Supplementary Table S1. Patient-reported outcomes instruments

Instrument	Description	Scales/Domains
EORTC QLQ-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(1,2)	• Mobility, self-care, usual activities, pain/discomfort, and anxiety/depression • VAS rating of global assessment of their current (day of assessment) state of health

Abbreviations: EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, EuroQol 5-dimension questionnaire using a 5-level scale; QoL, quality of care; VAS, visual analogue scale.

1. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ*, et al.* The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* **1993**;85(5):365-76.

2.Fayers P, Aaronson N, Bjordal K, MGroenvold, Curran D, Bottomley A*, et al.* The EORTC QLQ-C30 Scoring Manual (3rd Edition). Brussels: European Organisation for Research and Treatment of Cancer; 2001.

Supplementary Table S2. Axi-cel delivery and administration time

Median (range), days	Axi-Cel (*n* = 49)
Leukapheresis to axi-cel release	12 (10-19)
Leukapheresis to delivery of axi-cel at study site	18 (13-49)
Leukapheresis to axi-cel administration	25 (17-52)

Abbreviations: axi-cel, axicabtagene ciloleucel.

Supplementary Table S3. Summary of efficacy and safety outcomes in patients ≥65 years versus all patients in ZUMA-7

Outcome	All Patients		Patients ≥65 Years	
	Axi-Cel	**SOC**	**Axi-Cel**	**SOC**
EFS, median (95% CI), months	8.3 (4.5-15.8)	2.0 (1.6-2.8)	21.5 (5.0-NE)	2.5 (1.6-3.2)
ORR, %	83	50	88	52
CR rate, %	65	32	75	33
24-months OS rate, %	61	52	64	50
PFS, median (95% CI), months	14.7 (5.4-NE)	3.7 (2.9-5.3)	21.5 (5.1-NE)	5.0 (2.8-7.3)
Grade ≥3 treatment-emergent AEs, *n*/*N* (%)	155/170 (91)	140/168 (83)	46/49 (94)	45/55 (82)
Grade ≥3 CRS, *n*/*N* (%)	11/170 (6)	-	4/49 (8)	-
Grade ≥3 neurologic events, *n*/*N* (%)	36/170 (21)	1/168 (1)	13/49 (27)	1/55 (2)

Abbreviations: AE, adverse event; axi-cel, axicabtagene ciloleucel; CR, complete response; CRS, cytokine release syndrome; EFS, event-free survival; NE, not evaluable; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; SOC, standard of care.

Supplementary Table S4. Serious adverse events in at least 3 patients in patients ≥65 years

n (%)	Axi-Cel *n* = 49		SOC *n* = 55	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any serious adverse event	29 (59)	25 (51)	26 (47)	23 (42)
Pyrexia	12 (24)	1 (2)	2 (4)	0
Hypotension	6 (12)	2 (4)	1 (2)	1 (2)
Pneumonia	4 (8)	4 (8)	3 (5)	3 (5)
Acute kidney injury	1 (2)	0	5 (9)	3 (5)
Encephalopathy	6 (12)	4 (8)	0	0
Febrile neutropenia	0	0	6 (11)	6 (11)
Neutropenia[a]	4 (8)	3 (6)	2 (4)	2 (4)
Sepsis	1 (2)	1 (2)	3 (5)	3 (5)
Anemia	1 (2)	1 (2)	2 (4)	2 (4)
Confusional state	3 (6)	2 (4)	0	0
Dyspnea	2 (4)	2 (4)	1 (2)	1 (2)
Hypoxia	2 (4)	0	1 (2)	1 (2)
Sinus tachycardia	2 (4)	1 (2)	1 (2)	0
Somnolence	3 (6)	2 (4)	0	0
Thrombocytopenia[b]	0	0	3 (5)	3 (5)

The severity of all adverse events was graded with the use of the Common Terminology Criteria for Adverse Events, version 4.03, of the National Cancer Institute.
[a] Neutropenia refers to the combined preferred terms of neutropenia and neutrophil count decreased.
[b] Thrombocytopenia refers to the combined preferred terms of thrombocytopenia and platelet count decreased.
Abbreviations: axi-cel, axicabtagene ciloleucel; SOC, standard of care.

