

Supplementary Online Content

Camacho-Arteaga L, Iacoboni G, Kwon M, et al. Late adverse events after chimeric antigen receptor T-cell therapy for patients with aggressive B-cell non-Hodgkin lymphoma. *JAMA Netw Open*. 2025;8(2):e2461683.
doi:10.1001/jamanetworkopen.2024.61683

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Long-Term AEs Incidence Per 100 Person-Months (PM)

Adverse Events	Patients No. (%)	Episodes	Incidence rate per 100PM	95% CI
Infections	79 (45.9)	146	5.63	[4.50-7.04]
Neutropenia	69 (40.1)	93	3.59	[2.89-4.53]
Thrombocytopenia	46 (26.7)	58	2.24	[1.65-3.02]
Anemia	44 (25.6)	53	2.04	[1.48-2.83]
Others	25 (14.5)	30	1.16	[0.74-1.82]
Dermatological diseases	23 (13.4)	27	1.04	[0.71-1.54]
Neurologic disorders	15 (8.7)	15	0.58	[0.34-0.99]
Cardiovascular events	10 (5.8)	13	0.50	[0.26-0.97]
Secondary neoplasms	4 (2.3)	5	0.19	[0.09-0.44]
Psychiatric disorders	1 (0.6)	1	0.04	[0.01-0.18]
Immune-related events	1 (0.6)	1	0.04	[0.01-0.23]
GVHD	0 (0)	0	0	[0-0.14]

eTable 2. Long-Term AE Incidence Rate Per 100 Person-Months (PM) Per Infused CAR T-Cell Product

<i>Adverse Events</i>	<i>Tisagenlecleucel (n=55)</i>				<i>Axicabtagen ciloleucel (n=117)</i>				<i>p-value</i>
	<i>Patients n (%)</i>	<i>Episodes</i>	<i>Incidence rate per 100PM</i>	<i>95% CI</i>	<i>Patients n (%)</i>	<i>Episodes</i>	<i>Incidence rate per 100PM</i>	<i>95% CI</i>	
Infections	19 (34.5)	31	4.10	[2.42-6.94]	60 (51.3)	115	6.26	[4.88-8.02]	0.133
Neutropenia	23 (41.8)	33	4.37	[2.83-6.75]	46 (39.3)	60	3.27	[2.49-4.28]	0.233
Thrombocytopenia	19 (34.5)	26	3.44	[2.14-5.54]	27 (23.1)	32	1.74	[1.20-2.53]	0.022
Anemia	16 (29.1)	20	2.65	[1.50-4.66]	28 (23.9)	33	1.80	[1.21-2.66]	0.249
Others	10 (18.2)	13	1.72	[0.80-3.69]	15 (12.8)	17	0.93	[0.54-1.57]	0.161
Dermatological diseases	6 (10.9)	7	0.93	[0.37-2.35]	17 (14.5)	20	1.09	[0.72-1.65]	0.724
Neurologic disorders	7 (12.7)	7	0.93	[0.40-2.12]	8 (6.8)	8	0.44	[0.22-0.88]	0.159
Cardiovascular events	5 (9.1)	7	0.93	[0.37-2.30]	5 (4.3)	6	0.33	[0.13-0.82]	0.108
Neoplasms	0 (0)	0	0	[0-0.49]	4 (3.4)	5	0.27	[0.12-0.62]	0.960
Psychiatric disorders	0 (0)	0	0	[0-0.49]	1 (0.9)	1	0.05	[0.01-0.27]	0.960
Immune-related events	1 (1.8)	1	0.13	[0.02-0.76]	0 (0)	0	0	[0-0.20]	0.943
GVHD	0 (0)	0	0	[0-0.49]	0 (0)	0	0	[0-0.20]	-

eTable 3. Grade ≥3 Infectious and Cytopenia Incidence Rate Per 100 Person-Months (PM) Per Infused CAR T-Cell Product

