Supplementary material

Cost-Effectiveness of Chimeric Antigen Receptor T-Cell Therapy in Patients with Relapsed or Refractory Large B-Cell Lymphoma - No Impact of Site of Care

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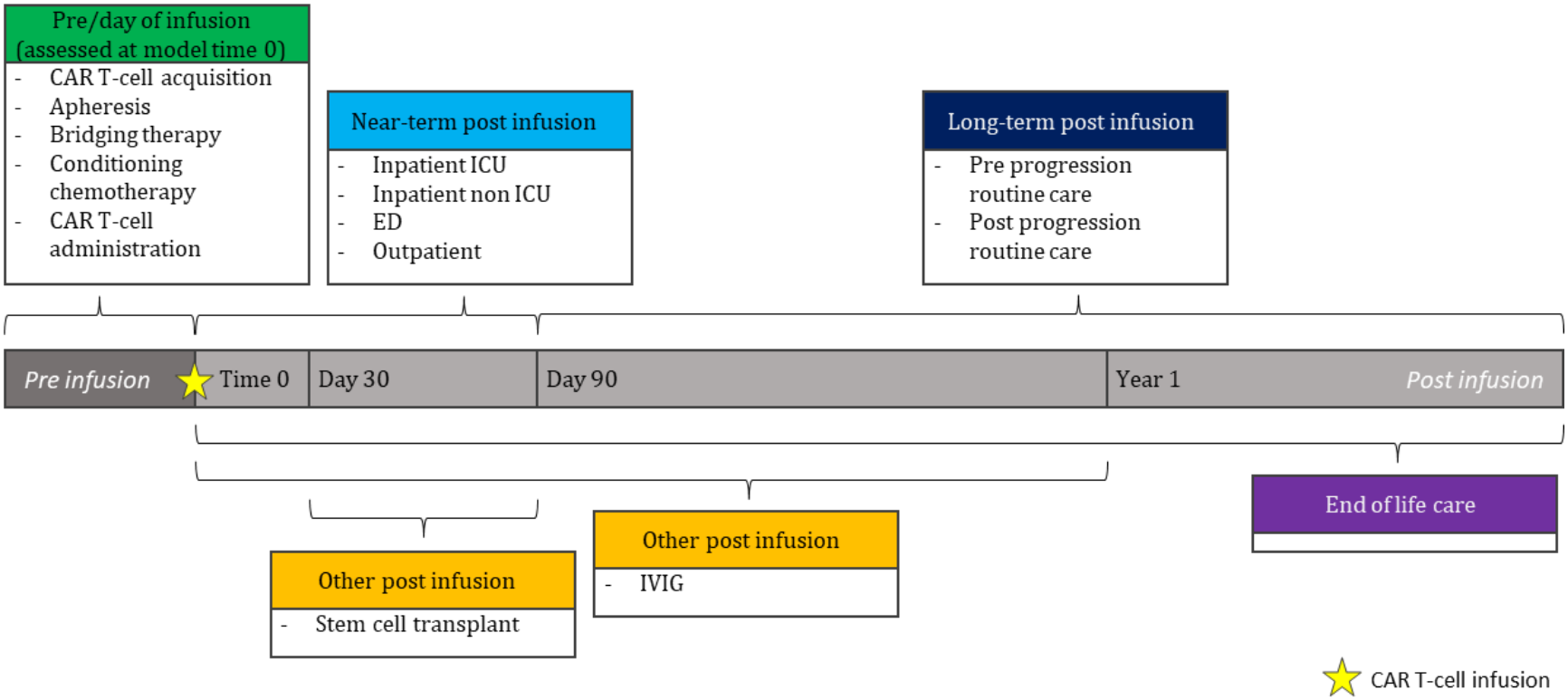
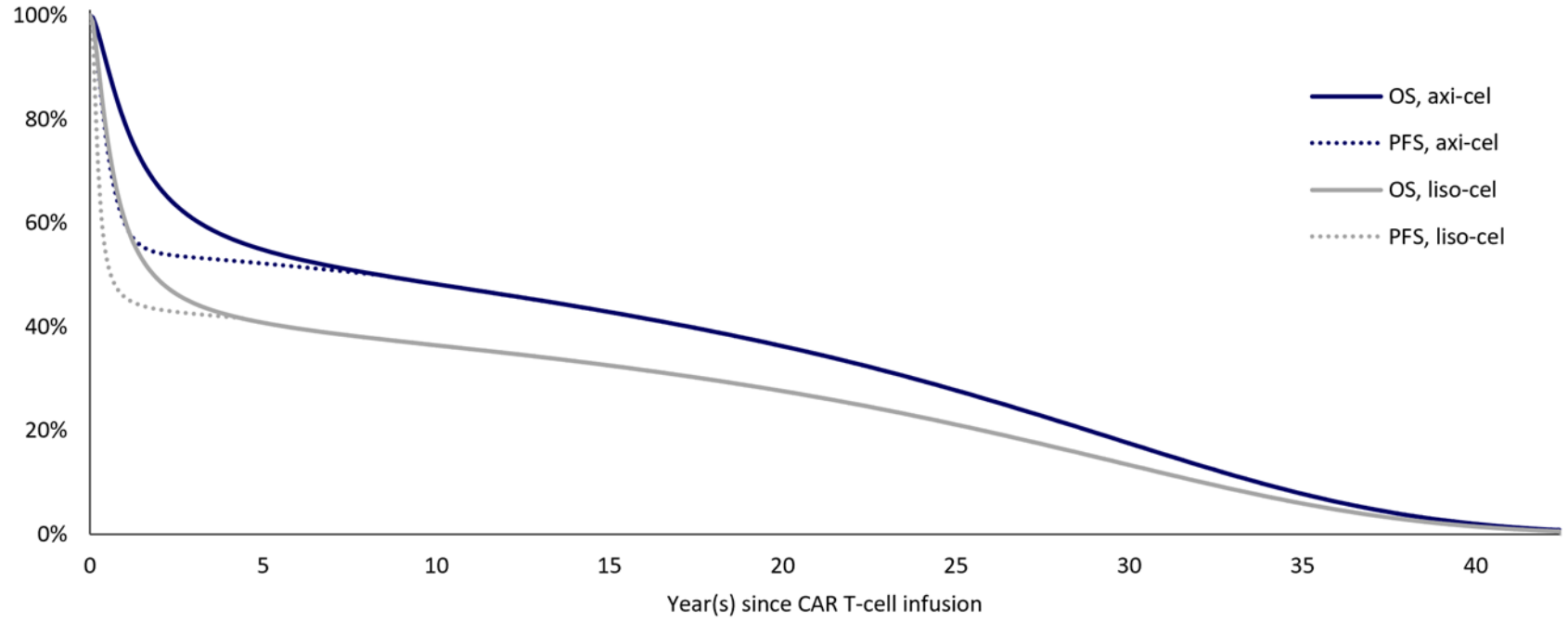
Figure S1 Costing types included in the model relative to date of CAR T-cell infusion



