LE INFEZIONI NEI PAZIENTI SOTTOPOSTI A TERAPIA CELLULARE: SIMILITUDINI E DIFFERENZE TRA IL CONTESTO ALLOTRAPIANTOLOGICO E LE CAR-T

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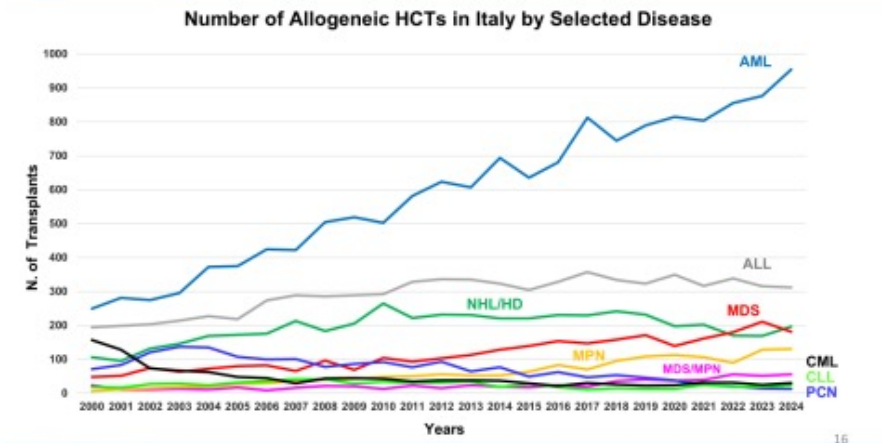
Infections in allo-HSCT and CAR-T: differences and analogies

- Underlying diseases
- Timing of infections: early, late
- Epidemiology of infections
  - Bacterial
  - Fungal
  - Viral
- Relevance of underlying disease
- Prophylaxis of infections
- Vaccinations

Current indications to allo-HSCT: underlying disease



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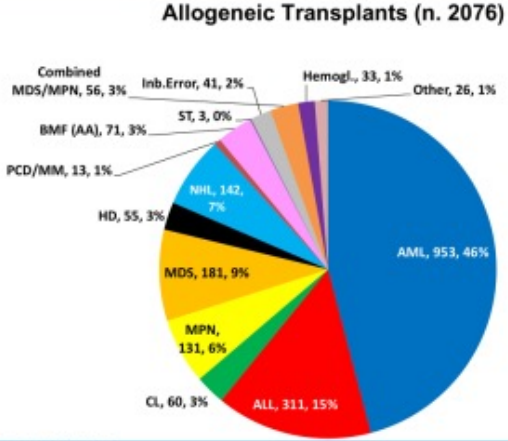


Disease	%
AML	46
ALL	15
MDS	9
NHL	7
MPN	6
HD	3

Export date 14/04/2025

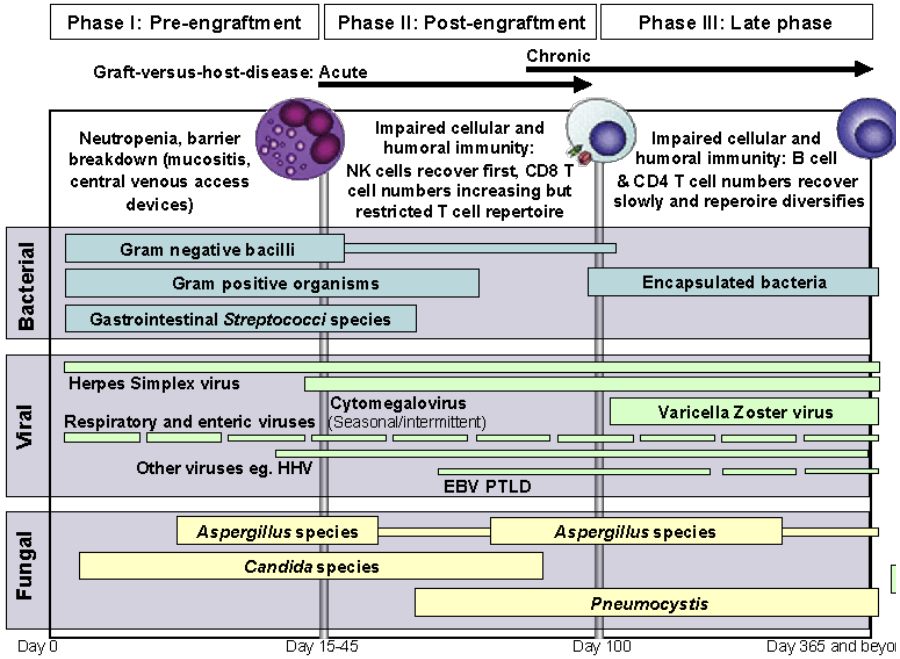
Stem Cell Research & Therapy

Kedia et al., J Stem Cell Res Ther 2013, S3
http://dx.doi.org/10.4172/2157-7633.S3-002

Review Article Open Access

Infectious Complications of Hematopoietic Stem Cell Transplantation

Shiksha Kedia[1], Pranab Sharma Acharya[1], Farhan Mohammad[1], Huy Nguyen[1], Deepak Asti[1], Suchita Mehta[1*], Manisha Pant[2] and Neville Mobarakai[3]



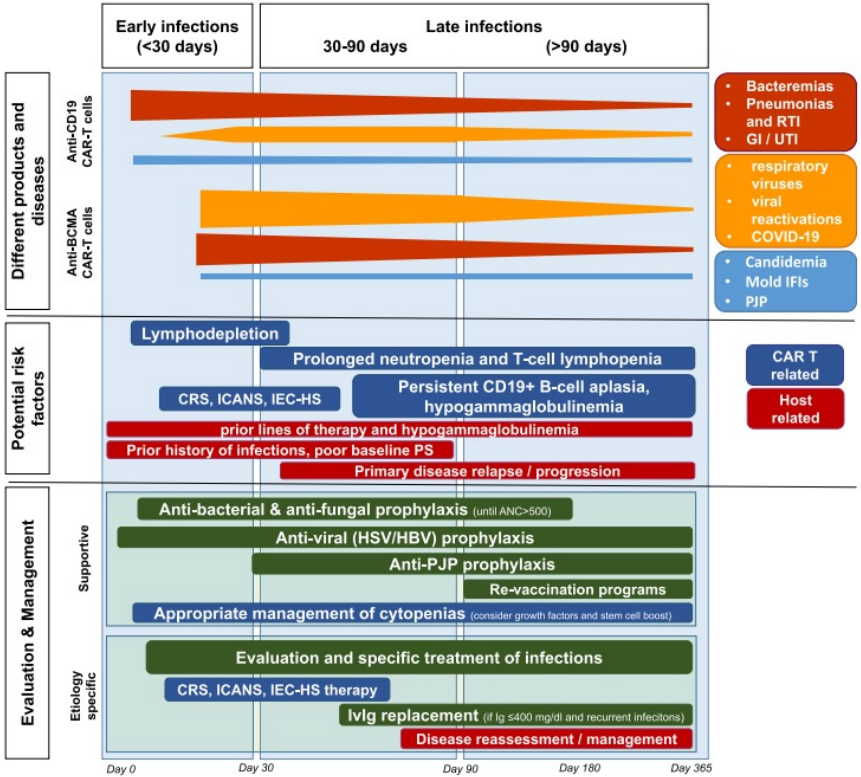
Transplantation and Cellular Therapy 30 (2024) 955–969

Transplantation and Cellular Therapy
journal homepage: www.astctjournal.org

Guideline

Best Practice Considerations by The American Society of Transplant and Cellular Therapy: Infection Prevention and Management After Chimeric Antigen Receptor T Cell Therapy for Hematological Malignancies

Zainab Shahid[1,*], Tania Jain[2], Veronica Dioverti[3], Martini Pennisi[4], Lekha Mikkilineni[5], Swetha Kambhampati Thiruvengadam[6], Nirali N Shah[7], Sanjeet Dadwal[8], Genovefa Papanicolaou[9], Mehdi Hamadani[10], Paul A. Carpenter[10], Gabriela Maron Alfaro[11], Susan K. Seo[1], Joshua A. Hill[12]



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Critical Reviews in Oncology / Hematology 192 (2023) 104134

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Infections in haematology patients treated with CAR-T therapies: A systematic review and meta-analysis

Gemma K. Reynolds [a,c,d,e,*,1], Beatrice Sim [a,d], Tim Spelman [d], Ashmitha Thomas [e], Anthony Longhitano [f], Mary Ann Anderson [b], Karin Thursky [a,c,d], Monica Slavin [a,c,d], Benjamin W. Teh [a,c,d,2]

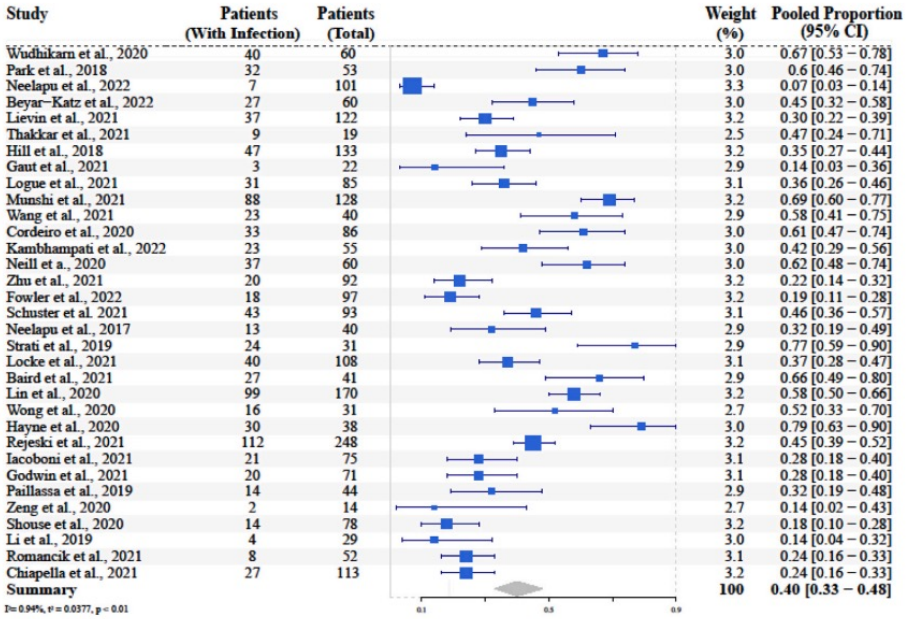

Fig. 2. Pooled proportion of CAR-T treated patients experience ≥ 1 infection.

2678 patients across 33 studies were included in the primary outcome. Forty-percent of patients experienced an infection of any grade. Twenty-five percent of infection events were severe.

Table 2
Pooled proportion of all-grade infection by underlying haematological malignancy.