Supplementary Table S5. Summary of cytopenias present on or after 90 days from initiation of definitive therapy on protocol in patients ≥65 years[a]

n (%)	Axi-Cel *n* = 49		SOC Patients Who Proceeded to ASCT *n* = 20	
	Any Grade	**Grade ≥3**	**Any Grade**	**Grade ≥3**
Any prolonged cytopenia	14 (29)	6 (12)	5 (25)	2 (10)
Prolonged thrombocytopenia	6 (12)	0	2 (10)	0
Platelet count decreased	5 (10)	0	2 (10)	0
Thrombocytopenia[b]	1 (2)	0	0	0
Prolonged neutropenia[c]	8 (16)	5 (10)	1 (5)	1 (5)
Neutrophil count decreased	4 (8)	3 (6)	0	0
Neutropenia	4 (8)	2 (4)	1 (5)	1 (5)
Febrile neutropenia	0	0	0	0
Prolonged anemia[d]	7 (14)	1 (2)	2 (10)	1 (5)
Anemia	6 (12)	1 (2)	2 (10)	1 (5)
Anemia macrocytic	1 (2)	0	0	0
Hematocrit decreased	0	0	0	0
Hemoglobin decreased	0	0	0	0

[a] 90 days from receipt of axi-cel infusion or the first dose of high-dose therapy. [b] Thrombocytopenia was identified with SMQ hematopoietic thrombocytopenia (narrow).[c] Neutropenia was identified using the MedDRA preferred terms of neutropenia, neutrophil count decreased, and febrile neutropenia. [d]Anemia was identified using the SMQ hematopoietic erythropenia (broad). Multiple instances of the same adverse event in one patient are counted once at the worst grade for each patient. Adverse events started on or after high-dose therapy were included. Adverse events were coded using MedDRA version 23.1 and graded per CTCAE version 4.03.
Abbreviations: ASCT, autologous stem cell transplant; axi-cel, axicabtagene ciloleucel; CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities; SMQ, Standardized MedDRA Queries; SOC, standard of care.

Supplementary Table S6. Deaths in axi-cel and SOC arms for patients ≥65 years (safety analysis set)

Reason for death, *n* (%)	Axi-Cel *n* = 49	SOC *n* = 55
Progressive disease	19 (39)	20 (36)
Fatal adverse event	1 (2)	1 (2)[a]
COVID-19	1 (2)	0
Definitive therapy-related mortality	0	1 (2)[a]
Other[b]	1 (2)	5 (9)
COVID-19	0	2 (4)

[a] Due to cardiac arrest. [b] Other reasons for death included natural progression from prior subdural hematoma (n = 1) in the axi-cel arm and COVID-19 (n = 2), cardiopulmonary arrest (n = 1), urosepsis (n = 1), and sepsis (n = 1) in the SOC arm.
Abbreviations: axi-cel, axicabtagene ciloleucel; SOC, standard of care.

Supplementary Table S7. Summary of serum analytes in patients <65 years versus ≥65 years in the axi-cel arm (*N* = 170)

