Patient-Reported Outcomes in a Phase 3, Randomized, Open-Label Study Evaluating the Efficacy of Axicabtagene Ciloleucel (Axi-Cel) Versus Standard of Care Therapy in Patients With Relapsed/Refractory Large B-Cell Lymphoma (ZUMA-7)

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Disclosures

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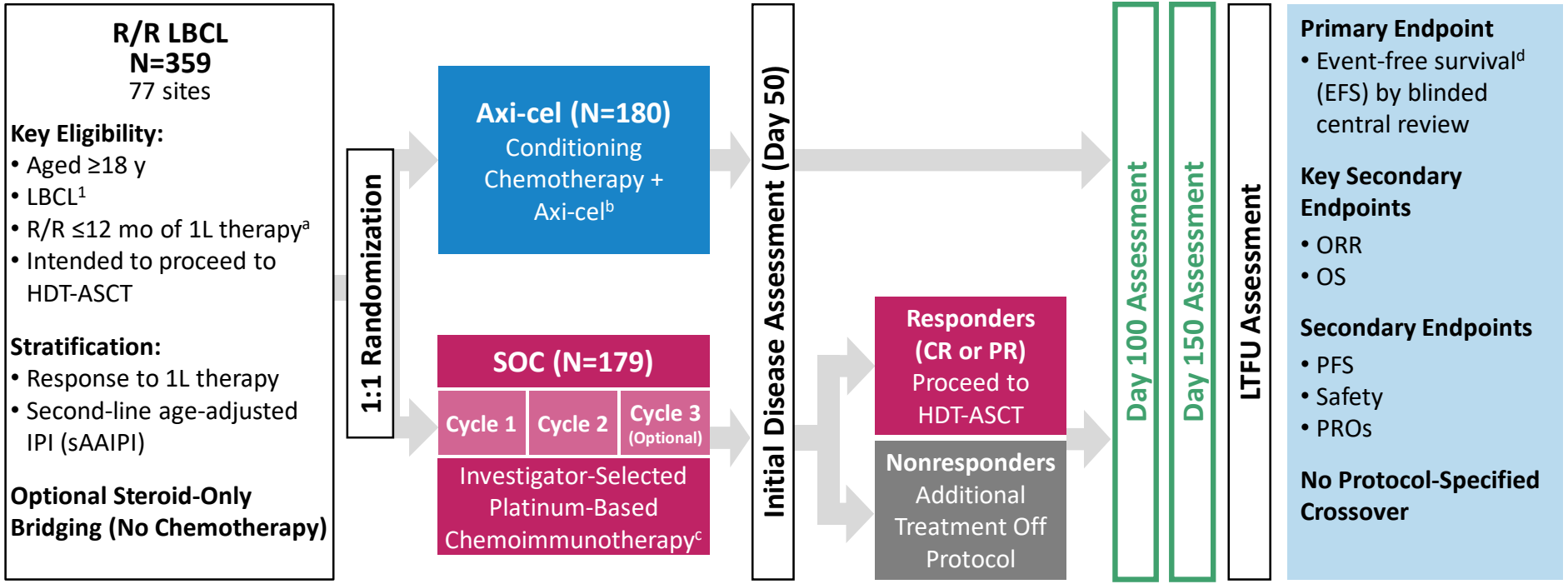
Background

- Outcomes are poor for patients with LBCL who relapse early or are refractory to first-line therapy. Furthermore, patients receiving second-line SOC therapy often report poor health-related QoL[1]
- ZUMA-7 (NCT03391466) is a pivotal Phase 3, randomized, open-label, multicenter study of axi-cel (an autologous anti-CD19 CAR T-cell therapy) versus SOC in second-line R/R LBCL
  - Primary analysis results will be presented at ASH 2021 (plenary, December 12)
- Axi-cel is an approved therapy for patients with relapsed or refractory LBCL after 2 or more lines of therapy
  - ZUMA-1 (NCT02348216) investigated the safety and efficacy of axi-cel in patients with refractory LBCL
  - A long-term follow-up analysis recently presented at ASH 2021 demonstrated a 5-year OS rate of 43% after a median follow-up of 63 months[2]
- Here, we report the first comparative analysis of PROs with CAR T-cell therapy versus SOC as second-line treatment in R/R LBCL in ZUMA-7

1. Lin V, et al. *J Clin Oncol*. 2020;38(15_suppl):e20070. 2. Jacobson CA, et al. ASH 2021. Abstract #1764.

ZUMA-7 Study Schema and Endpoints: Axi-Cel Versus SOC as Second-Line Therapy in Patients With R/R LBCL