Haematological malignancy	Pooled Incidence (95% CI)	Number of studies (patients)	Comment	Reference
ALL	0.49 (0.31 – 0.67)	4 (230)	High heterogeneity ($I^2 = 87\%$, $t^2 = 0.0375$, $p < 0.01$)	(Li et al., 2021; Hill et al., 2018; Park et al., 2018; Zhu et al., 2021)
MM	0.57 (0.39 – 0.75)	4 (265)	Moderate heterogeneity ($I^2 = 76\%$, $t^2 = 0.0091$, $p < 0.01$)	(Munshi et al., 2021; Li et al., 2021; Kambhampati et al., 2022; Wang et al., 2021).
NHL	0.36 (0.29 – 0.44)	28 (1883)	High heterogeneity ($I^2 = 93\%$, $t^2 = 0.0375$, $p < 0.01$)	(Neelapu et al., 2017; Wang et al., 2020; Logue et al., 2021; Beyar-Katz et al

All-grade infections, bacterial and viral infections were highest in myeloma patients at 57%, 37% and 28%, respectively.

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Late infections were as common as early infections (IRR = 0.86, 95% CI: 0.38 – 1.98).

Fig. 3. Comparison of early and late infections in ALL compared to NHL.

Late events after anti-CD19 CAR T-cell therapy for relapsed/refractory B-cell non-Hodgkin lymphoma

frontiers | Frontiers in Oncology
PUBLISHED 11 June 2024

Ana Costa Cordeiro[1*], George Durisek[2], Marjorie Vieira Batista[3], Jayr Schmidt[1], Marcos de Lima[4] and Evandro Bezerra[4*]

Before day 30, 2 infections/100 patient-day. After day 30, <0.5 infection/100 patient-day, (2 per patient-year) in most of cases managed as outpatients

Infections are more prevalent in the first month after CART19, the incidence declines over time, and it is a rare severe infection beyond the initial month from CART19. Early infections are more severe and mostly bacterial, in contrast with infections after 3 months, which are milder and mostly viral respiratory tract infections.

TABLE 3 Late infection after CART19.

Reference	Product	N	Late infection
Cordeiro et al. (17)	CART19 JCAR014	54 (NHL, B-ALL, and CLL)	Infection density beyond D90 from CART19 was 0.55 infection/100 patient-days at risk (2.1 per patient-year). Upper respiratory tract infections (48%), lower respiratory infections (23%), 80% managed as outpatients, 20% as inpatients, and 5% in ICU
Wudhikarn et al. (52)	Axi-cel and tisa-cel	60 NHL	Absolute number of infections post-CART19: 101 events. 23% between D30 and D100, 14% between D100 and D180, and 27.5% after D180
Baird et al. (50)	Axi-cel	41 NHL	Infection density through D28, 2.35; between D29 and D180, 0.38; D181–D365, 0.46; and beyond 1 year, 0.33 (#/100 patient-days)
Logue et al. (51)	Axi-cel	85 NHL	Infection rate 11.7 per 1,000 person-days within D30 from CART19, while 2.3 per 1,000 person-days between D30 and D90

JAMA Network Open. 2025;8(2):e2461683.

JAMA Network | Open.

Original Investigation | Hematology

Late Adverse Events After Chimeric Antigen Receptor T-Cell Therapy for Patients With Aggressive B-Cell Non-Hodgkin Lymphoma

Lina Camacho-Arteaga, MD, PhD; Gloria Iacoboni, MD, PhD; Mi Kwon, MD, PhD; Rebeca Bailén, MD, PhD; Rafael Hernani, MD, PhD; Ana Benzaquén, MD; Lucía López-Corral, MD, PhD; Estefanía Pérez-López, MD; Lina María Legulzamo-Martínez, MD; María Calvo-Orteu, BS; Manuel Guerreiro, MD, PhD; Aitana Balaguer-Rosello, MD, PhD; Carla Alonso-Martínez, PharmD; Xavier Vidal, MD, PhD; Pere Barba, MD, PhD; Antònia Agustí, MD, PhD

Patients meeting the inclusion criteria were enrolled into the study at 3 months after infusion, and their baseline information was then collected. This time point was selected based on the expected period for a complete resolution of the most common acute toxic effects (CRS and ICANS).

Figure. Long-Term Adverse Event Incidence Per 100 Person-Months

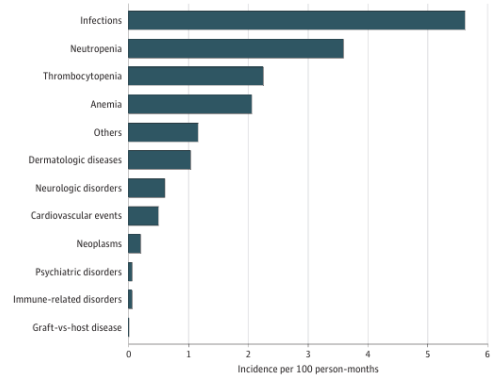

Table 2. Latency and Length of Adverse Event Episodes

	Latency		Length[a]	
Adverse event	Episodes, No.	Median (IQR) [range], d	Episodes with confirmed end date, No.	Median (IQR) [range], d
Infections	145[b]	251 (158-400) [9-751]	120	15 (9-34) [2-173]
Neutropenia	93	111 (57-211) [0-692]	53	92 (28-185) [5-495]
Thrombocytopenia	58	70 (1-258) [0-558]	19	126 (60-189) [9-556]
Anemia	53	90 (6-186) [0-721]	19	96 (35-148) [1-533]
Others	29[b]	191 (84-363) [2-754]	6	60 (3-97) [1-224]
Dermatologic diseases	27	165 (106-282) [57-518]	8	127 (70-152) [25-212]
Neurologic disorders	15	171 (63-279) [8-487]	10	169 (83-270) [1-295]
Cardiovascular events	13	265 (155-305) [0-752]	7	6 (1-126) [1-308]
Secondary neoplasms	5	514 (374-541) [217-693]	3	104 (29-433) [29-433]
Psychiatric disorders	1	550 (550-550) [550-550]	0	0
Immune-related events	1	458 (458-458) [458-458]	0	NA
Graft-vs-host disease	0	NA	0	NA

Seven patients (4.1%) experienced NRM during study follow-up, all from infections: 3 patients from COVID-19 pneumonia, 1 patient with Escherichia coli and Achromobacter sepsis, 1 with P aeruginosa sepsis, 1 with P aeruginosa and E coli pneumonia, and 1 with Streptococcus pneumoniae pneumonia.

The cumulative incidence of NRM was 4.4% at 12 months and 6.3% at 24 months

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blood advances

11 NOVEMBER 2025 • VOLUME 9, NUMBER 21

Real-world outcomes of infections following tisagenlecleucel in patients with B-cell ALL: a CIBMTR analysis

Hemalatha G. Rangarajan,[1] Prakash Satwani,[2] Megan M. Herr,[3] Min Chen,[4] Michael J. Martens,[4,5] Kitsada Wudhikarn,[6] Samuel John,[7] Vanessa A. Fabrizio,[8] Emily M. Hsieh,[9] Amar H. Kelkar,[10] Erin Doherty,[11] David I. Marks,[12] Olle Ringden,[13] Brian Friend,[14] Matthew S. Kelly,[15] Nosha Farhadfar,[16] Tim Prestidge,[17] Nasheed M. Hossain,[18] Hongtao Liu,[19] Shahrukh Hashmi,[20,21] Dipenkumar Modi,[22] Lena E. Winestone,[23] Zeinab El Boghdadly,[24] Hemant S. Murthy,[25] Miguel-Angel Perales,[26,27] Roy F. Chemaly,[14] Christopher E. Dandoy,[28] Joshua A. Hill,[29,30] Anna Huppler,[4,31] Marcie Riches,[4] and Jeffery J. Auletta[32,33]

We report infectious complications for 100 days (D100) following tisa-cel therapy in 471 pediatric and young adults (median age 13.8 years) with R/R B-ALL reported from September 2017 to June 2022.

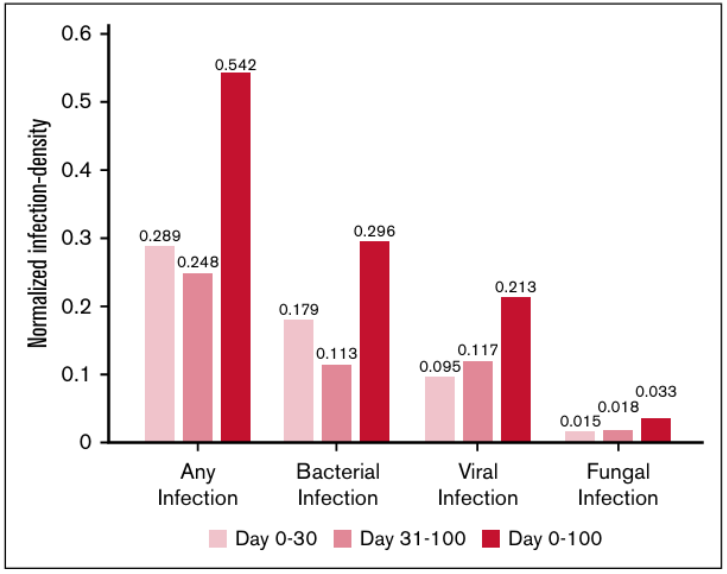

Figure 1. Normalized infection density by organism and time of tisa-cel therapy for R/R B-ALL. Each figure is normalized for the specified nonoverlapping time period.

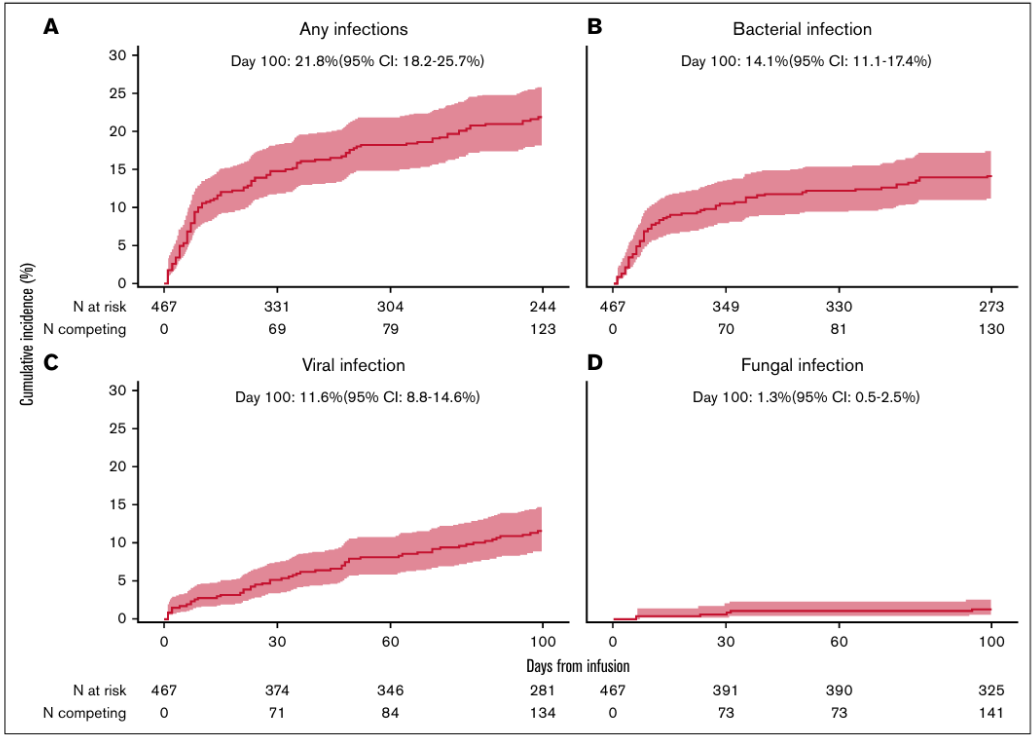

Figure 2. Cumulative incidence of infection with competing events following CD19 CAR T-cell therapy for R/R B-ALL. (A) Any infection; (B) bacterial infection;