Serum Analyte	<65 Years of Age (*n* = 121)		≥65 Years of Age *n* = 49		*P* value[a]
	n	Median (range)	*n*	Median (range)	
CRP (mg/L)					
Peak	129	86.0 (3.6-184.0)	50	83.7 (8.0-184.0)	.9269
AUC_{0-28}	129	1061.4 (27.8-5263.4)	50	1043.7 (68.9-2870.1)	.6538
Baseline	121	17.1 (0.2-184.0)	49	10.6 (0.7-184.0)	.4318
CXCL10 (pg/mL)					
Peak	129	1740.1 (386.9-9535.3)	50	2289.4 (508.4-19,360.0)	.0146
AUC_{0-28}	129	31723.3 (2967.7-140,224.1)	50	35,468.7 (8611.0-178,430.0)	.1097
Baseline	121	452.1 (145.8-2760.6)	49	576.3 (185.9-3640.0)	.0742
Ferritin (ng/mL)					
Peak	128	559.5 (67.0-82,900.0)	50	747.5 (107.0-12,544.0)	.0411
AUC_{0-28}	128	11,197.0 (637.0-1,104,878.5)	50	15,405.5 (1370.5-114,409.5)	.1161
Baseline	119	239.0 (1.0-4656.0)	49	274.0 (21.0-1593.0)	.3399
Granzyme B (pg/mL)					
Peak	129	44.5 (3.3-605.0)	50	47.3 (17.7-2379.5)	.4253
AUC_{0-28}	129	692.9 (39.8-12,968.0)	50	829.1 (98.6-17,722.2)	.6866
Baseline	121	9.1 (3.3-414.0)	48	8.9 (3.3-50.8)	.9482
ICAM-1 (ng/mL)					
Peak	129	791.9 (405.4-2925.5)	50	901.7 (424.6-3584.9)	.0749
AUC_{0-28}	129	20,318.2 (3304.2-62,508.7)	50	20,873.3 (5681.6-63,199.9)	.5704
Baseline	121	584.0 (333.0-2622.1)	49	569.0 (369.5-1834.7)	.9753
IFN-γ (pg/mL)					
Peak	129	227.9 (9.7-23,360.0)	50	432.1 (56.1-23,360.0)	.0135
AUC_{0-28}	129	1854.4 (47.7-315,565.1)	50	3241.4 (432.9-168,014.5)	.0784
Baseline	121	9.3 (1.4-288.1)	49	12.7 (1.4-160.3)	.1418
IL-1 RA (pg/mL)					
Peak	129	996.0 (237.0-12,954.0)	50	1206.0 (401.8-16,000.0)	.0566
AUC_{0-28}	129	20,309.6 (1539.7-218,174.4)	50	21,995.9 (4899.9-163,588.7)	.2836
Baseline	119	600.8 (140.8-3577.5)	48	562.3 (240.9-2585.1)	.9929
IL-2 (pg/mL)					
Peak	129	13.1 (0.4-147.3)	50	17.4 (1.4-173.1)	.0933
AUC_{0-28}	129	81.9 (2.5-913.4)	50	101.9 (23.0-694.4)	.1312
Baseline	121	0.4 (0.4-12.2)	49	0.4 (0.4-10.4)	.7803
IL-2 R alpha (ng/mL)					
Peak	129	6.6 (1.2-56.2)	50	9.3 (1.5-80.0)	.0062
AUC_{0-28}	129	120.0 (7.8-960.5)	50	158.9 (22.2-1216.0)	.0611
Baseline	121	1.6 (0.5-32.7)	48	1.7 (0.4-35.9)	.9292
IL-6 (pg/mL)					
Peak	129	41.8 (1.2-2972.0)	50	48.8 (2.2-2972.0)	.2598
AUC_{0-28}	129	534.3 (8.6-31,936.4)	50	778.7 (37.6-40,636.5)	.2722
Baseline	121	2.9 (0.5-49.8)	49	3.2 (0.5-19.6)	.9698
IL-7 (pg/mL)					
Peak	129	38.9 (17.9-129.7)	50	34.2 (19.2-62.0)	.0180
AUC_{0-28}	129	878.3 (235.1-2132.0)	50	711.9 (246.9-1646.8)	.0015
Baseline	121	21.0 (4.7-54.5)	49	18.5 (5.3-34.5)	.0485
IL-8 (pg/mL)					
Peak	129	60.3 (18.0-6718.0)	50	55.9 (10.8-1046.4)	.8660
AUC_{0-28}	129	965.0 (133.4-85,027.0)	50	900.8 (160.5-14,495.4)	.5466
Baseline	121	16.5 (4.4-7920.0)	49	19.3 (5.2-748.1)	.1011
IL-10 (pg/mL)					
Peak	129	11.2 (0.5-342.3)	50	17.3 (2.4-652.9)	.0733
AUC_{0-28}	129	150.9 (9.9-4480.7)	50	214.6 (25.1-4830.0)	.1413
Baseline	121	0.6 (0.2-101.0)	49	0.6 (0.2-54.7)	.9023
IL-15 (pg/mL)					
Peak	129	36.1 (12.7-144.6)	50	47.1 (20.5-173.0)	.0004
AUC_{0-28}	129	490.3 (129.1-1655.4)	50	568.7 (142.9-2093.2)	.2544
Baseline	121	3.1 (3.1-8.3)	49	3.1 (3.1-25.4)	.8854
TNF alpha (pg/mL)					
Peak	129	6.2 (2.2-58.4)	50	7.3 (3.2-72.1)	.0797
AUC_{0-28}	129	136.8 (15.3-1224.4)	50	144.7 (43.4-1072.3)	.4059
Baseline	121	3.9 (1.4-83.1)	49	3.8 (1.7-91.5)	.7739
VCAM-1 (ng/mL)					