Adverse Events	Tisagenlecleucel (n=55)				Axicabtagen ciloleucel (n=117)				p-value
	Patients n (%)	Episodes	Incidence rate per 100PM	95% CI	Patients n (%)	Episodes	Incidence rate per 100PM	95% CI	
Infections	10 (18.2)	15	1.98	[0.87-4.53]	25 (21.4)	40	2.18	[1.44-3.28]	0.829
Neutropenia	15 (27.3)	24	3.18	[1.82-5.53]	34 (29.1)	39	2.12	[1.50-3.01]	0.193
Thrombocytopenia	8 (14.5)	10	1.32	[0.57-3.09]	14 (12.0)	15	0.82	[0.45-1.48]	0.333
Anemia	6 (10.9)	6	0.79	[0.29-2.18]	8 (6.8)	8	0.44	[0.17-1.11]	0.396

eTable 4. Latency and Length of AE Episodes, According to Time of Onset

	Onset within 3 months and persisting beyond						Onset after 3 months					
	Episode s	Latency (median [IQR] Min- max)	Episode s with confirm ed end date	Length (median [IQR] Min- max)	Episode s w/out confirm ed end date	Length (median [IQR] Min- max)	Episode s	Latency (median [IQR] Min- max)	Episode s with confirm ed end date	Length (median [IQR] Min- max)	Episode s w/out confirm ed end date	Length (median [IQR] Min- max)
Infections	18	64.5 [42-84] 9-91	12	30.5 [17.5- 114.5] 7-173	6	337 [277- 494] 116-664	127*	271 [184- 421] 98-751	108	14 [8-32.5] 2-165	19	202 [35- 258] 3-558
Neutropenia	35	29 [1-64] 0-91	18	184 [102- 287] 12-495	17	375 [150- 494] 23-728	58	184 [123- 336] 90-692	35	64 [21- 100] 5-478	23	164 [42- 394] 2-616
Thrombocytope nia	31	1 [0-30] 0-86	9	162 [126- 189] 9-556	22	372 [251- 572] 44-803	27	284 [151- 365] 91-558	10	86 [32- 152] 15-215	17	291 [240- 356] 1-674
Anemia	28	11 [0-60.5] 0-91	11	140 [107- 196] 21-533	17	329 [263- 572] 44-728	25	259 [158- 380] 91-721	8	50.5 [7-91.5] 1-96	17	84 [19- 270] 0-357
Others	8	33.5 [14.5- 55.5] 2-84	3	97 [68-224] 68-224	5	391 [262- 462] 104-728	21*	278 [166- 525] 95-754	3	3 [1-52] 1-52	18	145 [46- 301] 19-542
Dermatological diseases	3	61 [57-78] 57-78	2	193.5 [175- 212] 175-212	1	262 [262] 262	24	177 [119- 289] 92-518	6	115 [35- 128] 25-129	18	307.5 [203- 595] 35-628
Neurologic disorders	5	63 [60-63] 8-67	4	167.5 [109.5- 246.5]	1	82 [82] 82	10	266.5 [171- 334]	6	185.5 [3-270] 1-295	4	368 [165.5- 516]

	83-294							131-487				54-573
Cardiovascular events	1	0 [0] 0	0	-	1	409 [409] 409	12	268 [164.5-319] 117-752	7	6 [1-126] 1-308	5	138 [87-287] 35-645
Neoplasms	0	-	0	-	0	-	5	514 [374-541] 217-693	3	104 [29-433] 29-433	2	127.5 [40-215] 40-215
Psychiatric disorders	0	-	0	-	0	-	1	550 [550] 550	0	-	1	189 [189] 189
Immune-related events	0	-	0	-	0	-	1	458 [458] 458	0	-	1	87 [87] 87
GVHD	0	-	0	-	0	-	0	-	0	-	0	-