Real-world outcomes of infections following tisagenlecleucel in patients with B-cell ALL: a CIBMTR analysis

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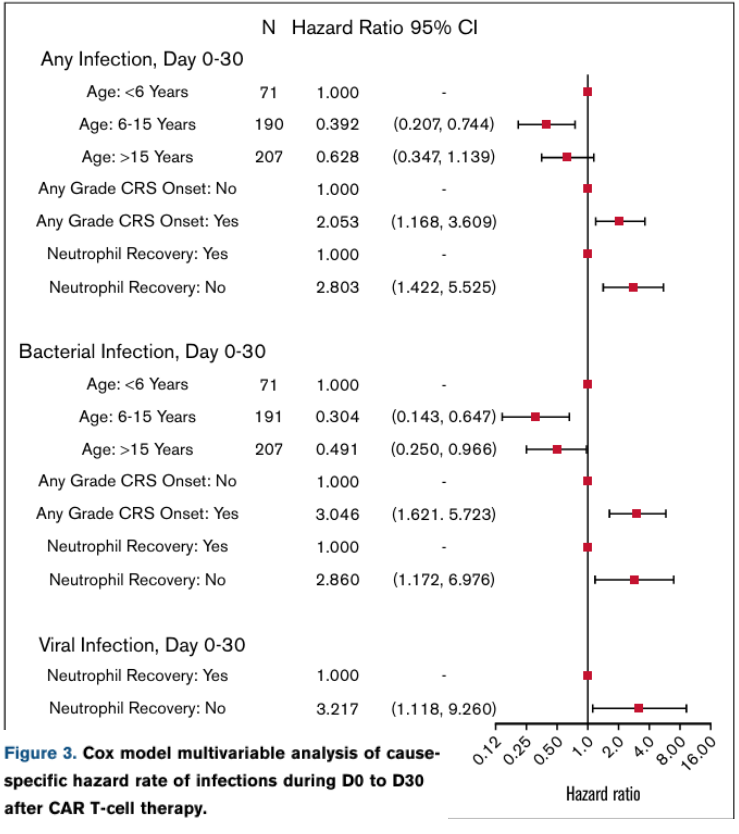
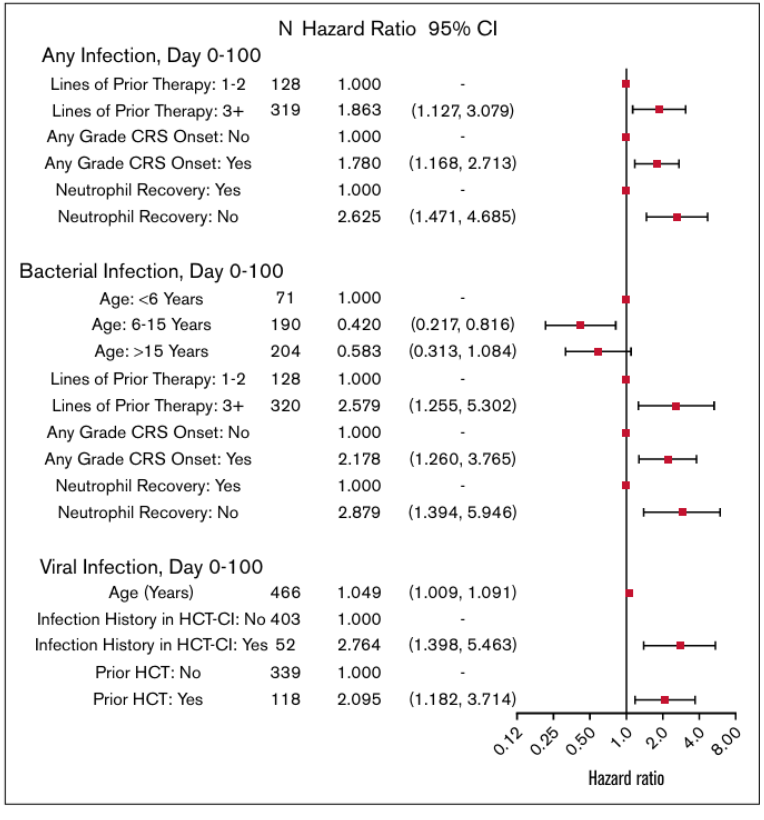


Figure 3. Cox model multivariable analysis of cause-specific hazard rate of infections during D0 to D30 after CAR T-cell therapy.

Figure 4. Cox model multivariable analysis of cause-specific hazard rate of infections during D0 to D100 after CAR T-cell therapy.



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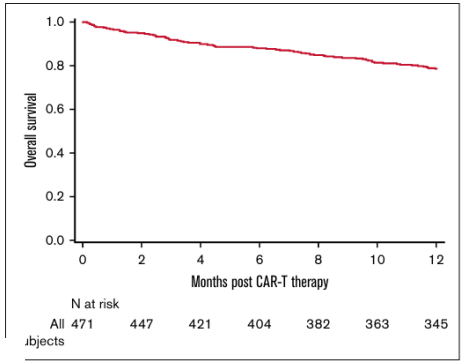

Figure 5. OS state probabilities within 1 year of CAR T-cell therapy.

Table 3. Cox model of overall mortality during days 100 to 365 after tisa-cel therapy

Variable	Category	HR, 95% CI	P value
Infection history after tisa-cel infusion	No infections	1.000	.718 (3 df)
	Infections during days 1-30 and 31-100	0.732 (0.292-1.838)	
	Infection during days 1-30 only	0.960 (0.566-1.629)	.880
	Infection during days 31-100 only	1.289 (0.725-2.291)	.386
Age, y	<6	1.000	**.003 (2 df)**
	6-15	0.406 (0.233-0.709)	.002
	>15	0.700 (0.419-1.170)	.174
Performance score (Lansky <16 years old; Karnofsky ≥16 years old)	90-100	1.000	**<.001 (3 df)**
	80	2.499 (1.610-3.880)	<.001
	<80	1.781 (1.036-3.060)	.037
	Missing	1.645 (0.850-3.183)	.140
Disease status at tisa-cel infusion	CR	1.000	**<.001**
	Not in CR	2.249 (1.491-3.393)	
Any-grade CRS onset*	No	1.000	**.020**
	Yes	1.536 (1.069-2.209)	

Analysis includes patients who are alive and free of subsequent HCT at day 100 landmark. Variables were chosen for inclusion by stepwise selection, with a *P* value of <.05 used as the criterion for inclusion. Infection history after CAR T-cell therapy was forced into the model. *P* values that are significant are indicated in bold.

*CRS onset was treated as a time-dependent covariate.

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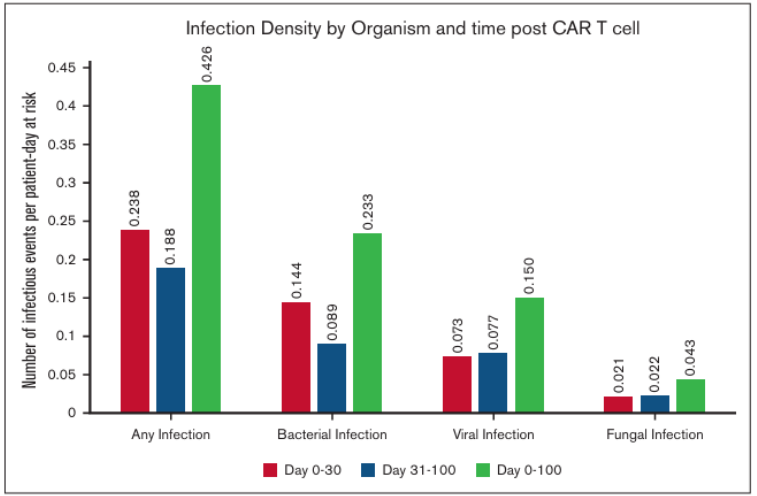
A total of 3350 patients with R/R LBCL received CD19 CAR T cell therapy, with 2804 patients (83.7%) receiving axi-cel and 546 patients (16.3%) receiving tisa-cel across 121 centers during the study period



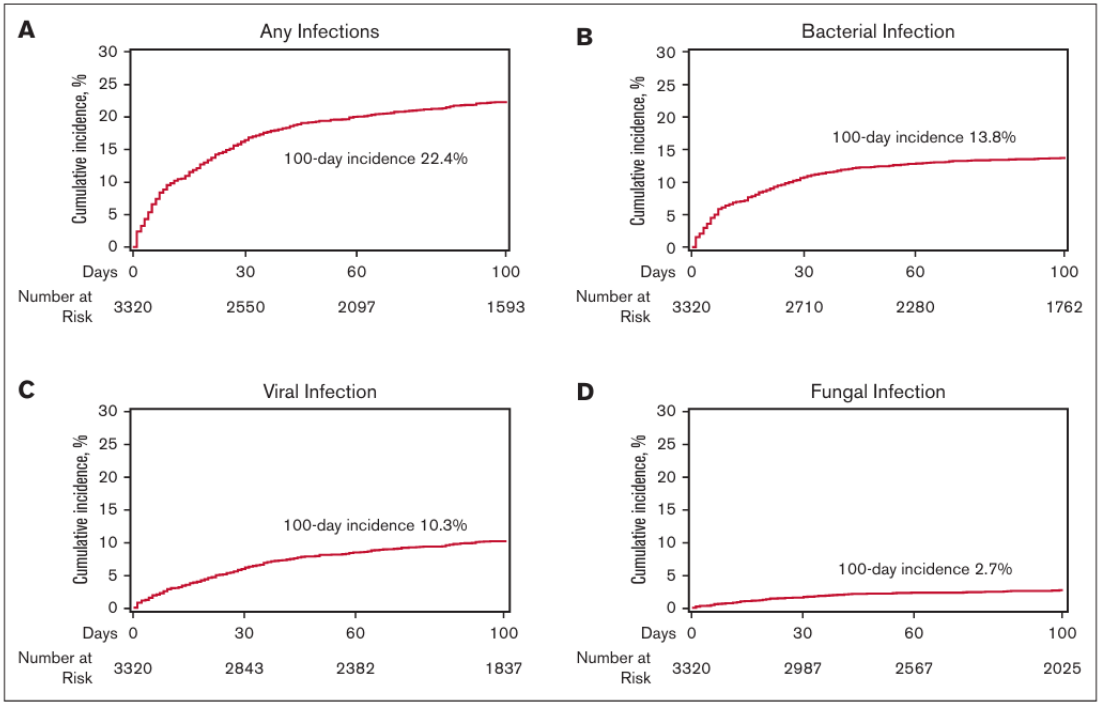


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Table 3. Multivariable analysis of risk factors associated with infection-related complication during day 0-100 after CAR T-cell therapy