Serum Analyte	<65 Years of Age (*n* = 121)		≥65 Years of Age *n* = 49		*P* value[a]
	n	Median (range)	*n*	Median (range)	
Peak	129	807.1 (358.4-2577.0)	50	1103.4 (545.2-2561.4)	<.0001
AUC_{0-28}	129	20,375.6 (2828.7- 70,016.1)	50	26,506.2 (6485.1-75,244.0)	.0023
Baseline	121	589.5 (293.0-5409.9)	49	706.9 (405.2-3195.5)	.0005
GM-CSF (pg/mL)					
Peak	129	1.9 (0.7-213.9)	50	2.9 (0.7-31.8)	.0073
AUC_{0-28}	129	25.3 (4.7-2687.7)	50	30.6 (12.7-430.7)	.0656
Baseline	121	0.7 (0.7-2.3)	49	0.7 (0.7-0.7)	.5330
IL-12 P40 (pg/mL)					
Peak	129	274.6 (61.1-1105.5)	50	302.7 (94.5-1885.9)	.6913
AUC_{0-28}	129	4859.9 (510.1-27,143.8)	50	4354.4 (714.6-29,015.9)	.3689
Baseline	121	187.7 (35.3-1328.4)	49	203.4 (24.2-3019.4)	.8177
IL-17 (pg/mL)					
Peak	129	12.4 (1.5-260.8)	50	13.3 (3.7-127.9)	.7454
AUC_{0-28}	129	155.7 (10.4-3083.1)	50	143.4 (55.1-1600.1)	.9040
Baseline	121	3.5 (1.5-98.6)	49	4.1 (1.5-58.2)	.3304
IL-4 (pg/mL)					
Peak	129	0.2 (0.2-6.1)	50	0.2 (0.2-3.8)	.2045
AUC_{0-28}	129	6.3 (1.3-74.2)	50	6.3 (2.3-40.0)	.8937
Baseline	121	0.2 (0.2-0.8)	49	0.2 (0.2-0.2)	.5330
IL-5 (pg/mL)					
Peak	129	9.4 (0.5-387.4)	50	14.1 (0.5-386.1)	.0537
AUC_{0-28}	129	85.9 (3.6-5247.4)	50	153.0 (6.2-5419.2)	.0872
Baseline	121	0.5 (0.5-3.7)	49	0.5 (0.5-10.3)	.8813
MCP-1 (pg/mL)					
Peak	129	1031.8 (214.3-3606.4)	50	1291.6 (390.2-9671.4)	.0846
AUC_{0-28}	129	13,575.9 (2349.2-60,160.8)	50	14,066.1 (5897.5-142,020.6)	.8710
Baseline	121	295.0 (92.8-17,184.0)	49	326.3 (69.5-737.8)	.6949
MCP-4 (pg/mL)					
Peak	129	176.9 (71.3-507.2)	50	194.2 (67.4-755.1)	.1193
AUC_{0-28}	129	3903.6 (388.8-9057.5)	50	3918.7 (1091.4-17,931.6)	.5814
Baseline	121	108.3 (42.3-294.3)	49	124.7 (39.1-341.0)	.2105
MDC (pg/mL)					
Peak	129	1127.0 (382.0-37,153.0)	50	1226.0 (382.0-24,330.0)	.5282
AUC_{0-28}	129	21,935.0 (2674.0-651,744.0)	50	20,252.0 (5799.0-453,529.0)	.4538
Baseline	121	1258.0 (382.0-149,600.0)	49	1186.0 (382.0-107,612.0)	.6103
MIP-1α (pg/mL)					
Peak	129	41.1 (8.0-2315.9)	50	45.6 (23.7-308.9)	.2368
AUC_{0-28}	129	964.7 (110.4-30,615.4)	50	867.0 (279.1-4765.4)	.6985
Baseline	121	26.9 (8.0-1366.6)	49	26.0 (8.0-574.9)	.7935
MIP-1β (pg/mL)					
Peak	129	255.0 (90.2-2987.5)	50	270.7 (78.7-1042.1)	.3292
AUC_{0-28}	129	4594.0 (671.3-41,014.0)	50	4277.7 (1397.2-16,068.5)	.6354
Baseline	121	132.3 (40.9-843.9)	49	120.4 (51.7-627.4)	.2823
SAA (mg/L)					
Peak	129	184.0 (3.1-184.0)	50	184.0 (3.7-184.0)	.7528
AUC_{0-28}	129	1518.5 (32.7-5890.1)	50	1500.6 (31.8-4154.4)	.6469
Baseline	121	16.5 (0.8-184.0)	49	12.4 (1.6-184.0)	.9945
TARC (pg/mL)					
Peak	129	1604.1 (73.2-50,723.0)	50	1609.4 (116.0-10,525.0)	.7248
AUC_{0-28}	129	26748.1 (1716.4-884,914.3)	50	20,803.1 (2524.1-203,873.3)	.3013
Baseline	121	513.5 (77.3-52,160.0)	49	484.8 (65.5-24,591.9)	.5426

Peak was defined as the maximum post-baseline level of the analyte from baseline to Week 4 post-treatment. AUC measures the total levels of analyte over time, and was defined as the AUC in a plot of levels of analyte against scheduled visit from baseline to Week 4 post-treatment.

