YESCARTA® (axicabtagene ciloleucel): Results of the ZUMA-7 Phase 3 Study

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The following information regarding the ZUMA-7 study is provided below as a professional courtesy in response to your unsolicited request.

Summary

Methods

The ZUMA-7 study is a randomized, open-label, multicenter, phase 3 study to assess the safety and efficacy of YESCARTA versus standard care as second-line therapy in patients with relapsed or refractory large B-cell lymphoma (LBCL) after failure of conventional first-line therapy.

Patients in the YESCARTA arm received low-dose lymphodepleting chemotherapy before receiving a single intravenous (IV) infusion of YESCARTA at a target dose of 2×10^6 CAR T cells/kg.

Patient Characteristics

Between January 25, 2018 and October 4, 2019, 359 patients were enrolled, including 180 in the YESCARTA arm and 179 in the standard-care arm. Of the patients enrolled in the YESCARTA arm, 170 (94%) patients received YESCARTA infusions. The median turnaround time from leukapheresis to product delivery to the trial site was 18 days. Of the 179 patients enrolled in the standard-care arm, 64 (36%) patients received high-dose therapy with autologous stem cell transplant (HDT-ASCT). Baseline characteristics were generally balanced between the YESCARTA and standard-care arms.

Efficacy

After a median follow-up of 24.9 months, YESCARTA was associated with significantly longer event-free survival (EFS, primary endpoint) than standard care (median EFS, 8.3 vs 2 months, respectively; stratified hazard ratio [HR], 0.40; 95% CI, 0.31–0.51; p<0.001). The estimated EFS rates at 24 months were 41% in the YESCARTA arm and 16% in the standard-care arm. Patients who received YESCARTA had significantly higher objective response rate (ORR) than those who received standard care (83% vs 50%, respectively; p<0.001). Complete response (CR) rates were 65% for patients who received YESCARTA and 32% for those who received standard care.

Results of the prespecified primary overall survival analysis was analyzed at 5 years after the first patient underwent randomization. At a median follow-up of 47.2 months (range 39.8 to 60.0), death was reported in 82 patients in the YESCARTA arm and 95 patients in the standard-care arm. The primary analysis of OS showed a significant improvement in overall survival with YESCARTA over standard care (HR of 0.73; 95% CI, 0.54 - 0.98; stratified two-sided log-rank p-value = 0.03). Median OS was not reached (95% CI, 28.6 months–NE) with YESCARTA, and was 31.1 months (95% CI, 17.1–NE) with standard care.

Approved for Use on 06 Aug 2024

The efficacy analysis as reported in the YESCARTA US Prescribing Information (USPI) is based on the FDA's clinical evaluation of the ZUMA-7 study data. Please see the full Prescribing Information for additional information on efficacy of YESCARTA in the ZUMA-7 study.

Safety

As part of the FDA adjudication, two patients received non-conformal products and was thus excluded from the safety analysis population. One hundred sixty-eight patients were included in the FDA's adjudicated safety analysis.

All patients experienced adverse events (AEs) of any grade. Grade ≥3 AEs were reported in 155/170 (91%) patients in the YESCARTA arm and in 140/168 (83%) of patients in the standard-care arm.

Grade ≥ 3 cytokine release syndrome (CRS) occurred in 11/170 (6%) patients who received YESCARTA. Grade ≥ 3 neurologic events occurred in 36/170 (21%) patients who received YESCARTA and in 1/168 (1%) patients who received standard care.

The safety outcomes in the USPI were based on the FDA's clinical evaluation of the ZUMA-7 study data. Please see the full Prescribing Information for additional information on safety of YESCARTA in the ZUMA-7 study.

The full indication, important safety information, and boxed warnings are available at:

https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.pdf

ZUMA-7 Phase 3 Study (NCT03391466)