	Overall infection				Bacterial infection				Viral infection				Fungal infection			
Variable	**n**	**Event**	**HR (95% CI)**	***P* value**	**n**	**Event**	**HR (95% CI)**	***P* value**	**n**	**Event**	**HR (95% CI)**	***P* value**	**n**	**Event**	**HR (95% CI)**	***P* value**
Age (decades)*	3296	695	1.067 (1.006-1.131)	.030	3304	439	1.117 (1.037-1.203)	.003	NA	NA	NA	NA	NA	NA	NA	NA
KPS				<.001 (3 df)				<.001				<.0001 (3 df)				.014 (3 df)
90-100	1344	207	Ref	Ref	1345	125	Ref	Ref	1349	89	Ref	Ref	1349	20	Ref	Ref
80	976	237	1.644 (1.366-1.979)	<.001	980	134	1.466 (1.152-1.864)	.002	979	114	1.867 (1.416-2.461)	<.001	981	25	1.708 (0.968-3.014)	.065
<80	627	196	2.089 (1.716-2.544)	<.001	629	138	2.343 (1.840-2.984)	<.001	633	89	2.194 (1.627-2.960)	<.001	635	28	2.347 (1.344-4.099)	.003
Missing	349	75	1.472 (1.129-1.920)	.004	350	42	1.320 (0.937-1.861)	.113	352	39	1.746 (1.196-2.548)	.004	353	13	2.467 (1.219-4.994)	.012
Baseline infection history				.004 (2 df)				.006 (2 df)								.002 (2 df)
No	2997	636	Ref	Ref	3004	388	Ref	Ref	NA	NA	NA	NA	3017	74	Ref	Ref
Yes	130	43	1.707 (1.246-2.338)	.001	131	30	1.831 (1.266-2.650)	.001	NA	NA	NA	NA	132	10	3.305 (1.675-6.520)	.001
Missing	169	36	0.972 (0.694-1.363)	.870	169	21	0.956 (0.621-1.473)	.840	NA	NA	NA	NA	169	2	0.656 (0.207-2.077)	.474
No. of lines of previous therapy				.017 (2 df)								.006 (2 df)				
1-2	977	177	Ref	Ref	NA	NA	NA	NA	981	76	Ref	Ref	NA	NA	NA	NA
≥3	2234	521	1.270 (1.073-1.503)	.005	NA	NA	NA	NA	2247	251	1.417 (1.095-1.834)	.008	NA	NA	NA	NA
Missing	85	17	1.021 (0.616-1.695)	.934	NA	NA	NA	NA	85	4	0.536 (0.194-1.477)	.228	NA	NA	NA	NA
CAR T-cell product																
Tisa-cel	538	82	Ref	Ref	539	44	Ref	Ref	NA	NA	NA	NA	NA	NA	NA	NA
Axi-cel	2758	633	1.483 (1.177-1.867)	.001	2765	395	1.800 (1.321-2.453)	<.001	NA	NA	NA	NA	NA	NA	NA	NA
Grade 3-5 CRS†																
No			Ref	Ref			Ref	Ref			Ref	Ref			Ref	Ref
Yes			1.762 (1.385-2.241)	<.001			1.898 (1.422-2.534)	<.001			1.546 (1.076-2.222)	.018			2.555 (1.418-4.603)	.002
Grade 3-5 ICANS†																
No			Ref	Ref			Ref	Ref			Ref	Ref			Ref	Ref
Yes			1.707 (1.408-2.070)	<.001			1.733 (1.356-2.214)	<.001			1.488 (1.125-1.968)	.005			2.629 (1.580-4.375)	<.001
Neutrophil recovery																
Yes			Ref	Ref			NA	NA			Ref	Ref			Ref	Ref
No			1.350 (1.075-1.694)	.01			NA	NA			1.471 (1.037-2.085)	.030			2.318 (1.362-3.945)	.001

Axicabtagene ciloleucel in relapsed or refractory indolent non-Hodgkin lymphoma (ZUMA-5): a single-arm, multicentre, phase 2 trial

Caron A Jacobson, Julio C Chavez, Alison R Sehgal, Basem M William, Javier Munoz, Gilles Salles, Pashna N Munshi, Carla Casulo, David G Maloney, Sven de Vos, Ran Reshef, Lori A Leslie, Ibrahim Yakoub-Agha, Olalekan O Oluwole, Henry Chi Hang Fung, Joseph Rosenblatt, John M Rossi, Lovely Goyal, Vicki Plaks, Yin Yang, Remus Vezan, Mauro P Avanzi, Sattva S Neelapu

Lancet Oncol 2022; 23: 91–103

- Grade 3 or worse infections occurred in 26 (18%) patients, including pneumonia in ten (7%) patients, opportunistic infections in four (3%), and upper respiratory tract infection in one.
- One (1%) patient with follicular lymphoma died of infection

Tisagenlecleucel in adult relapsed or refractory follicular lymphoma: the phase 2 ELARA trial

Nathan Hale Fowler[1,2], Michael Dickinson[3], Martin Dreyling[4], Joaquin Martinez-Lopez[5], Arne Kolstad[6], Jason Butler[7], Monalisa Ghosh[8], Leslie Popplewell[9], Julio C. Chavez[10], Emmanuel Bachy[11], Koji Kato[12], Hideo Harigae[13], Marie José Kersten[14], Charalambos Andreadis[15], Peter A. Riedell[16], P. Joy Ho[17], José Antonio Pérez-Simón[18], Andy I. Chen[19], Loretta J. Nastoupil[1], Bastian von Tresckow[20,21], Andrés José María Ferreri[22], Takanori Teshima[23], Piers E. M. Patten[24,25], Joseph P. McGuirk[26], Andreas L. Petzer[27], Fritz Offner[28], Andreas Viardot[29], Pier Luigi Zinzani[30,31], Ram Malladi[32], Aiesha Zia[33], Rakesh Awasthi[34], Aisha Masood[35], Oezlem Anak[33], Stephen J. Schuster[36,38] and Catherine Thieblemont[37,38]

NATURE MEDICINE | VOL 28 | FEBRUARY 2022 | 325–332 |

- 32% of the patients had grade ≥3 neutropenia
- None of the patients had prolonged grade ≥3 neutropenia
- Ten patients (10%) had grade ≥3 febrile neutropenia
- Any-grade infections occurred in 18.6% of patients 8 weeks post infusion; 5.2% had grade ≥3 events.
- No infection related death

Lisocabtagene maraleucel in follicular lymphoma: the phase 2 TRANSCEND FL study

Nature Medicine | Volume 30 | August 2024 | 2199–2207

- Grade ≥3 infections were reported in seven patients (5%, all 3L+) within the 90-d treatment-emergent period.
- Grade ≥3 late infections (that is, >90-d TEAE period) occurred in three patients (1 3L, 2 4L)
- Two patients died due to COVID-19

Cilta-cel or Standard Care in Lenalidomide-Refractory Multiple Myeloma

J. San-Miguel, B. Dhakal, K. Yong, A. Spencer, S. Anguille, M.-V. Mateos, C. Fernández de Larrea, J. Martínez-López, P. Moreau, C. Touzeau, X. Leleu, I. Avivi, M. Cavo, T. Ishida, S.J. Kim, W. Roeloffzen, N.W.C.J. van de Donk, D. Dytfeld, S. Sidana, L.J. Costa, A. Oriol, R. Popat, A.M. Khan, Y.C. Cohen, P.J. Ho, J. Griffin, N. Lendvai, C. Lonardi, A. Slaughter, J.M. Schecter, C.C. Jackson, K. Connors, K. Li, E. Zudaire, D. Chen, J. Gilbert, T. Yeh, S. Nagle, E. Florendo, L. Pacaud, N. Patel, S.J. Harrison, and H. Einsele

N Engl J Med 2023;389:335-47.

Table 3. Adverse Events (Safety Population).*

Adverse Event	Cilta-cel (N=208)		Standard Care (N=208)	
	All	Grade 3 or 4	All	Grade 3 or 4
Any adverse event — no. (%)	208 (100.0)	201 (96.6)	208 (100.0)	196 (94.2)
Hematologic event — no. (%)	197 (94.7)	196 (94.2)	185 (88.9)	179 (86.1)
Neutropenia	187 (89.9)	187 (89.9)	177 (85.1)	171 (82.2)
Thrombocytopenia	113 (54.3)	86 (41.3)	65 (31.2)	39 (18.8)
Anemia	113 (54.3)	74 (35.6)	54 (26.0)	30 (14.4)
Lymphopenia	46 (22.1)	43 (20.7)	29 (13.9)	25 (12.0)
Infection — no. (%)	129 (62.0)	56 (26.9)	148 (71.2)	51 (24.5)
Upper respiratory tract†	39 (18.8)	4 (1.9)	54 (26.0)	4 (1.9)
Covid-19‡	29 (13.9)	6 (2.9)	55 (26.4)	12 (5.8)
Lower respiratory tract or lung§	19 (9.1)	9 (4.3)	36 (17.3)	8 (3.8)

The incidence of all infections during the trial period was similar with cilta-cel and standard care (62.0% vs. 71.2%), which suggested that infection risk is generally treatable in patients receiving cilta-cel.

Open Forum Infectious Diseases
MAJOR ARTICLE
IDSA OXFORD
published online 18 September 2025

Infectious Complications Following CD30 Chimeric Antigen Receptor T-cell Therapy in Adults

Felicia Cao,[1,a,©] Yueling Xiu,[2,a,©] Michael Mohnasky,[3,a,©] Jonathan S. Serody,[4,5,©] Paul Armistead,[4,5,©] Gianpietro Dotti,[5,6] Melody Smith,[7,©] Jonathan Huggins,[8,©] Julia Messina,[8,©] Bhanu Ramachandran,[9] Jennifer Saullo,[4] Joseph Stromberg,[9] Manish K. Saha,[10] Megan Walsh,[1] Barbara Savoldo,[5,11] Natalie Grover,[4,5,©] Heather I. Henderson,[5,6] and Tessa M. Andermann[5,6,©]

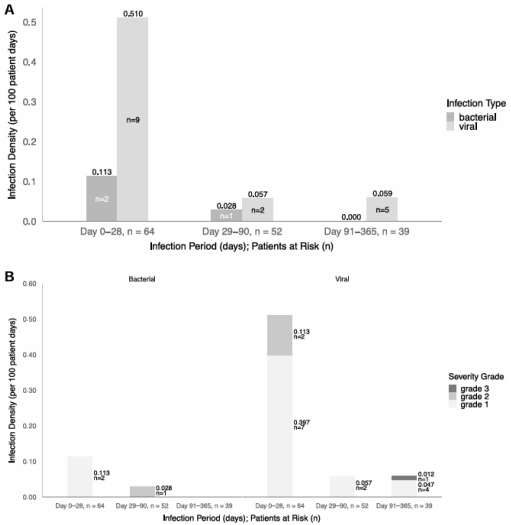


Figure 1. Increased density of mild viral infections observed within first 28 d after CD30 CAR-T. *A*, Density of bacterial and viral infections during the first 1 y following CAR T-cell therapy by infection periods (0–28, 29–90, and 91–365 d). Data shown are censored for relapse. No fungal infections were observed. *B*, Severity of infections including bacterial (left panel) and viral (right panel) occurring during the first 1 y following CAR-T therapy, divided into infection periods (0–28, 29–90, and 91–365 d) and censored for relapse.