[a] Nominal *P* value based on Wilcoxon rank-sum test.

Abbreviations: AUC, area under the curve; AUC_{0-28}, area under the curve from day 0 to 28; axi-cel, axicabtagene ciloleucel; CRP, C-reactive protein; CXCL10, CXC motif chemokine ligand 10; GM-CSF, granulocyte macrophage colony-stimulating factor; ICAM-1, intercellular adhesion molecule 1; IFN, interferon; IL, interleukin; IL-1RA, interleukin-1 receptor antagonist; IL-2Ra, interleukin-2 receptor alpha; MCP, monocyte chemotactic protein; MDC, macrophage-derived chemokine; MIP, macrophage inflammatory protein; SAA, serum amyloid A; TARC, thymus and activation regulated chemokine; TNF, tumor necrosis factor; VCAM, vascular cell adhesion molecule.

Supplementary Table S8. Most common adverse events, cytokine release syndrome, and neurologic events in patients ≥70 years

n (%)	Axi-Cel *n* = 24		SOC *n* = 26	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Any adverse event	24 (100)	22 (92)	26 (100)	20 (77)
Pyrexia	23 (96)	1 (4)	5 (19)	0
Neutropenia[a]	19 (79)	19 (79)	9 (35)	9 (35)
Nausea	10 (42)	1 (4)	16 (62)	0
Anemia	10 (42)	8 (33)	15 (58)	11 (42)
Thrombocytopenia[b]	10 (42)	6 (25)	17 (65)	16 (62)
Leukopenia[c]	10 (42)	9 (38)	3 (12)	3 (12)
Fatigue	8 (33)	2 (8)	12 (46)	0
Decreased appetite	8 (33)	0	8 (31)	0
Diarrhea	8 (33)	1 (4)	8 (31)	0
Cough	11 (46)	0	4 (15)	0
Constipation	5 (21)	0	9 (35)	0)
Hypokalemia	8 (33)	3 (13)	6 (23)	1 (4)
Hypophosphatemia	11 (46)	8 (33)	3 (12)	2 (8)
Hypotension	12 (50)	2 (8)	2 (8)	1 (4)
Confusional state	12 (50)	4 (17)	1 (4)	0
Hypoxia	9 (38)	5 (21)	2 (8)	1 (4)
Sinus tachycardia	9 (38)	1 (4)	2 (8)	0
Chills	8 (33)	0	2 (8)	0
Edema peripheral	4 (17)	0	6 (23)	0
Headache	5 (21)	0	4 (15)	0
Alanine aminotransferase increased	6 (25)	0	2 (8)	1 (4)

n (%)	Axi-Cel *n* = 24		SOC *n* = 26	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Hypocalcemia	7 (29)	0	1 (4)	0
Tremor	8 (33)	0	0	0
Aphasia	7 (29)	2 (8)	0	0
Dizziness	6 (25)	1 (4)	1 (4)	0
Hyperglycemia	5 (21)	0	2 (8)	0
Hypogammaglobulinemia	6 (25)	0	1 (4)	0
Encephalopathy	5 (21)	3 (13)	1 (4)	0
Hypoalbuminemia	5 (21)	0	1 (4)	0
Hyperglycemia	5 (21)	0	2 (8)	0
CRS	24 (100)	2 (8)	—	—
Pyrexia	23 (96)	1 (4)	—	—
Hypotension	11 (46)	2 (8)	—	—
Sinus tachycardia	8 (33)	1 (4)	—	—
Hypoxia	7 (29)	4 (17)	—	—
Chills	6 (25)	0	—	—
Neurologic events	18 (75)	8 (33)	5 (19)	0
Confusional state	12 (50)	4 (17)	1 (4)	0
Tremor	8 (33)	0	0	0
Aphasia	7 (29)	2 (8)	0	0
Encephalopathy	5 (21)	3 (13)	1 (4)	0
Somnolence	3 (13)	2 (8)	2 (8)	0
Cognitive disorder	1 (4)	0	1 (4)	0
Hallucination	0	0	1 (4)	0
Hallucination, visual	0	0	1 (4)	0

Shown are any adverse events of any grade that occurred in at least 20% of the patients in either the axi-cel arm or the SOC arm, as well as events of the cytokine release syndrome that occurred in at least 15% of the patients in the axi-cel arm and neurologic events of any grade that occurred in at least 15% of the patients in the axi-cel arm or at least 3% of those in the SOC arm. The severity of the cytokine release syndrome was graded according to Lee et

al.(1) Neurologic events were identified with the use of prespecified search list of preferred terms in MedDRA, version 23.1, on the basis of known neurotoxic effects associated with anti-CD19 immunotherapy, and were specifically identified with the use of methods that were based on the phase II study of blinatumomab.(2) The severity of all adverse events, including neurologic events and symptoms of the cytokine release syndrome, was graded with the use of the CTCAE, version 4.03, of the National Cancer Institute.

