refractory: 133 (73.9%)	• Primary refractory: 38 (55.10%)
• Primary refractory	• Relapse: 78 (31.32%)	• Relapse: 47 (26.11%)	• Relapse: 31 (44.90%)
• Relapse	○ < 6 months: 24 (9.63%)	○ <6 months: 9 (5.0%)	○ <6 months: 15 (21.73%)
○ <6 months	○ 6 to 12 months: 49 (19.67%)	○ 6 to 12 months: 38 (21.1%)	○ 6 to 12 months: 11 (15.94%)
○ 6 to 12 months	○ >12 months: 1 (0.40%)		○ >12 months: 1 (1.44%)
○ >12 months	○ Unknown duration: 4 (1.60%)		○ Unknown duration: 4 (5.79%)
○ Unknown duration			
Disease type by central review	• DLBCL: 186 (74.7%)	• DLBCL: 126 (70.0%)	• DLBCL: 60 (87.0%)
• DLBCL	• HGBCL: 35 (14.1%)	• HGBCL: 32 (17.8%)	• HGBCL: 3 (4.35%)
• HGBCL	• TFL: 0 (0.0%)	• Other: 5 (2.78%)	• TFL: 0 (0.00%)
• TFL	• B-NHL: 4 (1.61%)	• NR: 17 (9.44%)	• B-NHL: 4 (5.80%)
• B-NHL	• Other: 7 (2.81%)		• Other: 2 (2.90%)
• Other	• NR: 17 (6.83%)		
Best overall response to first-line therapy	• CR: 79 (31.73%)	• CR: 46 (25.6%)	• CR: 33 (47.82%)
• Complete response (CR)	• PR: 78 (31.32%)	• PR: 60 (33.3%)	• PR: 18 (28.09%)
• Partial response (PR)	• SD: 12 (4.82%)	• SD: 11 (6.11%)	• SD: 1 (1.44%)
• Stable disease (SD)	• PD: 79 (31.73%)	• PD: 63 (35.0%)	• PD: 16 (23.19%)
• Progressive disease (PD)	• Not evaluated: 1 (0.40%)		• Not evaluated: 1 (1.44%)

B-NHL: B-cell non-Hodgkin lymphoma; DLBCL: diffuse large B-cell lymphoma; ECOG: Eastern Cooperative Oncology Group; HGBCL: high-grade B-cell lymphoma; NR: not reported; TFL: transformed follicular lymphoma.

Efficacy

Efficacy analyses included 178 and 69 leukapheresed patients from ZUMA-7 and ALYCANTE, respectively, of which 170 and 62 received axi-cel. For all TTE, trends were very similar between the trials, see Table 2. Subgroup analysis for age in ZUMA-7 (< 65 and ≥ 65 years at baseline) did not show statistically significant differences between the groups, nor did the ZUMA-7 subgroups differ to ALYCANTE. EFS is presented for all populations, including subgroups, in Figure 1.

Table 2. Efficacy results

	Pooled	ZUMA-7	ALYCANTE
CMR, month 3	55.6%	51.2%	67.7%
ORR, month 12	46.6%	46.5%	46.8%
DOR, month 12	61.0%	60.6%	62.1%
EFS, month 24	45.2%	45.2%	44.7%
PFS, month 24	47.4%	47.6%	46.8%
OS, month 24	64.9%	62.8%	70.8%

Safety

Safety data from ZUMA-7 (N=170) and ALYCANTE (N=62) showed that all infused patients experienced at least one TEAE (Table 3). Table 4 displays causes of mortality across the populations.

Table 3. TEAEs in the pooled, ZUMA-7 and ALYCANTE populations

TEAE	Pooled N = 232	ZUMA-7 N = 170	ALYCANTE N = 62
Any TEAE	232 (100.00%)	170 (100.00%)	62 (100.00%)
- Worst Grade ≥ 3	210 (90.52%)	155 (91.18%)	55 (88.71%)
Any serious TEAE	118 (50.86%)	95 (55.88%)	23 (37.10%)
- Worst Grade ≥ 3	95 (40.95%)	78 (45.88%)	17 (27.42%)
Any TE neurologic event	135 (58.19%)	103 (60.59%)	32 (51.61%)
- Worst Grade ≥ 3	46 (19.83%)	36 (21.18%)	10 (16.13%)
Any TE CRS	215 (92.67%)	157 (92.35%)	58 (93.55%)
- Worst Grade ≥ 3	14 (6.03%)	11 (6.47%)	3 (4.84%)
Any TE neutropenia	156 (67.24%)	122 (71.76%)	34 (54.84%)
- Worst Grade ≥ 3	150 (64.66%)	119 (70.00%)	31 (50.00%)
Any TE thrombocytopenia	78 (33.62%)	50 (29.41%)	28 (45.16%)
- Worst Grade ≥ 3	45 (19.40%)	25 (14.71%)	20 (32.26%)
Any TE anemia	98 (42.24%)	73 (42.94%)	25 (40.32%)
- Worst Grade ≥ 3	64 (27.59%)	51 (30.00%)	13 (20.97%)
Any TE bacterial infections	26 (11.21%)	18 (10.59%)	8 (12.90%)
- Worst Grade ≥ 3	10 (4.31%)	8 (4.71%)	2 (3.23%)
Any fatal TEAE	18 (7.76%)	18 (10.59%)	1 (1.61%)