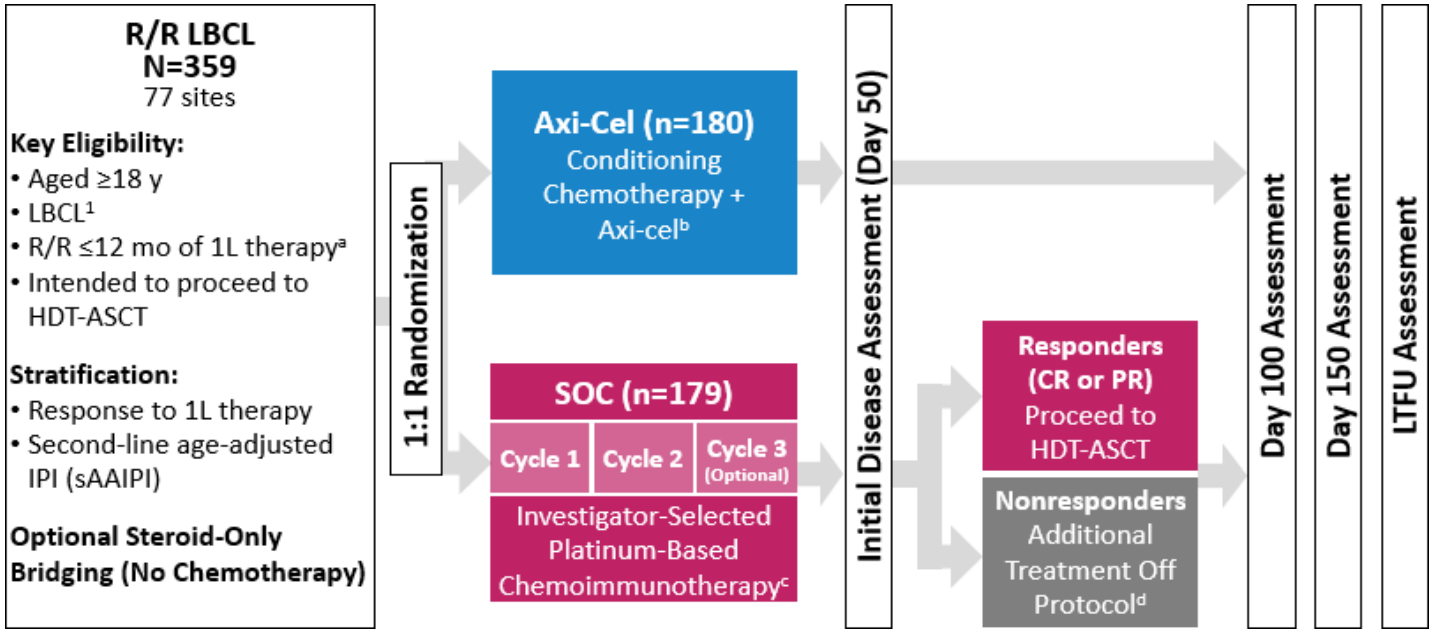
Methods

Study Design and Participants[1-3]

ZUMA-7 is a randomized, open-label, multicenter, phase 3 study conducted at 77 sites worldwide to assess the safety and efficacy of YESCARTA versus standard care as second-line therapy in patients with relapsed or refractory LBCL after failure of conventional first-line therapy. After screening, eligible patients were randomized 1:1 to YESCARTA or investigator-selected standard care. Stratification was according to response to first-line therapy and second-line age-adjusted IPI (sAAIPI).

Figure 1. ZUMA-7 Study Design[1,3]

Figure adapted with permission from Locke et al. ASH 2021.



[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]YESCARTA (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 YESCARTA infusion (target intravenous dose, 2×10^6 CAR T cells/kg).
[c]Protocol-defined standard-care regimens included R-GDP, R-DHAP, R-ICE, or R-ESHAP.
[d]56% of patients received subsequent cellular immunotherapy.
Abbreviations: 1L=first-line; CR=complete response; HDT-ASCT= high-dose therapy with autologous stem cell transplant; IPI= International Prognostic Index; LBCL=large B-cell lymphoma; PR=partial response; R/R=relapsed or refractory.

Key eligibility criteria:

- Adults ≥ 18 years of age
- Refractory or relapsed LBCL (including diffuse large B-cell lymphoma [DLBCL], high grade B-cell lymphoma with or without *MYC* and B-cell lymphoma 2 [*BCL2*] and/or *BCL6* rearrangement, DLBCL arising from follicular lymphoma, and T-cell/histiocyte-rich large B-cell lymphoma), and intended to proceed to HDT-ASCT
    - Refractory disease defined as no complete remission to first-line therapy
    - Relapsed disease defined as complete remission to first-line therapy followed by biopsy-proven disease relapse ≤12 months after completion of first-line therapy
- Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1
- Received prior anti-CD20 monoclonal antibody therapy and an anthracycline-containing chemotherapy regimen
- Adequate organ function

Key exclusion criteria:

- Previous autologous stem cell transplantation (ASCT) or allogeneic stem cell transplantation (alloSCT)
- Received prior CD19-targeted therapy or CAR T-cell therapy
- >1 line of therapy for DLBCL

Patients randomized to the YESCARTA arm underwent leukapheresis to obtain peripheral blood mononuclear cells for YESCARTA production. Before receiving YESCARTA, patients received a lymphodepleting chemotherapy regimen consisting of IV 30 mg/m^2/day fludarabine and 500 mg/m^2/day cyclophosphamide on days -5, -4, and -3. On day 0, patients received a single IV infusion of YESCARTA at a target dose of 2 × 10^6 CAR T cells/kg. Bridging therapy was optional and only corticosteroids were permitted. Patients in the standard-care arm received 2-3 cycles of investigator-selected platinum-based chemoimmunotherapy. Patients who achieved a CR or a partial response (PR) went on to receive HDT-ASCT. Patients who failed to respond to standard care could receive cellular immunotherapy off protocol (treatment switch), even though there was no planned crossover between the study arms. Toxicity management followed that of the ZUMA-1 pivotal study cohorts.