[a] Neutropenia refers to the combined preferred terms of neutropenia and neutrophil count decreased.

[b] Thrombocytopenia refers to the combined preferred terms of thrombocytopenia and platelet count decreased.

[c] Leukopenia refers to the combined preferred terms of leukopenia and white-cell count decreased.

Abbreviations: axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; MedDRA, Medical Dictionary for Regulatory Activities; SOC, standard of care.

1. Lee DW, Gardner R, Porter DL, Louis CU, Ahmed N, Jensen M*, et al.* Current concepts in the diagnosis and management of cytokine release syndrome. *Blood* **2014**;124(2):188-95.

2. Topp MS, Gokbuget N, Stein AS, Zugmaier G, O'Brien S, Bargou RC*, et al.* Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. *Lancet Oncol* **2015**;16(1):57-66.

Supplementary Table S9. Deaths in axi-cel and SOC arms for patients ≥70 years

Reason for death, *n* (%)	Axi-Cel *n* = 24	SOC *n* = 26
Progressive disease	12 (50)	13 (50)
Fatal adverse event	1 (4)	1 (4)[a]
COVID-19	1 (4)	0
Other	0	1 (4)[b]

[a] Due to cardiac arrest (related to high-dose chemotherapy). [b] Due to sepsis.
Abbreviations: axi-cel, axicabtagene ciloleucel; SOC, standard of care.

Supplementary Table S10. Baseline characteristics for quality-of-life analysis in patients ≥65 years[a]

Characteristic	Axi-Cel *n* = 46	SOC *n* = 42	Overall *N* = 88
Median age (range), years	69 (65-80)	69 (65-78)	69 (65-80)
Male sex, *n* (%)	24 (52)	28 (67)	52 (59)
Race or ethnic group, *n* (%)[b]			
American Indian or Alaska Native	0	1 (2)	1 (1)
Asian	2 (4)	1 (2)	3 (3)
White	42 (91)	40 (95)	82 (93)
Other	2 (4)	0	2 (2)
Hispanic or Latino ethnic group, *n* (%)[b]			
Yes	2 (4)	3 (7)	5 (6)
No	43 (93)	38 (90)	81 (92)
Not reported	1 (2)	1 (2)	2 (2)
ECOG performance status score of 1, *n* (%)[c]	25 (54)	13 (31)	38 (43)
Disease stage, *n* (%)			
I-II	7 (15)	9 (21)	16 (18)
III-IV	39 (85)	33 (79)	72 (82)
sAAIPI of 2-3, *n* (%)[d, e]	23 (50)	9 (21)	32 (36)
Molecular subgroup according to central laboratory, *n* (%)[f]			
Germinal center B-cell–like	29 (63)	28 (67)	57 (65)
Activated B-cell–like	3 (7)	2 (5)	5 (6)
Unclassified	4 (9)	2 (5)	6 (7)
Not applicable	6 (13)	6 (14)	12 (14)
Missing data	4 (9)	4 (10)	8 (9)
Disease type according to central laboratory, *n* (%)			
DLBCL not otherwise specified/without further classification possible[g,h]	31 (67)	35 (83)	66 (75)
HGBL, including rearrangement of *MYC* with *BCL2* or *BCL6* or both	11 (24)	3 (7)	14 (16)
Not confirmed or missing data	3 (7)	2 (5)	5 (6)