CRS, cytokine release syndrome; TE(AE), treatment-emergent (adverse event).

Table 4. Subject incidence of death, including causes of death*

Patient numbers (%)*	Pooled N = 232	ZUMA-7 N = 170	ALYCANTE N = 62
Subjects who died	93 (40.09%)	74 (43.53%)	19 (30.65%)
Primary cause of death			
Progressive disease	63 (27.16%)	51 (30.00%)	12 (19.35%)
Adverse event	13 (5.60%)	8 (4.71%)	5 (8.06%)
Secondary malignancy	2 (0.86%)	2 (1.18%)	0 (0.00%)
Other (total excluding COVID-19)	15 (6.47%)	13 (7.65%)	2 (3.23%)

**All causes of death excluded individuals with COVID-19 related deaths.*

HRQoL

HRQoL patterns were generally consistent across ZUMA-7 and ALYCANTE. Longitudinal analyses of mean changes in EORTC QLQ-C30 global health status (GHS), physical function (PF), and EQ-5D-5L VAS are presented in Figure 2. While both trials showed early declines in GHS and PF at Day 50, followed by recovery and improvement, only ALYCANTE reached clinical significance in GHS recovery by Month 24. Baseline GHS and PF scores in both trials (GHS: 68.6 & 68.1; PF: 83.5 & 86.4) were comparable to general population norms (GHS: 66.1; PF: 85.1).[3]

Figure 1. EFS for the pooled, ZUMA-7, ZUMA-7 for patients aged ≥ 65 years, ZUMA-7 for patients aged < 65 years and ALYCANTE populations

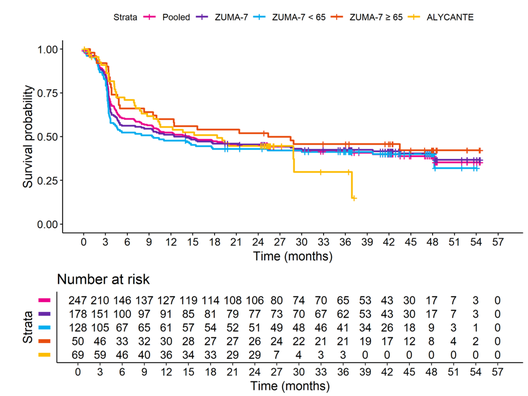
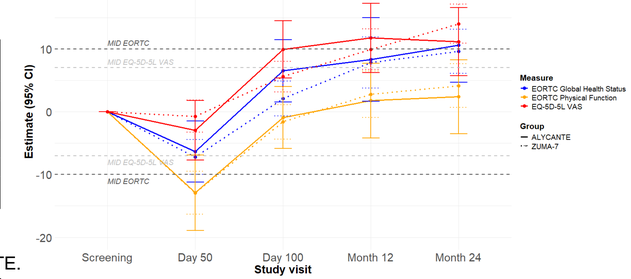


Figure 2. Estimated Change from Baseline
EORTC QLQ-C30 Global Health Status, Physical Function, and EQ-5D-5L VAS



CONCLUSIONS

Pooled data from ZUMA-7 and ALYCANTE demonstrate that axi-cel provides consistent and durable efficacy, predictable safety, and meaningful HR-QoL benefits in patients with R/R LBCL, regardless of ASCT eligibility. These results support the use of axi-cel as a standard 2L therapy, offering lasting responses with manageable toxicity across a broad patient population, including those ineligible for ASCT.

These findings are based on an unadjusted analysis and should be interpreted accordingly. The feasibility of pooling axi-cel patients from ZUMA-7 and ALYCANTE while adjusting for potential differences between the patient populations is currently being explored. As such, a limitation of these results is that the generalizability of these findings is to be confirmed.

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CONTACT INFORMATION

Professor Roch Houot, MD, PhD

CHU Rennes, Rennes, France

Email: roch.houot@chu-rennes.fr