Endpoints[1]

The primary endpoint was EFS according to blinded central review, defined as time from randomization to the earliest date of disease progression per Lugano Classification, commencement of new lymphoma therapy, death from any cause, or a best response of stable disease up to and including the response on the day 150 assessment after randomization).

Secondary endpoints included:

- ORR
- OS
- Investigator-assessed EFS
- Progression-free survival (PFS)
- Incidence of AEs
- Patient-reported outcomes (PROs)

Endpoints were assessed on Days 50, 100, and 150 after randomization, followed by every 3 months until 2 years of follow-up, and then every 6 months until 5 years of follow-up.

Statistical Analysis[1,3]

The primary efficacy analysis was to be conducted when 250 events by blinded central review were observed, which provides approximately 90% power at the 1-sided 2.5% significance level to detect an EFS improvement of 50%. Statistical testing was conducted hierarchically for the primary and key secondary end points.

- A subgroup analysis of EFS was conducted for predefined covariates.
- ORR was tested at the 2.5% level at the time of the primary EFS analysis, if a statistically significant improvement in EFS was found.
- A prespecified primary overall survival analysis was analyzed at 5 years after the first patient underwent randomization.

Efficacy analyses included all randomized patients (intent-to-treat population). Safety analyses included all randomized patients who received ≥1 dose of YESCARTA or standard care; patients were analyzed by the therapy received according to the protocol (patients were analyzed according to the protocol therapy they received).

Table 1. Summary of Analyses[1,3,6,8]

	Primary Efficacy Analysis	Primary OS Analysis
Data cutoff date	March 18, 2021	January 25, 2023
Median duration of follow-up	24.9 months	47.2 months
Efficacy Analysis		
Number of patients	Overall, n=359 YESCARTA, n=180 Standard care, n=179	
Disease response assessed by	Blinded central review	Log-rank test stratified according to randomization factors
Safety Analysis		
Number of patients	Overall, n=338 YESCARTA, n=170 Standard care, n=168	

Disposition and Manufacturing

Disposition[3]

Between January 25, 2018 and October 4, 2019, 359 patients were enrolled, including 180 in the YESCARTA arm and 179 in the standard-care arm.

- Of patients in the YESCARTA arm:
  - Two patients did not undergo leukapheresis due to progressive disease (PD) (n=1) and other reasons (n=1)
  - Six patients did not proceed to lymphodepleting chemotherapy due to AEs (n=2), death (n= 2), PD (n=1), or other reasons (n=1)
  - Two patients received lymphodepleting chemotherapy but did not proceed to YESCARTA infusion due to AEs
  - Overall, 170 (94%) patients received YESCARTA infusion
- Of patients in the standard-care arm:
  - Eleven patients did not receive ≥1 dose of salvage chemotherapy due to patient request (n=8), lost to follow-up (n=1), or other reasons (n=2)
  - Of the 168 patients that receive ≥1 dose of salvage chemotherapy, 88 patients could not proceed due to PD (n=56), SD (n=27), AE (n=1) and other reasons (n=4)
  - Of the 80 patients who responded to salvage chemotherapy, 11 did not undergo leukapheresis due to PD (n=9), AE (n=1), and insufficient response (n=1)
  - A total of 64 (36%) patients received HDT-ASCT; five patients did not receive HDT due to PD

Time From Leukapheresis to YESCARTA Delivery[1]

In patients who received YESCARTA (n=170), the median turnaround time from leukapheresis to YESCARTA delivery to the trial site was 18 days. YESCARTA was successfully manufactured for 100% (178 of 178) of patients who underwent leukapheresis; 94% (170 of 180) of patients received treatment.

Patient Characteristics

Baseline Patient Characteristics[1,3]

Baseline characteristics were generally balanced between the YESCARTA and standard-care arms (Table 2). Overall, patients had a median age of 59 years, 74% had primary refractory disease, 45% had high sAAIPI (2-3), 54% had high lactate dehydrogenase, 79% had stage III-IV disease, and 16% had high-grade B-cell lymphoma (HGBL, including double-/triple-hit lymphoma) according to central laboratory.

Table 2. Baseline Patient Characteristics[1,3]

	YESCARTA (n=180)	Standard Care (n=179)	Overall (N=359)
Age, years, median (range)	58 (21–80)	60 (26–81)	59 (21–81)
≥65 years, n (%)	51 (28)	58 (32)	109 (30)
Male, n (%)	110 (61)	127 (71)	237 (66)
ECOG performance status of 1, n (%)	85 (47)	79 (44)	164 (46)
Disease stage, n (%)			
I or II	41 (23)	33 (18)	74 (21)
III or IV	139 (77)	146 (82)	285 (79)
sAAIPI of 2-3[a], n (%)	82 (46)	79 (44)	161 (45)
Response to 1L therapy, n (%)			
Primary refractory	133 (74)	131 (73)	264 (74)
Relapse ≤12 months of 1L therapy	47 (26)	48 (27)	95 (26)
Disease type according to central laboratory, n (%)			
DLBCL[a]	126 (70)	120 (67)	246 (69)
HGBL, not otherwise specified	0	1 (1)	1 (<1)
HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both	31 (17)	25 (14)	56 (16)
Elevated LDH level[b], n (%)	101 (56)	94 (53)	195 (54)
Positive CD19 status by immunohistochemistry per central laboratory[c], n (%)	144 (80)	134 (75)	278 (77)
Bone marrow involvement[d], n (%)	17 (9)	15 (8)	32 (9)
Tumor burden per central laboratory[e], mm^2, median (range)	2123 (181–22538)	2069 (252–20117)	2118 (181–22538)