Abbreviations: CAR = chimeric antigen receptor; ED = Emergency Department; ICU = Intensive Care Unit; IVIG = intravenous immune globulin

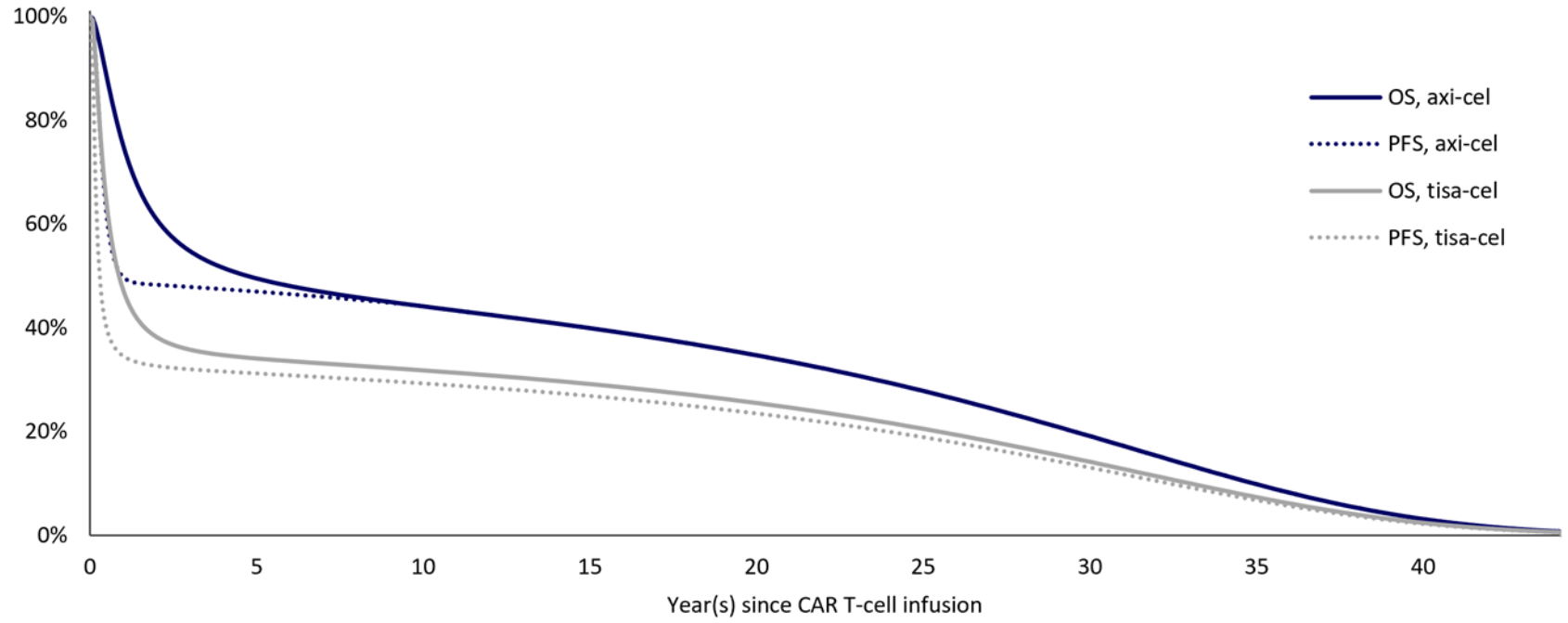
Figure S2a Overall and progression-free survival, axi-cel matched to liso-cel and liso-cel



Abbreviations: CAR = chimeric antigen receptor; OS = overall survival; PFS = progression-free survival

These survival curves are derived from partitioned survival models of axi-cel versus liso-cel in third-line large B-cell lymphoma (LBCL).[1]

Figure S2b Overall and progression-free survival, axi-cel matched to tisa-cel and tisa-cel



Abbreviations: CAR = chimeric antigen receptor; OS = overall survival; PFS = progression-free survival

These survival curves are derived from partitioned survival models of axi-cel versus tisa-cel in third-line LBCL.[2]

S3 Application of real-world data

Among sample patients identified in the Anlitiks All-Payor Claims data, average per patient numbers of Intensive Care Unit (ICU) days, non-ICU inpatient days, outpatient visits and Emergency Department (ED) visits occurring during the 91-day period beginning on the day of chimeric antigen receptor (CAR) T-cell infusion ("follow-up period") were evaluated separately for six mutually-exclusive patient groups defined by CAR T-cell site of care and adverse-event status:

- Inpatient site of care; evidence of cytokine release syndrome (CRS)
- Inpatient site of care; evidence of neurologic event (NE)
- Inpatient site of care; no evidence of CRS, NE, or infection
- Outpatient site of care; evidence of CRS
- Outpatient site of care; evidence of NE
- Outpatient site of care; no evidence of CRS, NE, or infection

In the model, resource use estimates for those with evidence of CRS were applied to patients with grade 3+ CRS without comorbid NE; estimates for those with evidence of NE were applied to patients with grade 3+ NE without comorbid CRS; and estimates for those without evidence of CRS, NE, or infection were applied to patients with neither grade 3+ CRS nor grade 3+ NE. For each category of resource use (i.e., ICU days, non-ICU inpatient days, outpatient visits and ED visits), the maximum of the average number of days/visits observed among patients with evidence of CRS and the average number of days/visits observed among patients with evidence of NE were applied to modeled patients with both grade 3+ CRS and grade 3+ NE.