1. Swerdlow SH, et al. *Blood.* 2016;127:2375-2390. 2. Cheson BD, et al. *J Clin Oncol.* 2014;32:3059-3068.

[a] Refractory disease was defined as no CR to 1L therapy; relapsed disease was defined as CR followed by biopsy-proven disease relapse ≤12 months from completion of 1L therapy. [b] Axi-cel patients underwent leukapheresis followed by conditioning chemotherapy with cyclophosphamide (500 mg/m^2/day) and fludarabine (30 mg/m^2/day) 5, 4, and 3 days before receiving a single axi-cel infusion (target intravenous dose, 2×10^6 CAR T cells/kg). [c] Protocol-defined SOC regimens included R-GDP, R-DHAP, R-ICE, or R-ESHAP. [d] EFS was defined as time from randomization to the earliest date of disease progression per Lugano Classification,[2] commencement of new lymphoma therapy, or death from any cause.

PRO Instruments and Schedule of Assessments

PRO instruments

Instrument	Description	Scales/Domains
EORTC QLC-C30	Cancer-specific 30-item questionnaire including global health status, functional, and symptom scales[1-2]	• Functional scales: physical, role, emotional, cognitive, and social functioning • Symptom scales: fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties
EQ-5D-5L	General questionnaire with 5 QoL domains plus a global assessment[3-4]	• Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression • Visual analog scale (VAS) rating of global assessment of their current (day of assessment) state of health
Work Productivity and Activity Impairment: General Health (WPAI)	Measure of work productivity and activity impairment[5]	• Absenteeism, presenteeism, overall work impairment, and activity impairment

Schedule of assessments

- Baseline (prior to treatment), Day 50, Day 100, Day 150, Month 9, and every 3 months thereafter from randomization up to 24 months or time of EFS event (disease progression, death from any cause, or new lymphoma therapy), whichever occurred first

1. Aaronson NK, et al. *J Natl Cancer Inst*. 1993;85(5):365-76. 2. Fayers P, et al. The EORTC QLQ-C30 Scoring Manual (3rd Edition). Published by: European Organisation for Research and Treatment of Cancer, Brussels 2001. 3. Herdman M, et al. *Qual Life Res*. 2011;20(10):1727-36. 4. Pickard AS, et al. *Value Health*. 2019;22(8):931-41. 5. Reilly MC, et al. *Pharmacoeconomics*. 1993;4(5):353-65.

Analysis Population and Statistical Methods

Analysis Population (QoL Analysis Set)

- All patients who had a baseline PRO and ≥1 measure completed at Day 50, Day 100, or Day 150

Statistical Methods

- Prespecified hypotheses for 3 PRO domains (EORTC QLQ-C30 Physical Functioning, EORTC QLQ-C30 Global Health Status/QoL, and EQ-5D-5L visual analog scale [VAS]) were tested using a mixed-effect model with repeated measures at Day 100 and subsequent time points if previous time points were statistically significant
- A clinically meaningful change was defined as 10 points for each EORTC QLQ-C30 score, 7 points for EQ-5D-5L VAS score, and 0.06 for the EQ-5D-5L index[1,2]
- Exploratory analyses on other domains of EORTC QLQ-C30 and EQ-5D-5L were also performed[1-3]

1. Maringwa JT, et al. *Support Care Cancer.* 2011;19(11):1753-60. 2. Pickard AS, et al. *Health Qual Life Outcomes.* 2007;5:70. 3. Thieblemont C, et al. *Br J Haematol.* 2020;189(1):84-96.

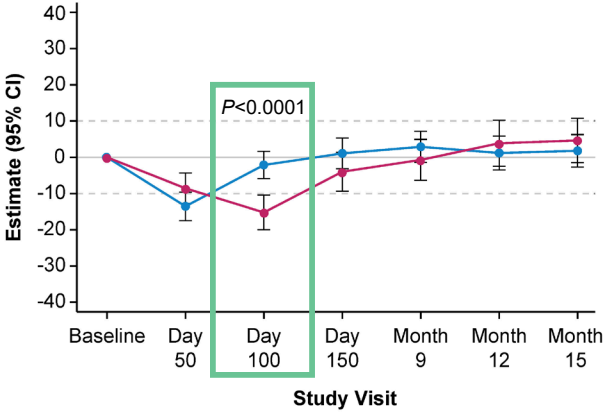
Baseline Demographic and Clinical Characteristics: QoL Analysis Set