Characteristic	Axi-Cel *n* = 46	SOC *n* = 42	Overall *N* = 88
Other	1 (2)	2 (5)	3 (3)
Disease type according to the investigator, *n* (%)			
DLBCL not otherwise specified	25 (54)	32 (76)	57 (65)
T-cell/histiocyte-rich LBCL	0	1 (2)	1 (1)
Large cell transformation from follicular lymphoma[i]	7 (15)	6 (14)	13 (15)
HGBL with/without *MYC* and *BCL2* and/or *BCL6* rearrangement	14 (30)	3 (7)	17 (19)
Prognostic marker according to central laboratory, *n* (%)			
HGBL, double- or triple-hit	11 (24)	3 (7)	14 (16)
Double-expressor lymphoma	19 (41)	19 (45)	38 (43)
MYC rearrangement	3 (7)	0	3 (3)
Not applicable	13 (28)	19 (45)	32 (36)
Missing data	0	1 (2)	1 (1)
Response to 1L therapy, *n* (%)[e]			
Primary refractory	32 (70)	24 (57)	56 (64)
Relapse ≤12 months after initiation or completion of 1L therapy	14 (30)	18 (43)	32 (36)
Bone marrow involvement, *n* (%)[j]	1 (2)	3 (7)	4 (5)
Elevated LDH level, *n* (%)[k]	27 (59)	14 (33)	41 (47)
Median tumor burden (range), mm^2 [l]	1826 (181-22538)	1657 (252-16649)	1762 (181-22538)

[a] Patients were randomly assigned to receive axi-cel or SOC. Percentages may not total 100 because of rounding.
[b] Race and ethnic group were determined by the investigator.
[c] Eastern Cooperative Oncology Group (ECOG) performance-status scores are assessed on a 5-point scale, with a score of 0 indicating no symptoms and higher scores indicating greater disability. A score of 1 indicates that the patient is ambulatory but restricted from strenuous activity. Only patients with an ECOG performance status score of 0-1 were included in the study.
[d] Values are the sAAIPI at randomization, which were similar to the sAAIPI according to the investigator as entered into the clinical database. The sAAIPI is used to assess prognostic risk on the basis of various factors after adjustment for patient age and extranodal status at the time of diagnosis of refractory disease; risk categories are assessed as low (0 factors), intermediate (1 factor), or high (2 or 3 factors).
[e] As reported by investigator at time of randomization via Interactive Voice/Web Response System.
[f] The molecular subgroup as assessed by the investigator was as follows: germinal center B-cell–like in 25 patients (54%) in the axi-cel arm, 15 (36%) in the standard-care arm, and 40 (45%) overall; non–germinal center B-cell–like in 14 (30%), 16 (38%), and 30 (34%), respectively. The molecular subgroup was not assessed in 7 patients (15%) in the axi-cel arm, 11 (26%) in the standard-care arm, and 18 (20%) overall.
[g] The definition of diffuse large B-cell lymphoma according to the central laboratory 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. Diffuse large B-cell lymphoma, not otherwise specified, according to the World Health Organization 2016 definition,(1) is also included.
[h] The definition of diffuse large B-cell lymphoma according to the central laboratory 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. Diffuse large B-cell lymphoma, not otherwise specified, according to the World Health Organization 2016 definition, is also included.

[i] Transformation was defined as the presence of large cells noted anywhere in the biopsy sample.

[j] The data shown were as collected on the diagnosis history case-report form.

[k] An elevated lactate dehydrogenase level was defined as a level that was above the upper limit of the normal range per local laboratory reference range.

[l] Tumor burden was determined on the basis of the sum of product diameters of the target lesions, according to the Cheson criteria,(2) and was assessed by the central laboratory.

Abbreviations: 1L, first-line; axi-cel, axicabtagene ciloleucel; DLBCL, diffuse large B-cell lymphoma; ECOG, Eastern Cooperative Oncology Group; HGBL, high-grade B-cell lymphoma; LBCL, large B-cell lymphoma; LDH, lactate dehydrogenase; sAAIPI, Second-line Age-Adjusted International Prognostic Index; SOC, standard of care.

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R*, et al.* The 2016 revision of the World Health Organization classification of lymphoid neoplasms. *Blood* **2016**;127(20):2375-90.

2. Cheson BD, Pfistner B, Juweid ME, Gascoyne RD, Specht L, Horning SJ*, et al.* Revised response criteria for malignant lymphoma. *J Clin Oncol* **2007**;25(5):579-86.