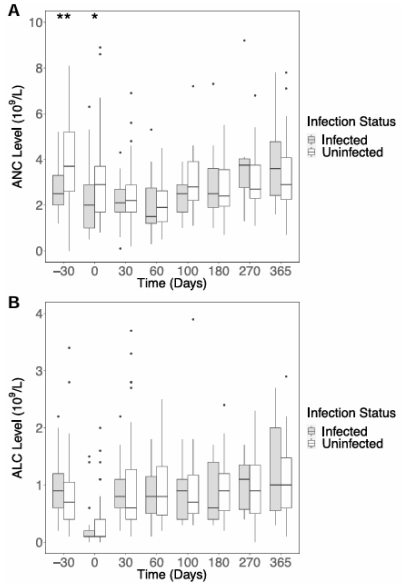


Figure 2. Immune recovery after CD30 CAR T-cell therapy demonstrates few differences between infected and uninfected patients within 1 y after infusion. *A*, Absolute neutrophil counts (ANC) and *B*, absolute lymphocyte counts (ALC) at time-points relative to the day of CAR-T infusion. Comparisons between infected and uninfected patients were performed using the Wilcoxon rank-sum test. $*P < .05$, $**P < .01$. Note: Seven ANC outlier values are missing from the plot (range, 13.2–40.8) and 2 ALC outlier values are missing from the plot (range, 5–14).

Infection density in the first year after CD30 CAR T-cell infusion was 0.131 per 100 patient-days-at-risk, with only 1 severe infection (1-year cumulative incidence of 32%). Infections were primarily viral (30%) and most common early after infusion.

Far fewer infections were bacterial in CD30 CAR-T recipients (4.9%), in contrast to the CD19 cohort in which bacterial infections predominated and were more severe. Microbiologically confirmed infections, primarily with respiratory viruses, were most common in the first 28 days after CD30 CAR-T infusion and most were mild.

Cancer Immunology, Immunotherapy (2025) 74:149
https://doi.org/10.1007/s00262-025-03998-1

RESEARCH

Infectious complications distribution following CLL1 CAR-T cell therapy for acute myeloid leukemiass

Jianmei Xu[1] · Huan Zhang[1] · Yifan Zhao[1] · Xiaomei Zhang[3] · Shujing Guo[1] · Xiaoxue Shi[1] · Xia Xiao[2] · Hairong Lyu[2] · Yu Zhang[2] · Xiaoyuan He[2] · Mingfeng Zhao[2]

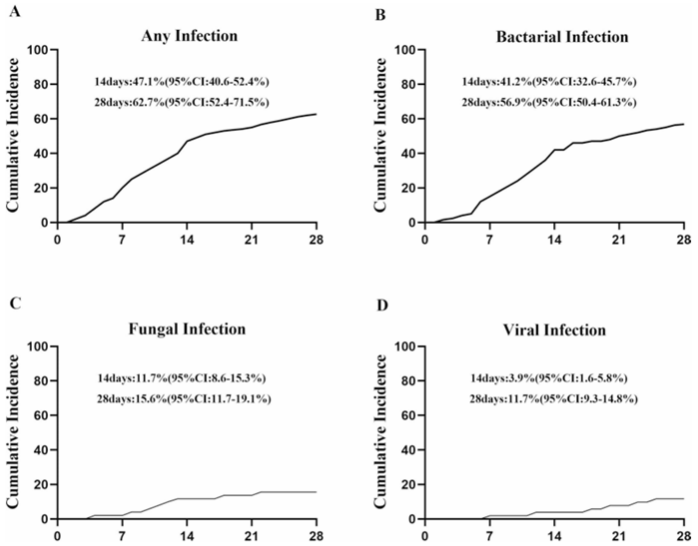


Fig. 2 Cumulative incidence and severity of infection after 28 days following CAR-T cell infusion The cumulative incidence rate of infections occurred in patients during the 14-day and 28-day periods following infusion of CLL1 CAR-T cells. **A–D** The cumulative incidence of any categories, including bacterial, viral, and fungal infections, was observed at 14 days and 28 days following the infusion of CAR-T cells

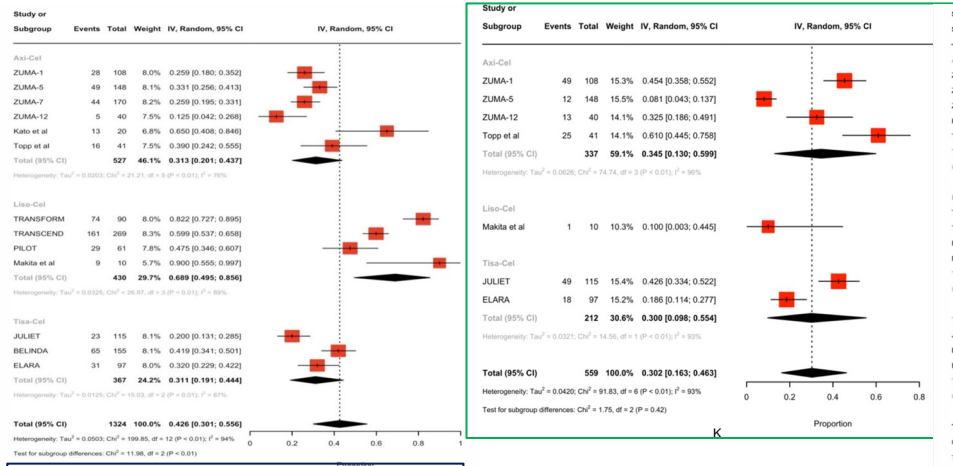
Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	*P* value	OR	95% CI	*P* value
Age						
≥40 versus < 40	1.048	0.295–3.569	0.941			
Sex						
Male versus female	0.625	0.181–2.104	0.447			
Prior antitumor treatment regimens						
< 3 versus ≥ 3	0.200	0.0403–0.757	0.027	0.230	0.039–1.042	0.071
Prior infections						
Yes versus No	8.909	1.522–170.400	0.045	1.013	0.217–4.603	0.986
Extramedullary infiltration						
Yes versus No	1.225	0.358–4.153	0.743			
Tumor burden, percentage						
≥50% versus < 50%	1.789	0.524–6.728	0.364			
CAR-T-cell dose, cells per kg						
$0.5–1.5\times10^6$ versus $1.6–3\times10^6$	3.674	0.838–25.870	0.119			
ALC cells at pre-lymphodepletion						
< 200 versus ≥ 200	0.440	0.124–1.548	0.197			
ANC cells at pre-lymphodepletion						
< 500 vs ≥ 500	3.850	1.087–16.100	0.046	3.785	0.870–20.340	0.041
lgG level at pre-lymphodepletion						
< 400 versus ≥ 400 mg/dL	3.900	1.127–14.550	0.035	2.879	0.695–12.870	0.149
CRS grade						
0 vs 1–2 versus 3–4	5.600	1.477–27.830	0.018	4.141	0.884–24.990	0.037
ICANS grade						
Yes versus No	0.382	0.0422–3.453	0.361			
Tocilizumab application						
Yes versus No	1.200	0.356–4.249	0.770			
Corticosteroid application						
Yes versus No	1.429	0.425–4.904	0.563			

CAR-T; chimeric antigen receptor T, ALC; antinuclear lymphocyte, ANC; antinuclear neutrophil cell, CRS; cytokine release syndrome, ICANS; immune effector cell associated neurotoxic syndrome

Safety and Toxicity Profiles of CAR T Cell Therapy in Non-Hodgkin Lymphoma: A Systematic Review and Meta-Analysis

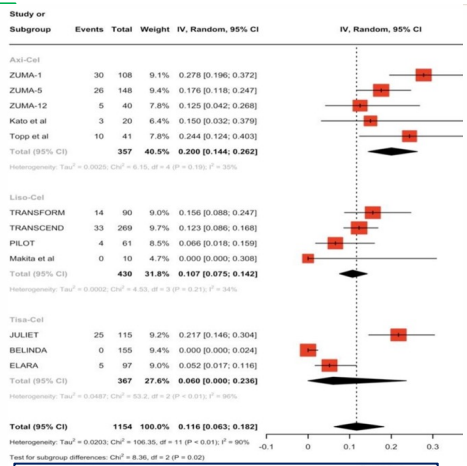
Samuel Yamshon,[1] Caitlin Gribbin,[1] Mohammad Alhomoud,[1] Nora Chokr,[1] Zhengming Chen,[2] Michelle Demetres,[3] Michelle Pasciolla,[4] John Leonard,[1] Tsiporah Shore,[1] Peter Martin[1]

Clinical Lymphoma, Myeloma and Leukemia, Vol. 24, No. 6, e235–e256 © 2024

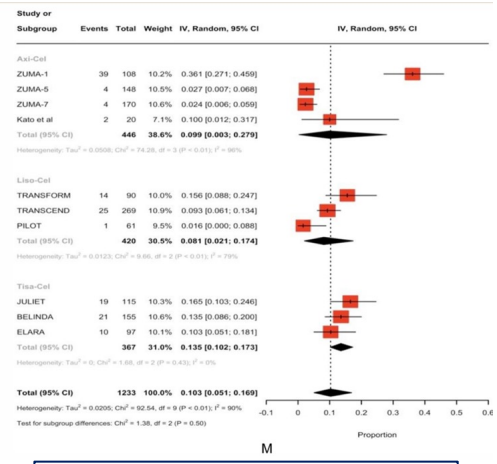


Forest plot of incidence of **severe neutropenia** (≥grade 3) among the 3 CART products (axi-cel**, liso-cel**, and tisa-cel).

Forest plot of incidence of **all-grade infection** among the 3 CART products (axi-cel, liso-cel, and tisa-cel).



Forest plot of incidence of **severe infections** (≥grade 3) among the 3 CART products (**axi-cel**, liso-cel, and tisa-cel).



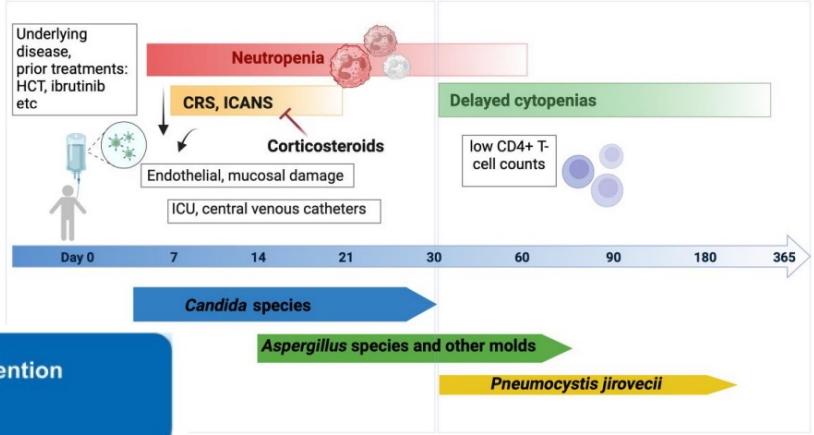
Forest plot of incidence of **febrile neutropenia** among the 3 CART products (axi-cel, liso-cel, and tisa-cel).