Characteristic, n (%)	Axi-cel N=165	SOC N=131	Overall N=296
Age ≥65 years	46 (28)	42 (32)	88 (30)
sAAIPI of 2-3	69 (42)	56 (43)	125 (42)
Response to 1L therapy at randomization			
Primary refractory	119 (72)	89 (68)	208 (70)
Relapse ≤12 mo of 1L therapy	46 (28)	42 (32)	88 (30)
Double/triple hit status per investigator			
HGBL (double-/triple-hit)	35 (21)	22 (17)	57 (19)
Negative	102 (62)	76 (58)	178 (60)
Not tested	28 (17)	33 (25)	61 (21)

- Of 359 patients enrolled in the ZUMA-7 study, 296 patients (82%) had baseline PROs and ≥1 follow-up measure and were included for analysis (QoL analysis set)
- Overall, 70% of patients had primary refractory disease, 42% had high sAAIPI (2-3), and 30% were ≥65 years old
- Using Global Health Status/QoL as a representative measure of the EORTC QLQ-C30, 208 patients (70%) completed the Day 100 assessment (88% axi-cel; 47% SOC)

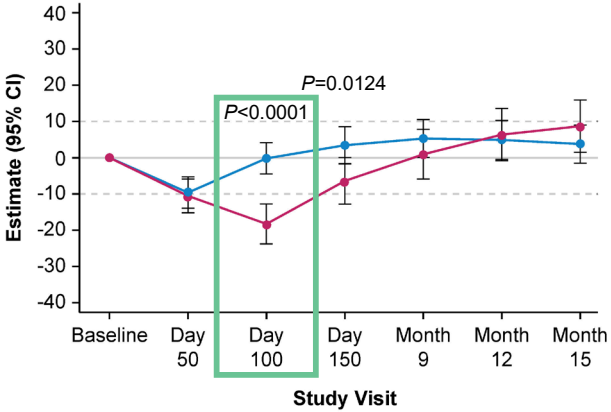
Change From Baseline for Prespecified PRO Endpoints

EORTC QLQ-C30 Physical Functioning



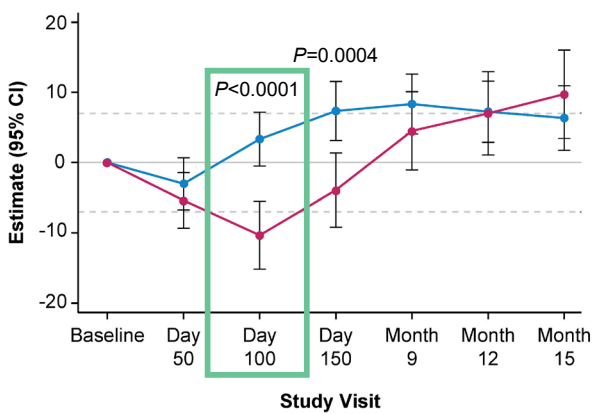
Axi-cel	164	163	146	109	88	79	67
SOC	131	126	64	56	40	33	26

EORTC QLQ-C30 Global Health Status/QoL



Axi-cel	165	163	146	110	88	79	67
SOC	130	125	62	56	40	33	26

EQ-5D-5L VAS



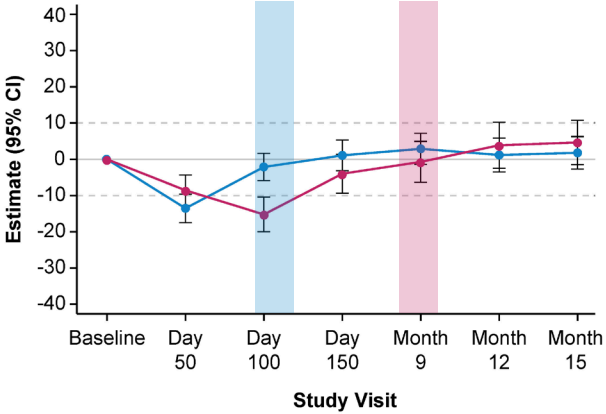
Axi-cel	165	163	145	110	88	80	67
SOC	129	126	65	56	40	32	26

- For patients in the QoL analysis set treated with axi-cel versus SOC, there was a statistically significant and clinically meaningful difference in mean change of scores from baseline at Day 100 in favor of axi-cel on all prespecified PRO domains
  - Sensitivity analyses controlling for covariates and patterns of missingness showed similar results with retained significance at Day 100

Evaluated via mixed-effect model with repeated measures. Statistical significance and clinical meaningfulness coincide for all except for EORTC QLQ-C30 Global Health Status/QoL at Day 150, which was less than a 10-point change (9.8).