[a]Definition of DLBCL, according to central read, included cases of incomplete evaluation that were due to inadequate sample amount or sample type, for which further classification of the subtype was not possible. DLBCL, not otherwise specified, is also included.
[b]Lactate dehydrogenase level greater than upper limit of normal per local laboratory reference range.
[c]CD19 staining was not required for participation in the study.
[d]As collected on the diagnosis history case report form.
[e]Tumor burden was measured by sum of product diameters of target lesions per Cheson criteria and assessed by central laboratory.
Abbreviations: 1L=first-line; ECOG=Eastern Cooperative Oncology Group; LDH=lactate dehydrogenase; sAAIPI=Second-line age-adjusted International Prognostic Index.

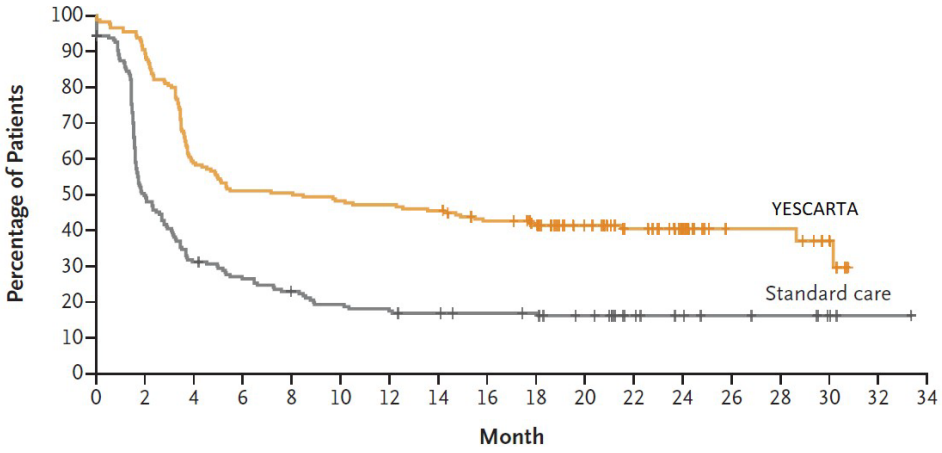
Efficacy

The primary efficacy analysis as reported in the YESCARTA USPI are based on FDA's clinical evaluation of the ZUMA-7 study data. Please see the full Prescribing Information for additional information on efficacy of YESCARTA in the ZUMA-7 study.

EFS[1,3,6]

After a median follow-up of 24.9 months, YESCARTA was associated with significantly longer EFS than standard care (median, 8.3 vs 2 months, respectively), with a stratified HR of 0.40 (95% CI, 0.31–0.51; p<0.001) (Figure 2). The estimated EFS rates at 24 months were 41% in the YESCARTA arm and 16% in the standard-care arm. Improvements in EFS for YESCARTA in comparison to standard care were consistent across key patient subgroups (including age [<65 vs ≥65 years], response to first-line therapy at randomization, sAAIPI, and prognostic markers per central laboratory).

Figure 2. Event-Free Survival (Primary Efficacy Endpoint)[1,3]



	No. of Patients	Median Event-free Survival (95% CI)
		mo
YESCARTA	180	8.3 (4.5–15.8)
Standard Care	179	2.0 (1.6–2.8)

Stratified hazard ratio for event or death, 0.40 (95% CI, 0.31–0.51)
P<0.001

No. at Risk

YESCARTA	180	163	106	92	91	87	85	82	74	67	52	40	26	12	12	6	
Standard care	179	86	54	45	38	32	29	27	25	24	20	12	9	7	6	3	1	0

Figure adapted with permission from *N Engl J Med.*
Abbreviations: CI=confidence interval; mo=months; no.=number.

Distinct from the primary endpoint of EFS per central review, a secondary endpoint of median EFS per investigator assessment continues to be assessed after the primary EFS analysis. Median investigator-assessed EFS was 10.8 months (95% CI, 5.0–25.5) with YESCARTA and 2.3 months (95% CI, 1.7–3.1) with standard care; estimated 4-year EFS rates of 38.9% and 17.3% were reported for YESCARTA and standard care, respectively (HR, 0.42; 95% CI, 0.33–0.55).