Open Forum Infectious Diseases
REVIEW ARTICLE
published online 13 March 2024

The Burden of Invasive Fungal Disease Following Chimeric Antigen Receptor T-Cell Therapy and Strategies for Prevention

Jessica S. Little,[1,2,©] Eleftheria Kampouri,[3,©] Daniel Z. Friedman,[4] Todd McCarty,[5] George R. Thompson III,[6] Dimitrios P. Kontoyiannis,[7,©] Jose Vazquez,[8] John W. Baddley,[9] and Sarah P. Hammond[1,10,11,©]

[1]Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA, [2]Division of Infectious Diseases, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA, [3]Infectious Diseases Service, Lausanne University Hospital and University of Lausanne, Lausanne, Switzerland, [4]Section of Infectious Diseases and Global Health, The University of Chicago, Chicago, Illinois, USA, [5]Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, Alabama, USA, [6]Division of Infectious Diseases, University of California Davis, Sacramento, California, USA, [7]Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas, M.D. Anderson Cancer Center, Houston, Texas, USA, [8]Division of Infectious Diseases, Medical College of Georgia/Augusta University, Augusta, Georgia, USA, [9]Division of Infectious Diseases, University of Maryland School of Medicine, Baltimore, Maryland, USA, [10]Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts, USA, and [11]Department of Medical Oncology, Massachusetts General Hospital Cancer Center, Boston, Massachusetts, USA



The Burden of Invasive Fungal Disease Following CAR T-cell Therapy and Strategies for Prevention

Little et al, 2024 | Open Forum Infectious Diseases

BACKGROUND

- CAR T-cell therapy is a novel immunotherapy with expanding use for multiple diseases.
- The characteristics of invasive fungal disease (IFD) after CAR T-cell therapy are not well described.
- Optimal approaches to prevention remain unclear but may vary across diseases and products.
- Herein we review the epidemiology of IFD after CAR T-cell therapy.

METHODS

- Clinical trials report few cases of IFD with limited detail on pathogen and/or timing of disease.
- 22 cohort studies evaluating infections after CD19 or BCMA-targeted CAR T-cell therapy were included.
- Only 50% of these studies reported using consensus definition of IFD.
- Antifungal prophylaxis practices varied widely across studies.

FINDINGS

- Among 2358 CD19 recipients, 66 proven/probable IFD cases reported.

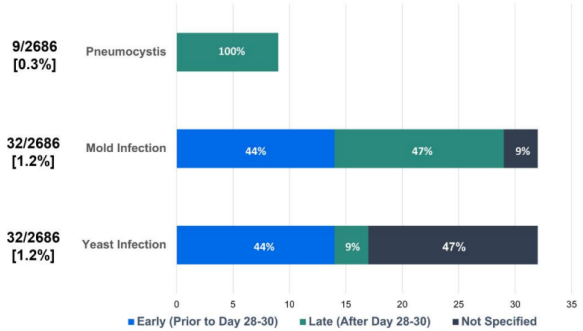
CD19 INCIDENCE, 3%

- Among 328 BCMA recipients, 8 proven/probable IFD cases reported.

BCMA INCIDENCE < 3%

The burden of invasive fungal disease after CAR T-cell therapy is low, but ongoing assessment of IFD in CAR T-cell recipients with novel disease indications is warranted. Improved understanding of risk factors for IFD may guide preventive strategies in the future.

Timing of Invasive Fungal Disease in Patients Receiving CAR T-Cell Therapy



Journal Pre-proof

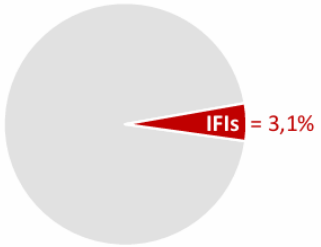
Invasive Fungal Infections after CD19 CAR T-cell Therapy for B-Cell Lymphoma: a LYSA study from the DESCAR-T Registry

Amélie Bouvier, Amandine Durand, Vivien Dupont, Nicolas Gower, Cristina Castilla Lorente, Arnaud Campidelli, Rémi Dulery, Jean-Pierre Gangneux, Magalie Joris, Martin Eloit, Christelle Latiere, Roberta di Blasi, Blandine Denis, Ludovic Gabellier, Franck Morschhauser, Olivier Casasnovas, Roch Houot, Cécile Angebault, Emmanuel Bachy, Fabien Le Bras, Thomas Gastinne, Jean-Jacques Tudesq, François Lemonnier, Giovanna Melica

- The median time to onset was 29.5 days.
- The median progression-free survival of patients with IFI was 3.2 months compared to 5.8 months in the non-infected population.
- The median overall survival of patients with IFI was 6 months compared to 25.4 months

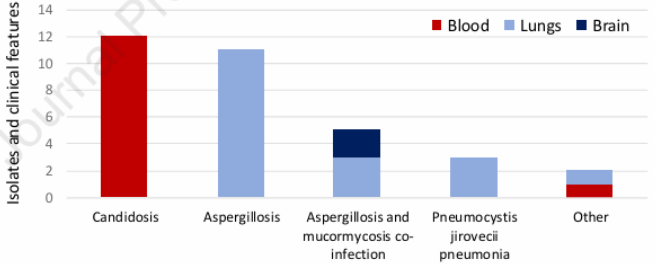
Landscape of invasive Fungal Infections after CD19 CAR T-Cell Therapy for B-Cell Lymphoma

DESCART registry
N = 1012
Refractory or relapsed
B cell lymphomas.



IFI-related mortality rate
22%

IFIs risk factors
Age at treatment decision
Number of prior treatment lines
At least one prior Allogenic transplant
Anti IL-1 treatment received
Bacterial infection



Conclusions: 1) Invasive fungal infection are a rare but often fatal complication following CD19 CAR T-Cell Therapy for B-Cell Lymphoma. 2) Following risk factors were identified : advanced age, number of prior lines of therapy, prior allogenic hematopoietic cell transplantation, anti-IL-1 receptor antagonist treatments, and pre-IFI bacterial infection.

Bouvier et al.

pathogens

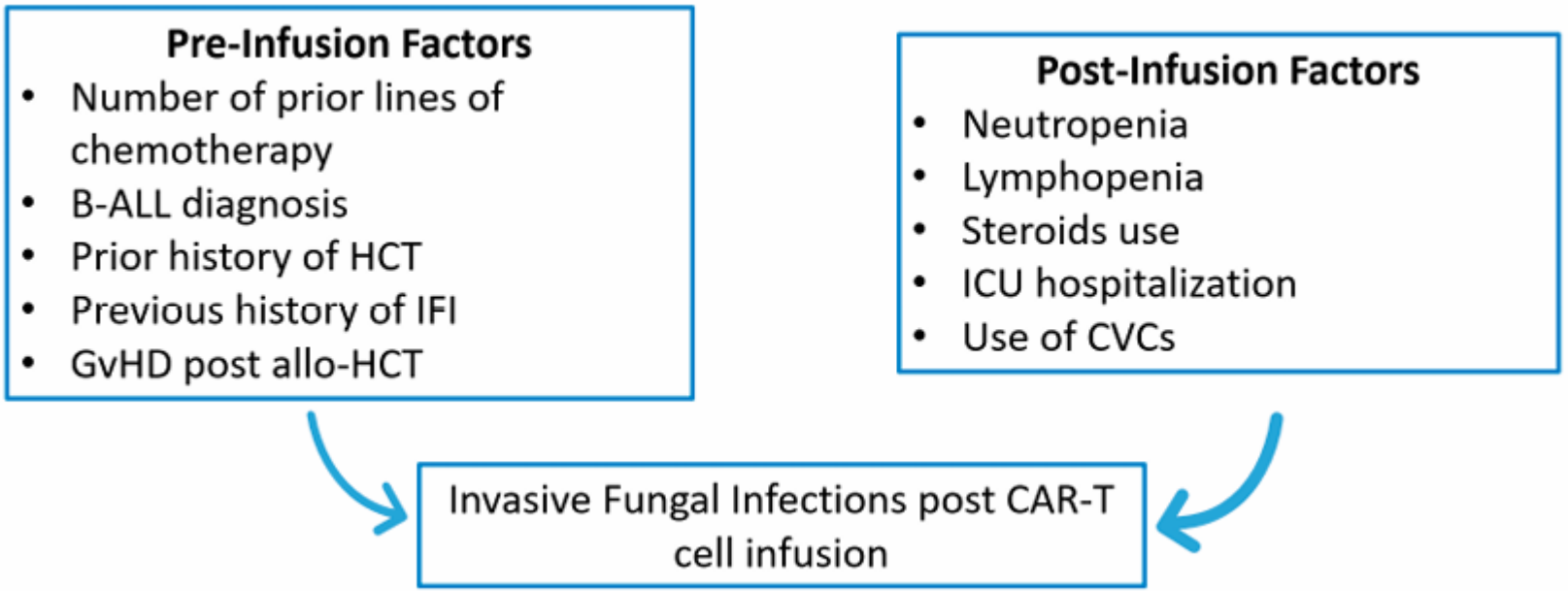
MDPI

Pathogens 2025, 14, 170

Review

Invasive Fungal Disease After Chimeric Antigen Receptor-T Immunotherapy in Adult and Pediatric Patients

Paschalis Evangelidis [1,†], Konstantinos Tragiannidis [2,†], Athanasios Vyzantiadis [3], Nikolaos Evangelidis [1], Panagiotis Kalmoukos [1], Timoleon-Achilleas Vyzantiadis [3], Athanasios Tragiannidis [2], Maria Kourti [2] and Eleni Gavriilaki [1,4,*]



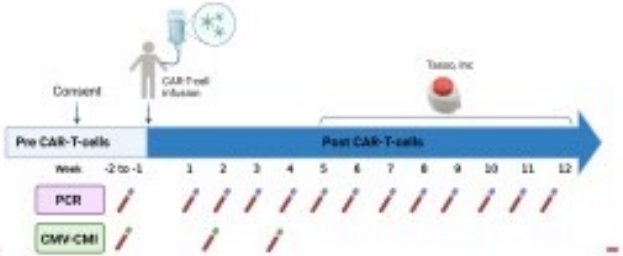
CMV Reactivation and CMV-Specific Cell-Mediated Immunity after Chimeric Antigen Receptor T-Cell Therapy

Kampouri et al., 2023 | *Clinical Infectious Diseases*

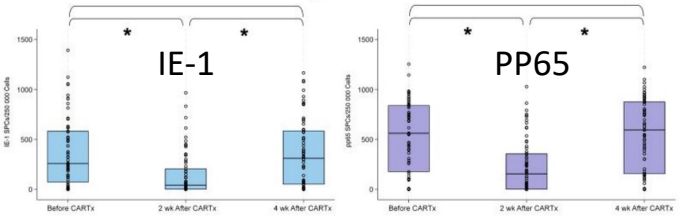
IDSA
Infectious Diseases Society of America

Prospective study, 72 adult CMV-seropositive CD19-, CD20-, BCMA CAR-T-cell therapy recipients.