Return to Baseline for Prespecified PRO Endpoints

EORTC QLQ-C30 Physical Functioning



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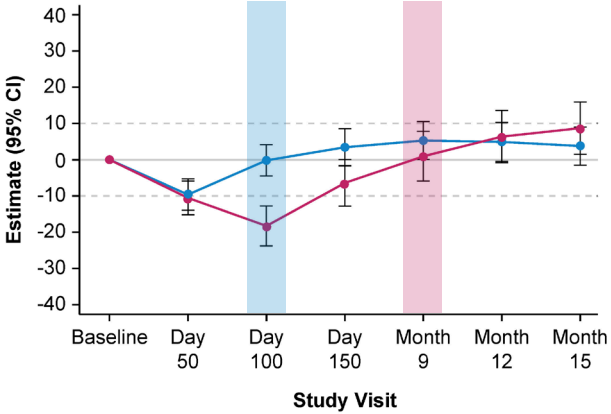
EORTC QLQ-C30 Global Health Status/QoL



Axi-cel	165	163	146	110	88	79	67
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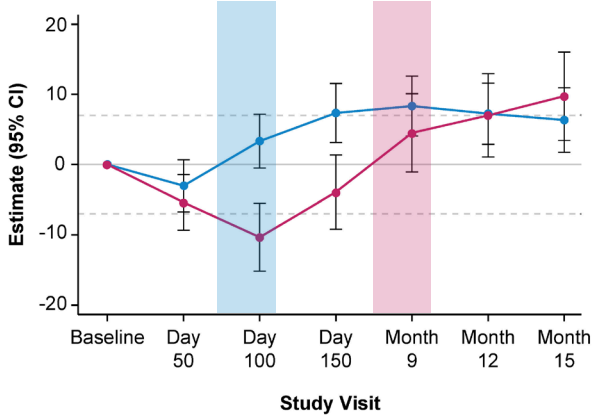
EQ-5D-5L VAS

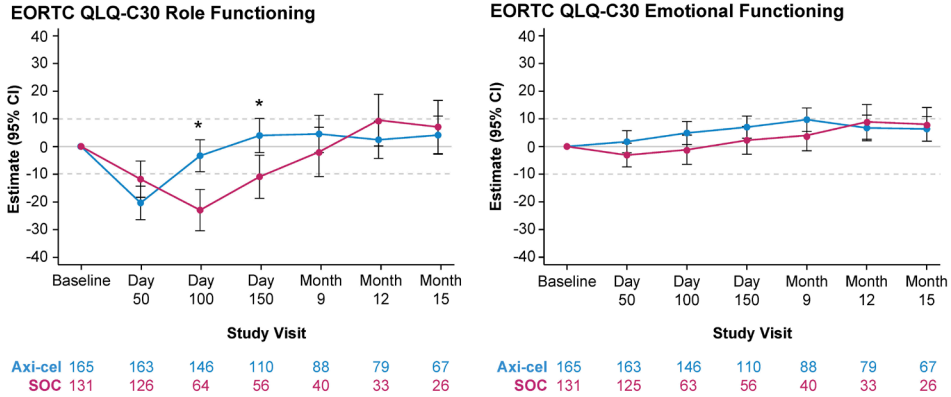


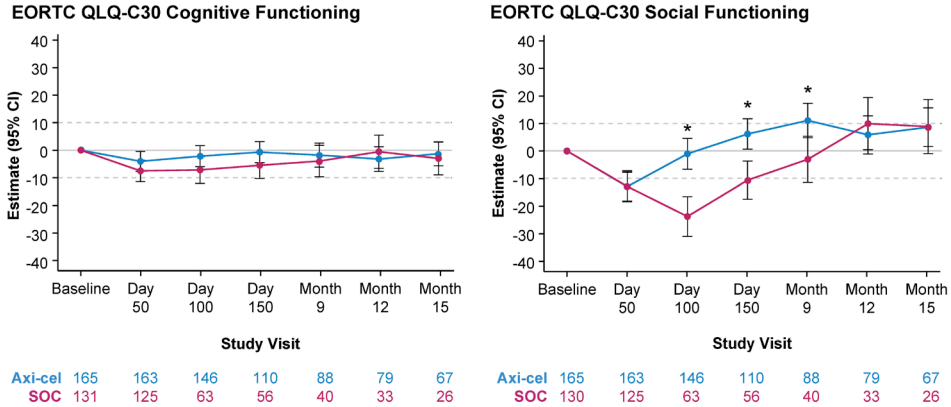
Axi-cel	165	163	145	110	88	80	67
SOC	129	126	65	56	40	32	26

- The mean estimated scores for the axi-cel arm returned to or exceeded scores at baseline by Day 100 – Day 150 (Months 3 – 5) versus Month 9 or later for the SOC arm

Evaluated via mixed-effect model with repeated measures. Statistical significance and clinical meaningfulness coincide for all except for EORTC QLQ-C30 Global Health Status/QoL at Day 150, which was less than a 10-point change (9.8). Shading indicates when the QOL measure is not statistically different from baseline.