ORR, OS, and PFS[1,3,4,6-8]

Patients who received YESCARTA had significantly higher ORR than those who received standard care (83% vs 50%, respectively; p<0.001; difference of 33% or 1.66-fold improvement).

- CR rates were 65% for patients who received YESCARTA and 32% for those who received standard care

Results of the prespecified primary overall survival analysis was analyzed at 5 years after the first patient underwent randomization. At a median follow-up of 47.2 months (range 39.8 to 60.0), death was reported in 82 patients in the YESCARTA arm and 95 patients in the standard-care arm. The primary analysis of OS showed a significant improvement in overall survival with YESCARTA over standard care (HR of 0.73; 95% CI, 0.54 - 0.98; stratified two-sided log-rank p-value = 0.03).

- Median overall survival was not reached (95% CI, 28.6 months–NE) with YESCARTA, and was 31.1 months (95% CI, 17.1–NE) with standard care
- Estimated 4-year overall survival was 54.6% (95% CI, 47.0–61.6) with YESCARTA and 46.0% (95% CI, 38.4–53.2) with standard care
- Risk of death was reduced by 27.4% with YESCARTA vs chemotherapy and HDT-ASCT
- 57% (n=102/179) of patients received subsequent off-protocol cellular immunotherapy after receiving standard care

Figure 3. Overall Survival[8]

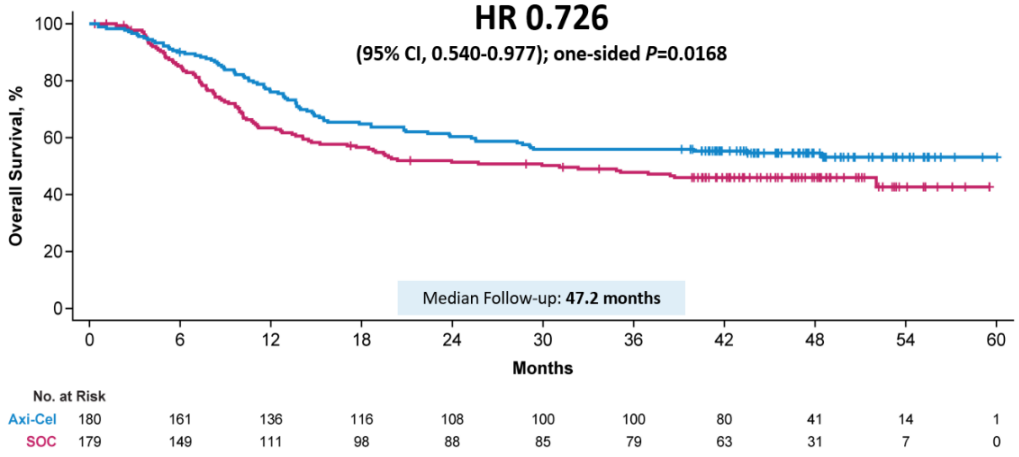


Figure adapted with permission from Westin et al. ASCO Meeting 2023.
Abbreviations: Axi-cel=axicabtagene ciloleucel; HR=hazard ratio; SOC=standard of care

Median PFS per investigator assessment was 14.7 months (95% CI, 5.4–43.5) in the YESCARTA arm and 3.7 months (95% CI, 2.9–5.3%) in the standard- care arm; stratified HR, 0.51 (95% CI, 0.38–0.67).

- Estimated 4 year PFS rate was 41.8% (95% CI, 34.1-49.2%) in the YESCARTA arm and 24.4% (95% CI, 17.2-32.2%) in the standard-care arm

Patient-Reported Outcomes[5]

The following PROs were compared between the YESCARTA and standard-care arms at baseline, Day 50, Day 100, Day 150, Month 9, and every 3 months thereafter from randomization through 24 months or time of EFS event, whichever occurred first:

- EORTC QLC-C30: cancer-specific 30-item questionnaire including global health status, functional, and symptom scales
- EQ-5D-5L: general questionnaire with 5 QoL domains plus a global assessment
- Work Productivity and Activity Impairment: General Health (WPAI): measure of work productivity and activity impairment

The QoL analysis set included all patients (Overall, N=296; YESCARTA, n=165; standard care, n=131) who had a baseline PRO assessment and ≥1 measure completed at Day 50, Day 100, or Day 150. A statistically significant and clinically meaningful difference was seen between the YESCARTA and standard-care arms in mean change of scores from baseline at Day 100 in favor of YESCARTA on all prespecified PRO domains, including EORTC QLC-C30 physical functioning, EORTC QLC-C30 global health status/QoL, and EQ-5D-5L visual analog scale (VAS) (Figure 4). The mean estimated scores for the YESCARTA arm returned to or exceeded scores at baseline by months 3-5, in comparison to month 9 or later for the standard-care arm. Patients in the YESCARTA arm had statistically significant (p<0.05) lower mean absenteeism and lower mean activities impairment at Day 100 compared with those in the standard-care arm.