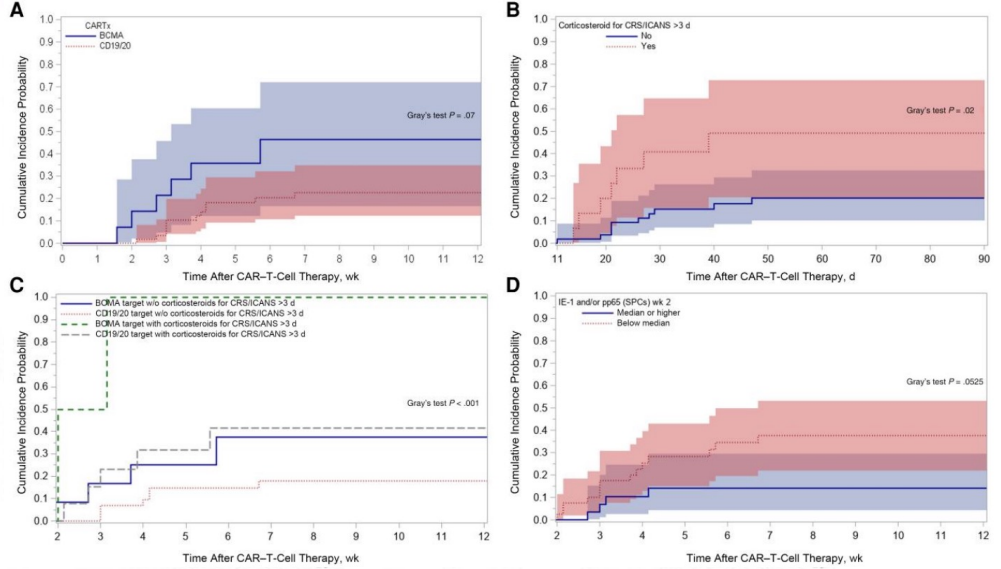
- CMV PCR weekly up to 12 weeks post-CAR-T-cell infusion, use of blood self-collection device after week 4 as needed.
- CMV-cell mediated immunity (CMI) assessed at baseline, week 2, and week 4 post-CAR-T-cell infusion using an IFN-γ release assay qantifying T-cell responses to IE-1 and pp65.



2. CMV-CMI values reached a nadir 2 weeks post-CAR-T-cell infusion and recovered by week 4.



1. CMV detected in 1 patient pre- and 18 patients post-CAR-T, overall incidence: 27%. No end-organ disease.



3. Patients receiving BCMA CAR-T-cell therapy or corticosteroids >3 days were at higher risk for CMV reactivation.

Possible associations were identified for more prior antitumor regimens and low week 2 CMV-CMI.

Open Forum Infectious Diseases
MAJOR ARTICLE

published online 18 July 2024

Cytomegaloviral Infections in Recipients of Chimeric Antigen Receptor T-Cell Therapy: An Observational Study With Focus on Oncologic Outcomes

Fareed Khawaja,[1,2] Sairah Ahmed,[2,3,4] Swaminathan P. Iyer,[2,4] Joseph Sassine,[1,4,5] Guy Handley,[1,5,6] Rishab Prakash,[2] Tracy VanWierren,[1] Jennifer Jackson,[1] Anna Zubovskaia,[1] Jeremy Ramdial,[3,5] Gabriela Rondon,[2] Krina K. Patel,[2] Amy Spallone,[1,2] Ella J. Ariza-Heredia,[1,5] Victor Mulanovich,[1,2] Georgios Angelidakis,[1] Ying Jiang,[1] and Roy F. Chemaly[1,2]

[1]Division of Internal Medicine, Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA, [2]Division of Cancer Medicine, Department of Lymphoma/Myeloma, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA, [3]Division of Cancer Medicine, Department of Stem Cell Transplantation and Cellular Therapy, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA, [4]Infectious Diseases Section, Department of Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA, and [5]Division of Infectious Disease and International Medicine, Department of Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida, USA

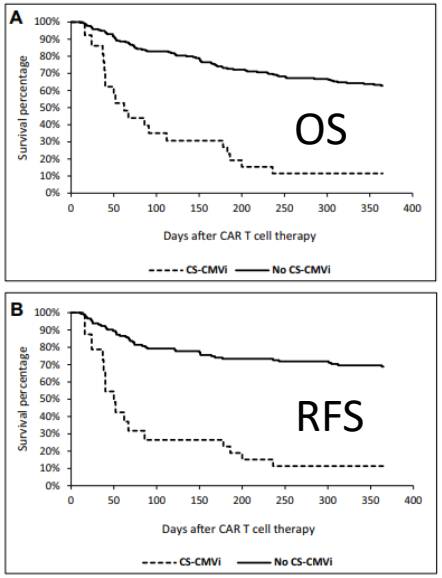


Figure 1. Kaplan-Meier curves illustrating survival differences between CAR T cell therapy recipients with and without CS-CMVi after 1 year. Patients with CS-CMVi had significantly worse overall survival ($P < .001$) (*A*), and relapse-free survival ($P < .001$) (*B*). Note: Patients' CS-CMVi status was treated as a time-dependent variable in the Kaplan-Meier analysis. Abbreviations: CMV, cytomegalovirus; CS-CMVi, clinically significant CMV infection; CAR, chimeric antigen receptor.

Of 230 patients identified, 22 (10%) had CS-CMVi.

Table 3. Cox Proportional Hazards Regression Model of Independent Risk Factors for Clinically Significant Cytomegalovirus Infection in Chimeric Antigen Receptor T-Cell Therapy Recipients

Independent Risk Factors	aHR	(95% CI)	*P* Value
Race			
Asian or Middle Eastern	13.71	(5.41–34.74)	<.0001
Other[a]	Reference		
LDH at time of CAR-T therapy (U/L) (every 100-unit increase)	1.09	(1.02–1.16)	.011
Treatment of CRS or ICANS with steroids[b]	6.25	(1.82–21.47)	.004
CMV surveillance	6.91	(2.77–17.25)	<.0001

Table 5. Cox Proportional Hazards Regression Model of Independent Risk Factors for Nonrelapse Mortality in Chimeric Antigen Receptor T-Cell Recipients

Independent Risk Factors	aHR	(95% CI)	*P* Value
Hypertension	1.94	(1.12–3.35)	.018
IPI for lymphoma at time of CAR-T therapy			<.0001
0–3	Reference		
4–5	3.16	(1.77–5.62)	
LDH at time of CAR-T therapy, U/L (every 100-unit increase)	1.13	(1.08–1.18)	<.0001
HLH or MAS within 1 y after CAR-T therapy	2.40	(1.18–4.88)	.016
Fungal infection within 1 y[a]	3.19	(1.39–7.31)	.006
CS-CMVi within 1 y[a]	2.49	(1.29–4.82)	.007

Herpesvirus Infections After Chimeric Antigen Receptor T-Cell Therapy and Bispecific Antibodies: A Review

Joseph Sassine [1], Emily A. Siegrist [2] and Roy F. Chemaly [3,*]

Viruses **2025**, *17*, 133

- CMV reactivations happen early, at a median of 14–21 days, in up to half of the patients.
- Most early CMV reactivations occur in the context of a dip in CMV-CMI and disproportionately affect patients with CRS/ICANS, particularly those receiving glucocorticoids, and possibly recipients of BCMA CAR-T compared to CD19 CAR-T.
- Risk factors for any CMV reactivation include two or more immunosuppressants, dexamethasone or the use of axi-cel
- CS-CMVi is uncommon, with prevalence ranging between 3% and 15%
- In summary, CMV reactivations are common after CAR-T, but CS-CMVi and CMV endorgan disease remain rare
- While CMV reactivations have been associated with a higher risk of mortality, including non-relapse mortality, in CAR-T recipients, **a direct causal relationship is still not established**, particularly given the low rates of CMV end organ disease.
- At this time, CMV monitoring could be considered in the first 2 to 6 weeks after CAR-T in these higher risk patients

Transplantation and Cellular Therapy 31 (2025) 727–741

Transplantation and Cellular Therapy

journal homepage: www.astctjournal.org

Guideline

American Society for Transplantation and Cellular Therapy Series #11: Updated Cytomegalovirus Guidelines in Hematopoietic Cell Transplant and Cellular Therapy Recipients

Fareed Khawaja[1], Danniel Zamora[2,3], Michelle K. Yong[4], Morgan Hakki[5], Breana K. Goscicki[6], Lara Danziger-Isakov[7], Andrew Lin[8], Paul A. Carpenter[9], Michael Boeckh[2,3], Genovefa A. Papanicolaou[10,11], Sanjeet S. Dadwal[12], Roy F. Chemaly[1,*]

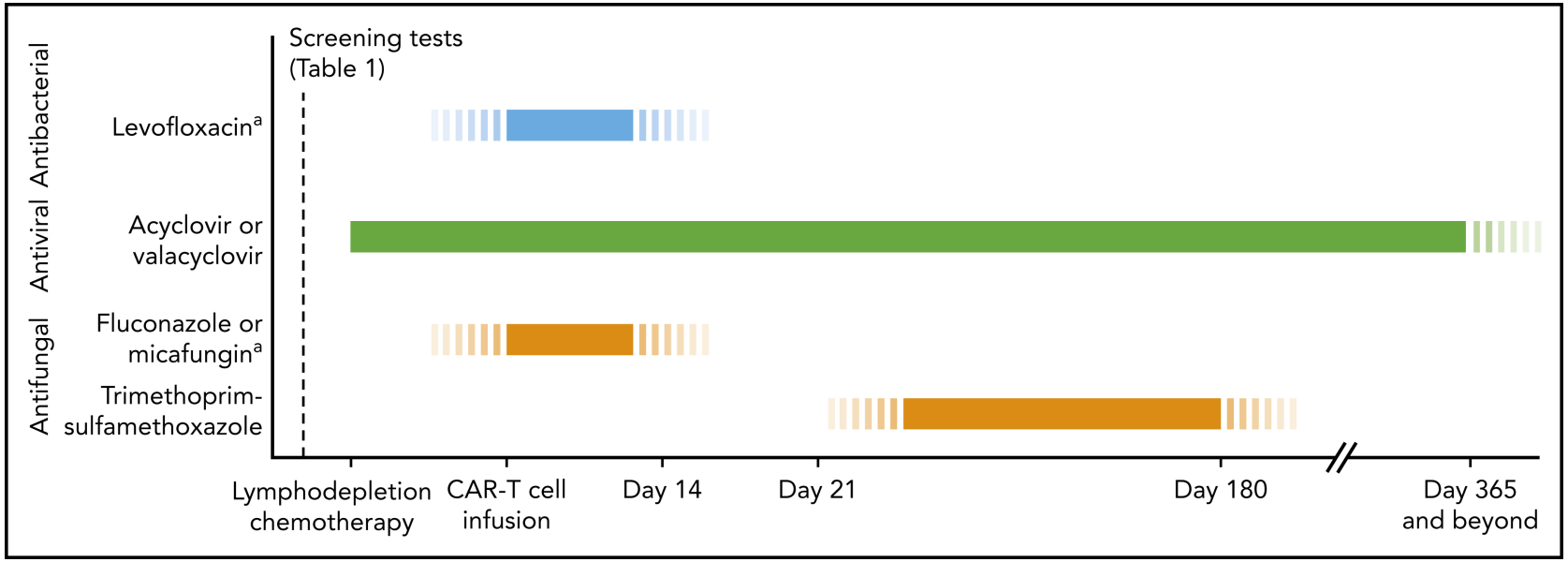
What is the Burden and Management of CMV Infection in CAR T-Cell Therapy Recipients?