Change From Baseline for EORTC QLQ-C30 Functional Scales

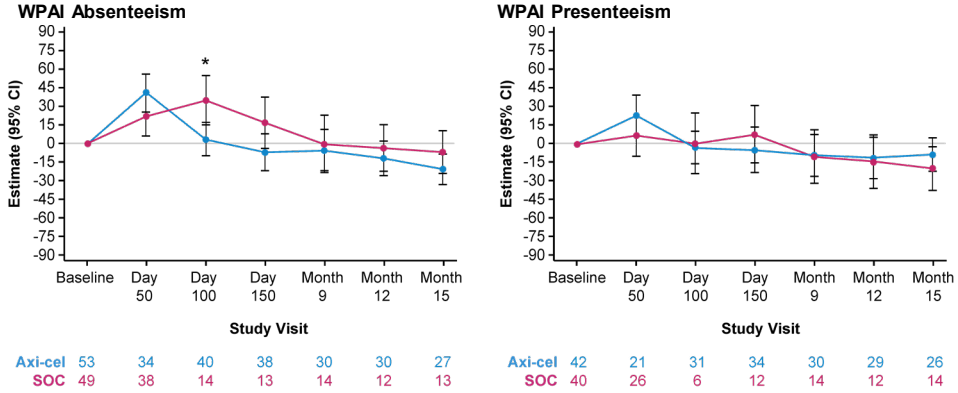


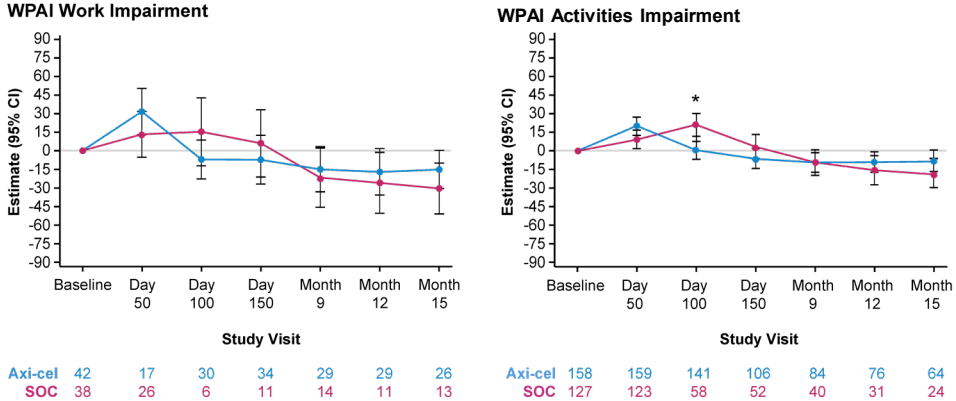


- Additional exploratory analyses of PRO endpoints also showed improvements with axi-cel over SOC
- The differences in change from baseline were statistically significant ($P<0.05$) in favor of axi-cel for
  - Nausea and vomiting, diarrhea, insomnia, and appetite loss measures at Day 100
  - Role functioning at Day 100 and Day 150
  - Social functioning, fatigue, and dyspnea measures at Day 100, Day 150, and Month 9

Evaluated via mixed-effect model with repeated measures. Symptom scales not shown. *$P<0.05$.

Change From Baseline for Work Productivity and Activity Impairment





- Patients treated with axi-cel had statistically significant (P<0.05) lower mean absenteeism and lower mean activities impairment at Day 100

Evaluated via mixed-effect model with repeated measures. *P<0.05. WPAI activities impairment included both employed and not employed patients. The other three questions were asked of employed patients only.

Conclusions

- ZUMA-7, the first randomized, global, multicenter Phase 3 study of axi-cel versus SOC in second-line R/R LBCL, demonstrates that treatment with axi-cel results in clinically meaningful improvement in QoL over SOC at Day 100 as measured by multiple validated PRO instruments
  - Score comparisons at later timepoints warrant cautious interpretation because attrition due to disease progression, new lymphoma therapy, or death was disproportionately higher on the SOC arm and may select patients with the best outcomes
- The data also suggest faster recovery to pretreatment QoL with axi-cel compared with SOC
- The superior clinical outcomes and patient experience with axi-cel over SOC should help inform treatment choices in second-line R/R LBCL

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