Figure 4. Key Patient-Reported Outcomes

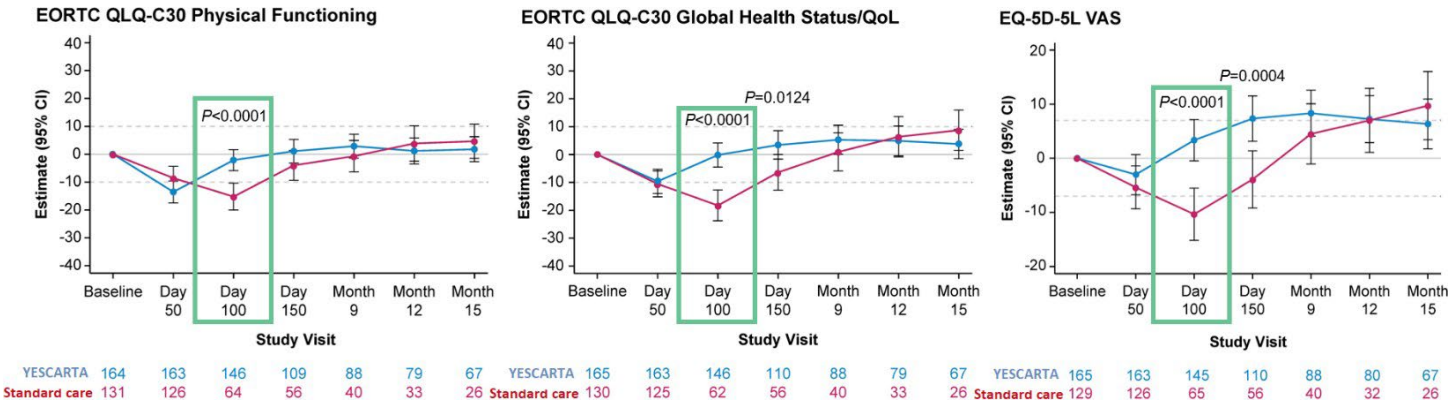


Figure adapted with permission from Elsawy et al. ASH 2021.
Abbreviations: CI=confidence interval; EORTC QLQ-C30=European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire; EQ-5D-5L=EuroQol 5 Dimension 5 Level; VAS=visual analog scale.

Safety

The safety outcomes as reported in the YESCARTA USPI were based on the FDA's clinical evaluation of the ZUMA-7 study data. Please see the full Prescribing Information for additional information on safety of YESCARTA in the ZUMA-7 study.

AEs[1,3,6,7]

All patients experienced ≥1 AE of any grade (Table 3).

- Grade ≥3 AEs were reported in 155/170 (91%) patients in the YESCARTA arm and in 140/168 (83%) of patients in the standard-care arm
    - The most commonly reported Grade ≥3 AE was neutropenia (YESCARTA, 69%; standard care, 41%)

Table 3. Summary of AEs[1,3]

Treatment-Emergent AEs, n (%)[a]	YESCARTA n=170		Standard Care n=168	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any AE	170 (100)	155 (91)	168 (100)	140 (83)
Pyrexia	158 (93)	15 (9)	43 (26)	1 (1)
Neutropenia[b]	121 (71)	118 (69)	70 (42)	69 (41)
Hypotension	75 (44)	19 (11)	25 (15)	5 (3)
Fatigue	71 (42)	11 (6)	87 (52)	4 (2)
Anemia	71 (42)	51 (30)	91 (54)	65 (39)
Diarrhea	71 (42)	4 (2)	66 (39)	7 (4)
Headache	70 (41)	5 (3)	43 (26)	2 (1)
Nausea	69 (41)	3 (2)	116 (69)	9 (5)
Sinus tachycardia	58 (34)	3 (2)	17 (10)	1 (1)
Leukopenia[c]	55 (32)	50 (29)	43 (26)	37 (22)

[a]Included are any AEs of any grade that occurred in ≥20% of patients in either the YESCARTA or standard-care cohort.
[b]Combined preferred terms of neutropenia and neutrophil count decreased.
[c]Combined preferred terms of leukopenia and white blood cell count decreased. Abbreviation: AE=adverse event.

In the YESCARTA arm, infections of any grade were reported in 76 (44.7%) patients and in 53 (31.5%) patients in the standard care arm. Grade 3 or higher infections were reported in 28 (16.5%) patients in the YESCARTA arm and 20 (11.9%) patients in the standard care arm.

Among all patients treated in the ZUMA-7 study, there was an increase in incidence of SAEs in the YESCARTA arm from data cutoff for primary EFS analysis (50%) to primary OS analysis (55.8%).There was an increase in subject incidence of fatal AEs within the YESCARTA arm from primary EFS analysis in 7 patients (4.1%) to primary OS analysis in 8 patients (4.7%), excluding those from progressive disease. Incidence of treatment emergent SAEs (46.4%) as well as fatal AEs in 2 patients (1.1%) remained unchanged in the standard care arm.

Disease progression was the most common cause of death in both the YESCARTA arm (51 patients) and the standard-care arm (71 patients).