*One episode with missing start date

eTable 5. Any Grade AE Episodes According to Onset*

Adverse Events	3 months (n=172) n (%)		>3 - 6 months (n=171) n (%)		>6 - 9 months (n=148) n (%)		>9 - 12 months (n=124) n (%)		>12 - 18 months (n=102) n (%)		>18 - 24 months (n=68) n (%)	
Patients with any AE	73 (42.4)		64 (37.4)		43 (29.1)		37 (29.8)		35 (34.3)		22 (32.4)	
	Patients	Episodes	Patient s	Episodes	Patient s	Episodes	Patient s	Episodes	Patients	Episodes	Patient s	Episodes
Infections	18 (10.5)	18	26 (15.2)	30	27 (18.2)	36	15 (12.1)	18	17 (16.7)	21	14 (20.6)	23
Neutropenia	34 (19.8)	35	25 (14.6)	27	10 (6.8)	10	9 (7.3)	10	7 (6.9)	7	4 (5.9)	4
Thrombocytopenia	31 (18)	31	8 (4.7)	9	3 (2.0)	4	7 (5.6)	7	6 (5.9)	6	1 (1.5)	1
Anemia	28 (16.3)	28	7 (4.1)	9	4 (2.7)	4	5 (4.0)	5	5 (4.9)	5	2 (2.9)	2
Others	6 (3.5)	8	6 (3.5)	6	5 (3.4)	5	4 (3.2)	4	2 (2.0)	2	5 (7.4)	5
Dermatological diseases	3 (1.7)	3	11 (6.4)	12	5 (3.4)	5	4 (3.2)	4	3 (2.9)	3	0 (0)	0
Neurologic disorders	5 (2.9)	5	4 (2.3)	4	1 (0.7)	1	3 (2.4)	3	2 (2.0)	2	0 (0)	0
Cardiovascular events	1 (0.6)	1	4 (2.3)	4	3 (2.0)	3	3 (2.4)	3	0 (0)	0	2 (2.9)	2
Neoplasms	0 (0)	0	0 (0)	0	1 (0.7)	1	0 (0)	0	2 (2.0)	3	1 (1.5)	1
Psychiatric disorders	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	1 (1.5)	1
Immune-related events	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	1 (1.0)	1	0 (0)	0
GVHD	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0

*One patient could have more that one AE episode

eTable 6. Grade ≥ 3 AE Episodes According to Onset

Adverse Events	3 months (n=172) n (%)		>3 - 6 months (n=171) n (%)		>6 - 9 months (n=148) n (%)		>9 - 12 months (n=124) n (%)		>12 - 18 months (n=102) n (%)		>18 - 24 months (n=68) n (%)	
Patients with any grade 3-5 AE	42 (24.4)		25 (14.6)		20 (13.5)		11 (8.9)		12 (11.8)		9 (13.2)	
	Patients	Episodes	Patients	Episodes	Patients	Episodes	Patients	Episodes	Patients	Episodes	Patients	Episodes
<i>Infections</i>	8 (4.7)	8	10 (5.8)	10	14 (9.5)	15	6 (4.8)	6	4 (3.9)	4	6 (8.8)	12
<i>Neutropenia</i>	25 (14.5)	26	15 (8.8)	17	7 (4.7)	7	5 (4.0)	6	5 (4.9)	5	2 (2.9)	2
<i>Thrombocytopenia</i>	15 (8.7)	15	4 (2.3)	5	1 (0.7)	1	3 (2.4)	3	1 (1.0)	1	0 (0)	0
<i>Anemia</i>	7 (4.1)	7	3 (1.8)	3	2 (1.4)	2	0 (0)	0	2 (2.0)	2	0 (0)	0
<i>Others</i>	1 (0.6)	1	0 (0)	0	0 (0)	0	1 (0.8)	1	0 (0)	0	2 (2.9)	2
<i>Dermatological diseases</i>	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0
<i>Neurologic disorders</i>	2 (1.2)	2	2 (1.2)	2	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0
<i>Cardiovascular events</i>	0 (0)	0	0 (0)	0	1 (0.7)	1	0 (0)	0	0 (0)	0	0 (0)	0
<i>Neoplasms</i>	0 (0)	0	0 (0)	0	1 (0.7)	1	0 (0)	0	1 (1.0)	1	1 (1.5)	1
<i>Psychiatric disorders</i>	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0
<i>Immune-related events</i>	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0
<i>GVHD</i>	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0	0 (0)	0