Table S4 Model inputs related to healthcare resource utilization

	Base	Low	High
Healthcare resource utilization, days 0-90[a]			
CAR T-cell site of care: inpatient			
Patients with CRS but not NE			
ICU days / patient	2.08	1.66	2.49
Non-ICU inpatient days / patient	17.16	13.73	20.59
ED visits / patient	0.06	0.05	0.07
Outpatient visits / patient	5.04	4.03	6.04
Patients with NE but not CRS			
ICU days / patient	2.32	1.86	2.78
Non-ICU inpatient days / patient	16.83	13.47	20.20
ED visits / patient	0.12	0.09	0.14
Outpatient visits / patient	4.70	3.76	5.65
Patients with both CRS and NE			
ICU days / patient	2.32	1.86	2.78
Non-ICU inpatient days / patient	17.16	13.73	20.59
ED visits / patient	0.12	0.09	0.14
Outpatient visits / patient	5.04	4.03	6.04
CAR T-cell site of care: outpatient			
Patients with CRS but not NE			
ICU days / patient	2.35	1.88	2.82
Non-ICU inpatient days / patient	7.81	6.24	9.37
ED visits / patient	0.01	0.01	0.01
Outpatient visits / patient	3.38	2.70	4.06
Patients with NE but not CRS			
ICU days / patient	2.01	1.61	2.41
Non-ICU inpatient days / patient	4.76	3.81	5.71
ED visits / patient	0.02	0.02	0.03
Outpatient visits / patient	2.16	1.73	2.59
Patients with both CRS and NE			
ICU days / patient	2.35	1.88	2.82
Non-ICU inpatient days / patient	7.81	6.24	9.37
ED visits / patient	0.02	0.02	0.03
Outpatient visits / patient	3.38	2.70	4.06

[a] Derived from Anlitiks All-Payor Claims data. Refer to S3 for more information.

Abbreviations: CAR = chimeric antigen receptor; CRS = cytokine release syndrome; ED = Emergency Department; ICU = Intensive Care Unit; NE = neurologic event

Table S5 PSA inputs related to costs, CAR T-cell site of care, healthcare resource utilization, and health utilities

	Mean	Standard error	Distribution
Unit costs ($)			
CAR T-cell administration cost	$148	$15	GAMMA
Apheresis cost / patient	$112	$11	GAMMA
Cost / package			
Bendamustine	$2,474	$252	GAMMA
Cyclophosphamide	$280	$29	GAMMA
Fludarabine	$95	$10	GAMMA
IVIG	$999	$102	GAMMA
Bridging therapy cost / patient	$3,426	$350	GAMMA
Lymphodepleting chemotherapy administration cost	$148	$15	GAMMA
SCT cost / episode	$309,356	$31,567	GAMMA
IVIG administration cost	$148	$15	GAMMA
Inpatient hospitalization cost / day			
ICU day	$6,305	$643	GAMMA
Non-ICU day	$2,875	$293	GAMMA
ED visit cost	$124	$13	GAMMA
Outpatient/other visit cost	$183	$19	GAMMA
Routine care costs / patient / month, months 4+			
Pre progression, months 4-60	$1,829	$187	GAMMA
Pre progression, months 60+	$365	$37	GAMMA
Post progression	$1,829	$187	GAMMA
End of life care cost / patient	$19,529	$1,993	GAMMA
CAR T-cell site of care[a]			
Inpatient %	82.9%	0.085	BETA
Relative CRS and NE incidence between CAR T-cell sites of care, inpatient/outpatient	1.38	0.14	GAMMA
Healthcare resource utilization, days 0-90			
CAR T-cell site of care: inpatient			
Patients with CRS but not NE			
ICU days / patient	2.08	0.21	GAMMA
Non-ICU inpatient days / patient	17.16	1.75	GAMMA
ED visits / patient	0.06	0.01	GAMMA
Outpatient visits / patient	5.04	0.51	GAMMA
Patients with NE but not CRS			
ICU days / patient	2.32	0.24	GAMMA
Non-ICU inpatient days / patient	16.83	1.72	GAMMA
ED visits / patient	0.12	0.01	GAMMA
Outpatient visits / patient	4.70	0.48	GAMMA