Fatal Grade 5 AE-related deaths occurred in 8 (4.7%) patients in the YESCARTA arm (COVID-19 [n=2], sepsis [n=2], myocardial infarction, progressive multifocal leukoencephalopathy, acute respiratory distress syndrome, cardiac arrest, pneumonia, and hepatitis B reactivation [n=1 each]. Only hepatitis B reactivation was related to YESCARTA treatment. Two patients (1.1%) in the standard care arm had fatal Grade 5 AE related deaths (cardiac arrest and acute respiratory distress syndrome [n=1 each]; both were HDT-related).

CRS and Neurologic Events[1,3,6]

CRS occurred in 157/170 (92%) patients who received YESCARTA (Table 4).

- Grade ≥3 CRS occurred in 11/170 (6%) patients
- The median onset of CRS was 3 days (range, 1 – 10) after infusion; median duration of CRS was 7 days (range, 2 – 43)
- No deaths due to CRS occurred, and all events resolved.
- Tocilizumab, glucocorticoids, and vasopressors were used for management of CRS in 65%, 24%, and 6% of patients,

respectively.

Neurologic events occurred in 102/170 (60%) patients who received YESCARTA and in 33/168 (20%) patients who received standard care (Table 4).

- Grade ≥ 3 neurologic events occurred in 36/170 (21%) patients who received YESCARTA and in 1/168 (1%) patients who received standard care
- The median onset of neurologic events was 7 days in the YESCARTA arm and 23 days in the standard-care arm; median duration of neurologic events was 9 days in the YESCARTA arm and 23 days in the standard-care arm
- No deaths due to neurologic events occurred
- At the time of data cutoff, 2 patients had ongoing neurologic events (YESCARTA, Grade 2 paresthesia and Grade 1 memory impairment [n=1]; standard care, Grade 1 paresthesia [n=1]).

Table 4. Summary of CRS and Neurologic Events[1]

n (%)[a]	YESCARTA n=170		Standard Care n=168	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
CRS	157 (92)	11 (6)	-	-
Pyrexia	155/157 (99)	14/157 (9)	-	-
Hypotension	68/157 (43)	18/157 (11)	-	-
Sinus tachycardia	49/157 (31)	3/157 (2)	-	-
Chills	38/157 (24)	0 (0)	-	-
Hypoxia	31/157 (20)	13/157 (8)	-	-
Headache	32/157 (20)	2/157 (1)	-	-
Neurologic event	102 (60)	36 (21)	33 (20)[b]	1 (1)
Tremor	44 (26)	2 (1)	1(1)	0 (0)
Confusional state	40 (24)	9 (5)	4 (2)	0 (0)
Aphasia	36 (21)	12 (7)	0 (0)	0 (0)
Encephalopathy	29 (17)	20 (12)	2 (1)	0 (0)
Paresthesia	8 (5)	1 (1)	14 (8)	0 (0)
Delirium	3 (2)	3 (2)	5 (3)	1 (1)

[a]Included are any CRS and neurologic events of any grade occurring in ≥15% of patients in the YESCARTA cohort or ≥3% in the standard-care cohort
[b]Other preferred terms reported in the standard-care cohort (in ≤2 patients) included somnolence, agitation, hypoesthesia, lethargy, depressed level of consciousness, cognitive disorder, memory impairment, bradyphrenia, taste disorder, hallucination, hallucination visual, nystagmus, head discomfort, and neuralgia.
Abbreviation: CRS=cytokine release syndrome.

Safety results of the primary OS analysis of the ZUMA-7 study showed no new cases of CRS or neurologic events in either trial group since the primary EFS analysis.

Cytopenias[1,6]

In the primary EFS analysis, prolonged Grade ≥3 cytopenias that occurred on or after 30 days from receipt of YESCARTA infusion or first dose of HDT occurred in 49 (29%) patients in the YESCARTA arm and 12 (19%) patients that received on-protocol ASCT in the standard-care arm. In the primary OS analysis, prolonged Grade ≥3 cytopenia that occurred ≥6 months from receipt of YESCARTA infusion was reported in 8 patients (4.7%) in the axi-cel group, including 6 patients (3.5%) with prolonged neutropenia and 2 (1.2%) with prolonged anemia.

Other AEs of Interest[1,6,7]

Among the 160 YESCARTA patients in the primary EFS analysis who were tested for B-cell aplasia, 47% and 36% of patients had B-cell aplasia (undetectable B cells) up to 6 and 12 months post-infusion, respectively. Additionally, safety results of the primary OS analysis of the ZUMA-7 (n=162) study showed B-cell aplasia occurred in 62.3% of the patients at 3 months and in 22.6% at 24 months after infusion in the patients in the YESCARTA arm who were evaluated for B-cell levels at these time points.

Hypogammaglobulinemia was reported in 19/170 (11.2%) of patients in the YESCARTA arm and 1/168 (0.6%) in the standard care arm.