Supplementary Table S11. Mixed model with repeated measures estimated difference in change from baseline for prespecified patient-reported outcomes measures (quality-of-life analysis set) in patients ≥65 years

		Model 1: Base model			Sensitivity analyses: Model 2: Pattern mixture model			Sensitivity analyses: Model 3: Pattern mixture + covariates		
PRO score	Visit	Estimate (95% CI)	Unadjusted *P* value[a]	Adjusted *P* value[a]	Estimate (95% CI)	Unadjusted *P* value[a]	Adjusted *P* value[a]	Estimate (95% CI)	Unadjusted *P* value[a]	Adjusted *P* value[a]
EORTC QLQ-C30 Physical Functioning	Day 100	15.3 (6.8, 23.7)	0.0006	0.0019	16.4 (7.5, 25.3)	0.0004	0.0011	15.2 (5.4, 25.0)	0.0030	0.0074
	Day 150	11.3 (1.7, 21.0)	0.0220	0.0419	11.9 (2.2, 21.7)	0.0168	0.0251	10.8 (0.7, 20.9)	0.0359	0.0513
	Month 9	13.0 (1.9, 24.2)	0.0226	0.0419	13.6 (2.4, 24.8)	0.0176	0.0251	12.7 (1.3, 24.0)	0.0291	0.0485
	Month 12	-0.2 (-14.6, 14.2)	0.9746	0.9746	0.2 (-14.2, 14.6)	0.9760	0.9760	-0.7 (-15.2, 13.7)	0.9190	0.9190
	Month 15	2.5 (-11.7, 16.7)	ND	ND	3.4 (-10.9, 17.7)	ND	ND	2.0 (-12.7, 16.6)	ND	ND
EORTC QLQ-C30 Global Health Status/QoL	Day 100									
	Day 150	27.5 (16.2, 38.8)	<.0001	<.0001	25.7 (13.8, 37.7)	<.0001	0.0003	22.2 (9.5, 35.0)	0.0009	0.0044
	Month 9	22.5 (8.5, 36.5)	0.0020	0.0052	20.8 (6.2, 35.4)	0.0057	0.0115	17.2 (2.5, 32.0)	0.0230	0.0459
	Month 12	13.4 (0.3, 26.4)	0.0456	0.0633	12.0 (-1.6, 25.5)	0.0820	0.0911	8.7 (-5.2, 22.6)	0.2145	0.2383
	Month 15	8.1 (-7.2, 23.4)	0.2967	0.3214	6.6 (-9.3, 22.5)	ND	ND	3.1 (-12.9, 19.2)	ND	ND
EQ-5D-5L VAS	Day 100	9.7 (-3.9, 23.2)	ND	ND	8.5 (-5.6, 22.5)	ND	ND	4.6 (-10.4, 19.7)	ND	ND
	Day 150									
	Month 9	19.9 (12.1, 27.7)	<.0001	<.0001	18.9 (10.5, 27.2)	<.0001	0.0002	17.8 (8.8, 26.9)	0.0002	0.0020
	Month 12	19.5 (10.0, 29.1)	ND	ND	–0.2 (–6.9, 6.5)	ND	ND	–2.6 (–9.4, 4.2)	ND	ND
	Month 15	10.8 (0.1, 21.4)	ND	ND	–3.9 (–11.1, 3.3)	ND	ND	–6.3 (–13.5, 1.0)	ND	ND

Results populated only through month 15 due to lack of model convergence when using time points. Model 1 included variables for treatment, time, and treatment by time interaction (primary analysis) and controlled for response to first-line therapy (primary refractory, relapse ≤6 months of first-line therapy, relapse >6 and ≤12 months of first-line therapy) and age-adjusted IPI (0 to 1 vs 2 to 3) at time of screening. Model 2 included all variables in Model 1 with additional covariates to control for patterns of missingness through Day 150. Model 3 included all variables in Model 2 with additional covariates for: geographic region (rest of world, United States); ECOG performance status at screening (0, 1); sex; race/ethnicity (Asian, Black or African American, Other, White); disease type (diffuse large B-cell lymphoma, HGBL with or without *MYC* and *BCL2* and/or *BCL6* rearrangement, large-cell transformation from follicular lymphoma, other); molecular subgroup (germinal center B-cell like, non-germinal center B-cell like, not tested); and double/triple-hit status (double expressor lymphoma, HGBL-double hit, HGBL-triple hit, missing).

[a] *P* values only presented for Day 100 and only for subsequent visits when the previous visit was statistically significant (*P*<.05). Adjusted *P* values were calculated using the false discovery rate methodology.

Abbreviations: ECOG, Eastern Cooperative Oncology Group; EORTC, European Organization for Research and Treatment of Cancer; EQ-5D-5L, EuroQoL 5-dimension questionnaire using a 5-level scale; QLQ-C30, Quality of Life Questionnaire-Core 30; HGBL, high-grade B-cell lymphoma; IPI, International Prognostic Index; MMRM, mixed-effect model with repeated measures; ND, not displayed; VAS, visual analogue scale.