Patients with both CRS and NE			
ICU days / patient	2.32	0.24	GAMMA
Non-ICU inpatient days / patient	17.16	1.75	GAMMA
ED visits / patient	0.12	0.01	GAMMA
Outpatient visits / patient	5.04	0.51	GAMMA
CAR T-cell site of care: outpatient			
Patients with CRS but not NE			
ICU days / patient	2.35	0.24	GAMMA
Non-ICU inpatient days / patient	7.81	0.80	GAMMA
ED visits / patient	0.01	0.00	GAMMA
Outpatient visits / patient	3.38	0.34	GAMMA
Patients with NE but not CRS			
ICU days / patient	2.01	0.21	GAMMA
Non-ICU inpatient days / patient	4.76	0.49	GAMMA
ED visits / patient	0.02	0.00	GAMMA
Outpatient visits / patient	2.16	0.22	GAMMA
Patients with both CRS and NE			
ICU days / patient	2.35	0.24	GAMMA
Non-ICU inpatient days / patient	7.81	0.80	GAMMA
ED visits / patient	0.02	0.00	GAMMA
Outpatient visits / patient	3.38	0.34	GAMMA
Health utilities			
On CAR T-cell therapy (month 1)	0.740	0.076	BETA
Off therapy, months 2+			
Pre progression, months 2-60	0.782	0.080	BETA
Pre progression, months 61+	0.820	0.084	BETA
Post progression	0.390	0.040	BETA

[a] Varied for each CAR T-cell therapy independently.

Abbreviations: CAR = chimeric antigen receptor; CRS = cytokine release syndrome; ED = Emergency Department; ICU = Intensive Care Unit; IVIG = intravenous immune globulin; NE = neurologic event; PSA = probabilistic sensitivity analysis; SCT = stem-cell transplant

Table S6 Treatment-related PSA inputs

	Mean	SE *or* ESS[a]	Distribution
Axi-cel			
CAR T-cell acquisition cost / patient ($)	$399,000	$20,358	GAMMA
% receiving bridging therapy	1.0%	0.051	BETA
% receiving lymphodepleting chemotherapy			
Bendamustine	1.0%	101	DIRICHLET
Cyclophosphamide-fludarabine	98.0%	101	DIRICHLET
% receiving SCT post CAR T-cell infusion	7.9%	0.008	BETA
Grade ≥ 3 AE incidence (%)			
MAIC-matched axi-cel versus liso-cel			
CRS but not NE	3.0%	44.80	DIRICHLET
NE but not CRS	22.8%	44.80	DIRICHLET
Both CRS and NE	6.0%	44.80	DIRICHLET
MAIC-matched axi-cel versus tisa-cel			
CRS but not NE	2.9%	47.65	DIRICHLET
NE but not CRS	20.7%	47.65	DIRICHLET
Both CRS and NE	6.4%	47.65	DIRICHLET
% receiving IVIG	30.6%	0.031	BETA
Tisa-cel			
CAR T-cell acquisition cost / patient ($)	$373,000	$19,031	GAMMA
% receiving bridging therapy	91.9%	0.068	BETA
% receiving lymphodepleting chemotherapy			
Bendamustine	19.8%	111	DIRICHLET
Cyclophosphamide-fludarabine	73.0%	111	DIRICHLET
% receiving SCT post CAR T-cell infusion	5.4%	0.006	BETA
Grade ≥ 3 AE incidence (%)			
CRS but not NE	7.2%	111	DIRICHLET
NE but not CRS	4.5%	111	DIRICHLET
Both CRS and NE	9.9%	111	DIRICHLET
% receiving IVIG	30.0%	0.031	BETA
Liso-cel			
CAR T-cell acquisition cost / patient ($)	$410,300	$20,934	GAMMA
% receiving bridging therapy	59.1%	0.060	BETA
% receiving lymphodepleting chemotherapy			
Bendamustine	1.0%	269	DIRICHLET
Cyclophosphamide-fludarabine	99.0%	269	DIRICHLET
% receiving SCT post CAR T-cell infusion	7.6%	0.008	BETA
Grade ≥ 3 AE incidence (%)			
CRS but not NE	0.9%	228	DIRICHLET
NE but not CRS	8.8%	228	DIRICHLET

Both CRS and NE	1.8%	228	DIRICHLET
% receiving IVIG	21.0%	0.021	BETA

[a] Reflects ESS when distribution is Dirichlet and SE otherwise.