New or secondary cancers were reported in 8/170 (4.7%) patients in the YESCARTA arm and 3/168 (1.8%) patients in the standard-care arm, including 1 patient with 2 new cancers. No cases of replication-competent retrovirus were reported.

Pharmacokinetics

Please see the full Prescribing Information for additional information on pharmacokinetics of YESCARTA in the ZUMA-7 study.

CAR T-Cell Levels[1,6]

The median time to peak CAR T-cell levels following YESCARTA infusion was 7 days (range, 2–233). The median peak CAR T-cell level was 25.84 cells/mm^3, and CAR T cells remained detectable in 12/30 (40%) evaluable patients by 24 months. A correlation was seen between post-treatment CAR T-cell peak and area under the curve within the first 28 days (AUC_{0-28}) and objective response. There were no confirmed occurrences of anti–axi-cel antibodies.

Additionally, peak CAR T-cell levels and AUC_{0-28} were not significantly associated with overall survival.

References

1. Locke FL, Miklos DB, Jacobson CA et al. Axicabtagene ciloleucel as second-line therapy for large B-cell lymphoma. *N Engl J Med*. 2022;386(7):640-654. DOI: 10.1056/NEJMoa2116133
2. [Supplementary Appendix] Locke FL, Miklos DB, Jacobson CA et al. Axicabtagene ciloleucel as second-line therapy for large B-cell lymphoma. *N Engl J Med*. 2022;386(7):640-654. DOI: 10.1056/NEJMoa2116133
3. Locke FL, Miklos DB, Jacobson CA, et al. Primary analysis of ZUMA-7: a phase 3 randomized trial of axicabtagene ciloleucel versus standard-of-care therapy in patients with relapsed/refractory large B-cell lymphoma. Oral presentation at the American Society of Hematology (ASH) Annual meeting; December 11-14, 2021; Atlanta, GA.
4. Locke FL, Miklos DB, Jacobson CA, et al. Primary analysis of ZUMA-7: a phase 3 randomized trial of axicabtagene ciloleucel versus standard-of-care therapy in patients with relapsed/refractory large B-cell lymphoma. Presented at the European CAR T-cell Meeting; February 10-12, 2022; Abstract 55.
5. Elsawy M, Chavez JC, Avivi I, et al. 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). Oral presentation at the American Society of Hematology (ASH) Annual meeting; December 11-14, 2021; Atlanta, GA.
6. Westin JR, Oluwole OO, Kersten MJ, et al. Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma [published online ahead of print, 2023 Jun 5]. *N Engl J Med*. 2023;10.1056/NEJMoa2301665. doi:10.1056/NEJMoa2301665
7. [Supplementary Appendix] Westin JR, Oluwole OO, Kersten MJ, et al. Survival with Axicabtagene Ciloleucel in Large B-Cell Lymphoma [published online ahead of print, 2023 Jun 5]. *N Engl J Med*. 2023;10.1056/NEJMoa2301665. doi:10.1056/NEJMoa2301665
8. Westin JR, Oluwole OO, Kersten MJ, et al. Primary Overall Survival Analysis of the Phase 3 Randomized ZUMA-7 Study of Axicabtagene Ciloleucel Versus Standard-of-Care Therapy in Relapsed/Refractory Large B-Cell Lymphoma. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL.

Abbreviations

AE=adverse event
alloSCT=allogeneic stem cell transplantation
ASCT=autologous stem cell transplantation
AUC_{0-28}=area under the curve from day 0 to day 28
CAR=chimeric antigen receptor
CR=complete response
CRS=cytokine release syndrome
DLBCL=diffuse large B-cell lymphoma
DOR=duration of response
ECOG=Eastern Cooperative Oncology Group
EORTC QLQ-C30=European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire
EQ-5D-5L=EuroQol 5 Dimension 5 Level
FDA=US Food and Drug Administration
HDT-ASCT=high-dose therapy with autologous stem cell transplant
HGBL= high-grade B-cell lymphoma
HR=hazard ratio
IPI=International Prognostic Index
IV=intravenous
LBCL=large B-cell lymphoma
ORR=objective response rate
NE=not estimable
NR=not reached
NS=not significant
OS=overall survival
PD=progressive disease
PFS=progression-free survival
PR=partial response
PRO=patient reported outcome
QoL=quality of life
sAAIPI=second-line age-adjusted International Prognostic Index
VAS=visual analog scale
WPAI=Work Productivity and Activity Impairment

Product label

For the full indication, important safety information, and Boxed Warning(s), please refer to the YESCARTA® (axicabtagene ciloleucel) US Prescribing Information available at:

https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.pdf

Follow up

For any additional questions, please contact Kite at:

☎1-844-454-KITE (1-844-454-5483) or ✉ medinfo@kitepharma.com

Adverse event reporting

Please report all adverse events to:

Kite ☎ 1-844-454-KITE (1-844-454-5483)

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or 🌐 www.accessdata.fda.gov/scripts/medwatch

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