*One patient could have more than one AE episode

eTable 7. All Infectious Episodes*

<i>Infectious AEs</i>	<i>Episodes</i>
SARS-CoV2 infection	45
Unspecified acute lower respiratory infection	14
Unspecified acute upper respiratory infection	12
Cystitis, unspecified	4
Enterocolitis due to Clostridium difficile	4
Gingivitis and periodontal diseases	4
Pneumonia without isolation	4
Urinary tract infection, site not specified	4
Herpes zoster	3
Influenza due to identified influenza virus	3
Pneumonia due to Pseudomonas	3
Campylobacter enteritis	3
Acute bronchitis due to respiratory syncytial virus	2
Candidal stomatitis	2
Diarrhoea and gastroenteritis of presumed infectious origin	2
Pneumonia due to Haemophilus influenzae	2
Pneumonia due to other infectious organisms, not elsewhere classified	2
Pseudomonas aeruginosa sepsis	2
Respiratory syncytial virus as the cause of diseases classified to other chapters	2
Septicaemia due to Klebsiella oxytoca	2
Actinomycosis, unspecified	1
Acute bronchitis due to other specified organisms	1
Acute bronchitis due to parainfluenza virus	1
Acute pharyngitis, unspecified	1
Acute tubulo-interstitial nephritis	1

Acute upper respiratory infections of multiple and unspecified sites	1
Candidiasis	1
Catheter infection without isolation	1
Cholecystitis, unspecified	1
Cytomegaloviral disease	1
Escherichia coli in sputum	1
Haemophilus influenza in bronchoalveolar lavage	1
Herpes simplex infections	1
Infective spondylopathies without isolation	1
Influenza and pneumonia	1
Iridocyclitis, unspecified	1
Orchitis and epididymitis	1
Orchitis, epididymitis and epididymo-orchitis with abscess	1
Other interstitial pulmonary diseases with fibrosis	1
Otitis media, unspecified	1
Parvovirus infection, unspecified	1
Pilonidal cyst with abscess	1
Pneumocystosis	1
Pneumonia due to Acinetobacter	1
Salmonella enteritis	1
Scabies	1
Suppurative otitis media without isolation	1
Total	146

*A patient could have more than one episode

eTable 8. Dermatologic Adverse Events

<i>Dermatological AEs</i>	<i>n</i>
Eczematous dermatoses	5
Eosinophilic dermatoses	5
Acne, unspecified	1
Actinic keratosis	1
Allergic urticaria	1
Benign lipomatous neoplasm	1
Erythema intertrigo	1
Erythema multiforme	1
Follicular disorder, unspecified	1
Other disorders of pigmentation	1
Postoperative seroma abdominal	1
Pruritus, unspecified	1
Psoriasis	1
Rash and other nonspecific skin eruption	1
Recurrent oral aphthae	1
Scabies	1
Secondary dermatitis due to malignant neoplasia	1
Spontaneous ecchymoses	1
Viral warts	1
Total	27

eTable 9. Neurologic Adverse Events

<i>Neurological AEs</i>	<i>n</i>
Paresthesias	4
Unspecified encephalopathy	3
Polyneuropathy	1
Non-traumatic subdural hemorrhage	1
Intracerebral hemorrhage	1
Vocal cord paralysis	1
Tremor	1
Central vertigo	1
Postherpetic neuralgia	1
Bilateral psoas paresis	1
Total	15

eTable 10. Cardiovascular Adverse Events

<i>Cardiovascular AEs</i>	<i>n</i>
Heart failure	6
Hypertrophic cardiomyopathy	1
Pericarditis	1
Syncope	1
Thoracic pain. unspecified	1
Interstitial fibrosis	1
Atrial fibrillation and flutter	1
Tachycardia. unspecified	1
Total	13

eTable 11. Other Adverse Events

<i>Other AEs</i>	<i>n</i>
Functional diarrhoea	4
Abnormal laboratory results	3
Dyslipidemia	2
Embolism and thrombosis of unspecified vein	2
Benign neoplasm of colon, rectum, anus and anal canal	1
Bicipital tendinitis	1
Bronchitis, not specified as acute or chronic	1
Cholelithiasis	1
Fatty liver	1
Hypothyroidism	1
Idiopathic thrombocytopenic purpura	1
Interstitial pulmonary disease, unspecified	1
Lung diseases due to external agents	1
Magnesium deficiency	1
Other complications of internal prosthetic devices, implants and grafts, not elsewhere classified	1
Other diseases of lip and oral mucosa	1
Pain localized to upper abdomen	1
Postoperative intestinal obstruction	1
Pulmonary embolism	1
Rectal polyp	1
Renal failure	1
Tinnitus	1
Unilateral or unspecified inguinal hernia, with obstruction, without gangrene	1
Total	30

eFigure. Cumulative Incidence of NRM