Abbreviations: AE = adverse event; CAR = chimeric antigen receptor; CRS = cytokine release syndrome; ESS = effective sample size; IVIG = intravenous immune globulin; MAIC = matching-adjusted indirect comparison; NE = neurologic event; SCT = stem-cell transplant; SE = standard error

Table S7 Axi-cel-related inputs for scenario analyses[a]

	ZUMA-1 cohorts 1 & 2 with unadjusted AE incidence rates[b]	ZUMA-1 cohort 4[3]	ZUMA-1 cohort 6[4]
% receiving bridging therapy	-	68.3%	52.5%
% receiving SCT post CAR T-cell infusion	-	-	2.5%
Grade ≥ 3 AE incidence (%)[c]			
CRS but not NE	3.4%	0.8%	0.0%
NE but not CRS	23.2%	15.4%	12.5%
Both CRS and NE	7.5%	1.7%	0.0%

[a] Only input values different from those used in the base case analysis are reported here. In general, inputs for which data specific to the cohort of interest were not available were instead informed by ZUMA-1 cohorts 1 and 2.

[b] Unadjusted AE incidence rates for ZUMA-1 cohorts 1 and 2 came from Kite data on file [manuscript under review]. These rates reflect AE incidence over 2 years (the period during which AE data were systematically collected) for the Phase 2 ZUMA-1 patients.

[c] Data on the share of patients experiencing both CRS and NE were not available for any ZUMA-1 cohort. For each scenario, shares of patients with CRS but not NE, NE but not CRS, and both CRS and NE were derived from available data on the share of patients with CRS with or without NE and the share of patients with NE with or without CRS, assuming that the ratio of the share of patients with both CRS and NE to the smaller of the former two shares equals that reported for tisa-cel in the JULIET trial.[5]

Abbreviations: AE = adverse event; CAR = chimeric antigen receptor; CRS = cytokine release syndrome; NE = neurologic event; SCT = stem-cell transplant

Table S8a Scenario analysis results: Axi-cel versus liso-cel

	NMB		INMB (Axi-cel – liso-cel)	ICER
	Axi-cel	Liso-cel		
Base case	$518,624	$263,711	$254,913	$8,946
ZUMA-1 cohorts 1 & 2 with unadjusted AE incidence rates (scenario)	$518,617	$263,711	$254,906	$8,950
ZUMA-1 cohort 4 with unadjusted AE incidence rates (scenario)	$516,216	$263,711	$252,505	$10,278
ZUMA-1 cohort 6 with unadjusted AE incidence rates (scenario)	$533,047	$263,711	$269,336	$965
0% outpatient CAR T-cell site of care (scenario)	$514,983	$260,453	$254,530	$9,158
34% outpatient CAR T-cell site of care (scenario)	$522,335	$266,993	$255,342	$8,708

Abbreviations: AE = adverse event; CAR = chimeric antigen receptor; ICER = incremental cost-effectiveness ratio; INMB = incremental net monetary benefit; NMB = net monetary benefit

Table S8b Scenario analysis results: Axi-cel versus tisa-cel

	NMB		INMB (Axi-cel – tisa-cel)	ICER
	Axi-cel	Tisa-cel		
Base case	$454,719	$174,246	$280,472	$24,506
ZUMA-1 cohorts 1 & 2 with unadjusted AE incidence rates (scenario)	$454,744	$174,246	$280,498	$24,494
ZUMA-1 cohort 4 with unadjusted AE incidence rates (scenario)	$452,344	$174,246	$278,097	$25,568
ZUMA-1 cohort 6 with unadjusted AE incidence rates (scenario)	$469,139	$174,246	$294,892	$18,053
0% outpatient CAR T-cell site of care (scenario)	$451,123	$170,863	$280,260	$24,601
34% outpatient CAR T-cell site of care (scenario)	$458,379	$177,656	$280,723	$24,394

Abbreviations: AE = adverse event; CAR = chimeric antigen receptor; ICER = incremental cost-effectiveness ratio; INMB = incremental net monetary benefit; NMB = net monetary benefit

References

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2. Liu R, Oluwole OO, Diakite I, Botteman MF, Snider JT, Locke FL. Cost effectiveness of axicabtagene ciloleucel versus tisagenlecleucel for adult patients with relapsed or refractory large B-cell lymphoma after 2 or more lines of systemic therapy in the United States. J Med Econ. 2021:1.

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