- CMV surveillance in high-risk CAR T-cell recipients for 2 to 6 weeks after cellular infusion is recommended (B-II).
- Although a viral load threshold for the initiation of treatment has not yet been determined, prior studies have reported initiating treatment at viral loads from at least 500 IU/mL or 10,000 IU/mL.
- The viral load threshold needed to initiate CMV infection treatment may be affected by the type of CAR T-cell therapy, complications after CAR T-cell therapy (eg, ICANS,CRS), the disease state before CAR T cell therapy, and clinical concern for CMV end organ disease.
- No primary prophylaxis treatment is currently recommended to prevent CMV infection in CAR T cell therapy recipients (D-III).

Infections in allo-HSCT and CAR-T: differences and analogies

- Underlying diseases
- Timing of infections: early, late
- Epidemiology of infections
  - Bacterial
  - Fungal
  - Viral
- Relevance of underlying disease
- Prophylaxis of infections
- Vaccinations

How I prevent infections in patients receiving CD19-targeted chimeric antigen receptor T cells for B-cell malignancies



Joshua A. Hill,Susan K. Seo, How I prevent infections in patients receiving CD19-targeted chimeric antigen receptor T cells for B-cell malignancies, Blood, 2020, Figure 2.

Transplantation and Cellular Therapy 30 (2024) 955–969

Transplantation and Cellular Therapy

journal homepage: www.astctjournal.org

Guideline

Best Practice Considerations by The American Society of Transplant and Cellular Therapy: Infection Prevention and Management After Chimeric Antigen Receptor T Cell Therapy for Hematological Malignancies

Zainab Shahid[1,*], Tania Jain[2], Veronica Dioverti[3], Martini Pennisi[4], Lekha Mikkilineni[5], Swetha Kambhampati Thiruvengadam[6], Nirali N Shah[7], Sanjeet Dadwal[8], Genovefa Papanicolaou[1], Mehdi Hamadani[9], Paul A. Carpenter[10], Gabriela Maron Alfaro[11], Susan K. Seo[1], Joshua A. Hill[12]

Recommended Antimicrobial Prophylaxis Before and After CAR T Therapy

	Agent	Dose Regimen	Duration
Antibacterials*	Fluoroquinolones		At lymphodepletion therapy until 2 consecutive days of ANC $>0.5\times10^9$/L
	- Levofloxacin	500-750 mg PO QD	
	- Moxifloxacin	400 mg PO QD	
Antivirals			
- HSV/VZV	Acyclovir Valacyclovir	400 mg PO BID 500 mg PO BID	At lymphodepletion therapy until ≥6 m post-CAR T
- HBV	Entecavir	0.5 mg PO QD	At lymphodepletion therapy until ≥12 m post-CAR T
Antifungals†			
	Fluconazole‡ Echinocandins§	200 mg PO QD	Start with lymphodepletion therapy until 2 consecutive days of ANC $>0.5\times10^9$/L
Pneumocysitis jirovecii	TMP/SMX Dapsone Atovaquone Pentamidine	1 SS tablet PO QD or 1 DS PO TIW 100 mg PO QD 1500 mg PO QD inhaled or IV monthly	Start with ANC recovery (at least by d 30 post-CAR T) therapy until ≥6 m post-CAR T

CAR-HEMATOTOX: a model for CAR T-cell–related hematologic toxicity in relapsed/refractory large B-cell lymphoma

blood® 16 DECEMBER 2021 | VOLUME 138, NUMBER 24

Kai Rejeski,[1-3] Ariel Perez,[4] Pierre Sesques,[5] Eva Hoster,[1,6] Carolina Berger,[7] Liv Jentzsch,[8] Dimitrios Mougiakakos,[9] Lisa Frölich,[1,3] Josephine Ackermann,[1] Veit Bücklein,[1,2] Viktoria Blumenberg,[1,2] Christian Schmidt,[1] Laurent Jallades,[5] Boris Fehse,[7] Christoph Faul,[8] Philipp Karschnia,[3,10] Oliver Weigert,[1,3] Martin Dreyling,[1] Frederick L. Locke,[4] Michael von Bergwelt-Baildon,[1,3] Andreas Mackensen,[9] Wolfgang Bethge,[8] Francis Ayuk,[7] Emmanuel Bachy,[5] Gilles Salles,[5] Michael D. Jain,[4] and Marion Subklewe[1-3]

Baseline Features	0 Point	1 Point	2 Points
Platelet Count	> 175,000/µl	75,000 – 175,000/µl	< 75,000/µl
Absolute Neutrophil Count (ANC)	> 1200/µl	< 1200/µl	-
Hemoglobin	> 9.0 g/dl	< 9.0 g/dl	-
C-reactive protein (CRP)	< 3.0 mg/dl	> 3.0 mg/dl	-
Ferritin	< 650 ng/ml	650 – 2000 ng/ml	> 2000 ng/ml
Low: 0-1	High: ≥ 2		

Figure 4. CAR-HEMATOTOX. Determined before lymphodepletion, the score comprises 5 markers of hematotoxicity with additional weighting of the baseline platelet count and ferritin levels. The score discriminates between a high (CAR-HEMATOTOX score ≥2) and low (CAR-HEMATOTOX score 0-1) risk for hematotoxicity.

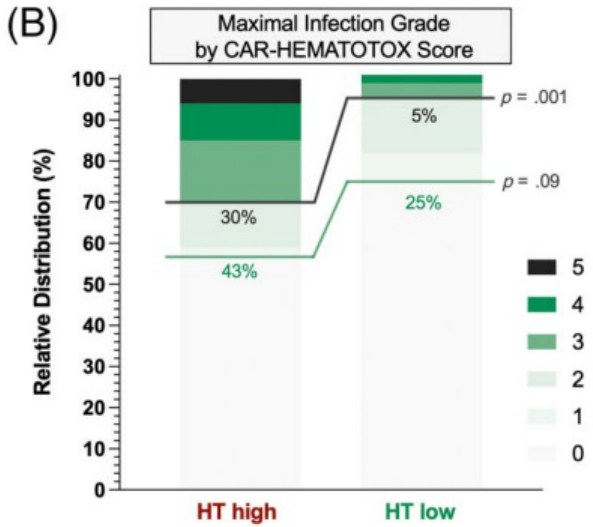
The score implicates bone marrow reserve and inflammation prior to CAR T-cell therapy as key features associated with delayed cytopenia and will be useful for risk-adapted management of hematotoxicity.

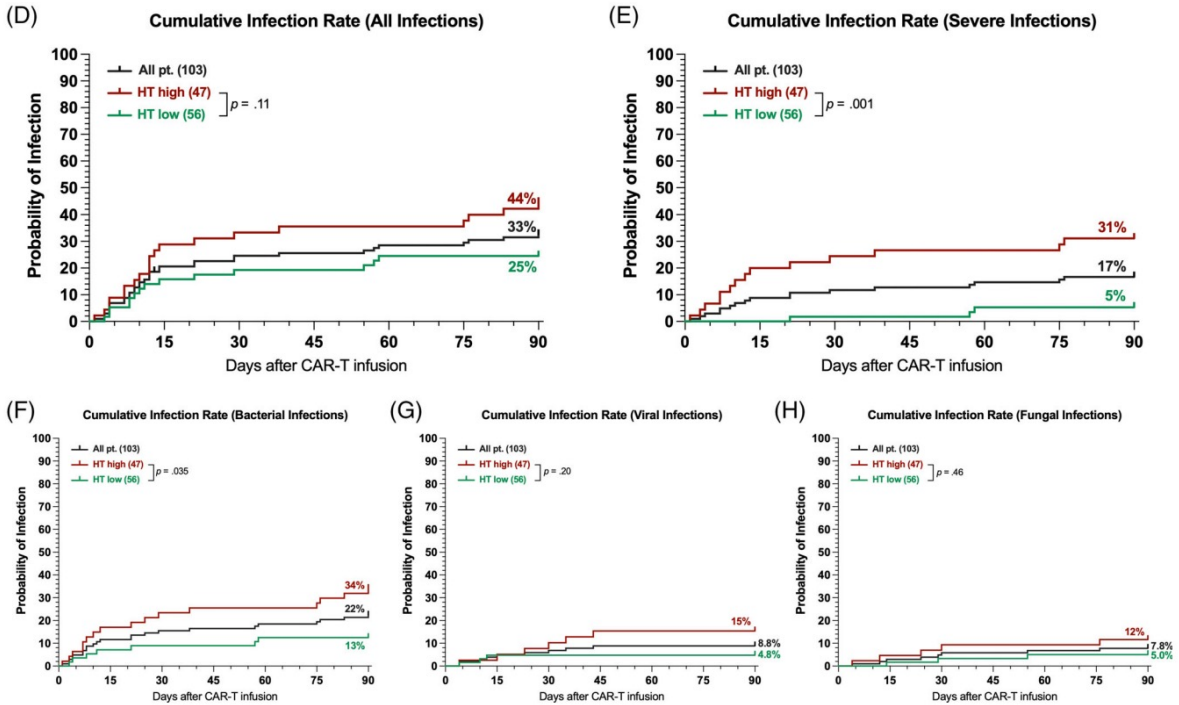
The CAR-HEMATOTOX score identifies patients at high risk for hematological toxicity, infectious complications, and poor treatment outcomes following brexucabtagene autoleucel for relapsed or refractory MCL

Am J Hematol. 2023;98:1699–1710.

Kai Rejeski[1,2,3] | Yucai Wang[4] | Omar Albanyan[5] | Javier Munoz[6] | Pierre Sesques[7] | Gloria Iacoboni[8,9] | Lucia Lopez-Corral[10,11] | Isabelle Ries[12] | Veit L. Bücklein[1,2] | Razan Mohty[5] | Martin Dreyling[1] | Aliyah Baluch[13] | Bijal Shah[14] | Frederick L. Locke[5] | Georg Hess[12] | Pere Barba[8] | Emmanuel Bachy[7] | Yi Lin[4] | Marion Subklewe[1,2,3] | Michael D. Jain[5]

The CAR-HEMATOTOX score was associated with severe infectious complications which represented the most common cause of non-relapse mortality.





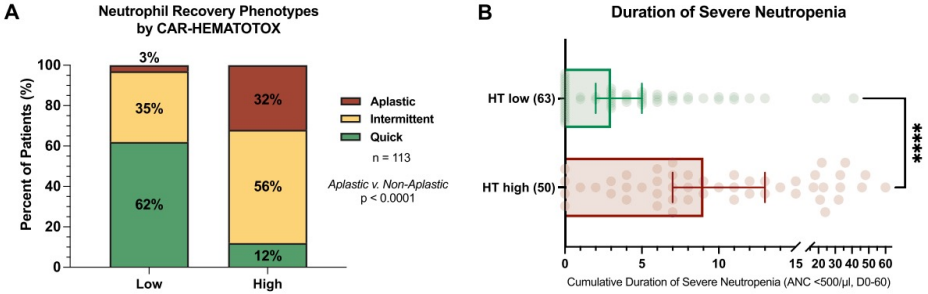
Rejeski *et al.*
Journal of Hematology & Oncology (2023) 16:88
https://doi.org/10.1186/s13045-023-01465-x

Journal of
Hematology & Oncology

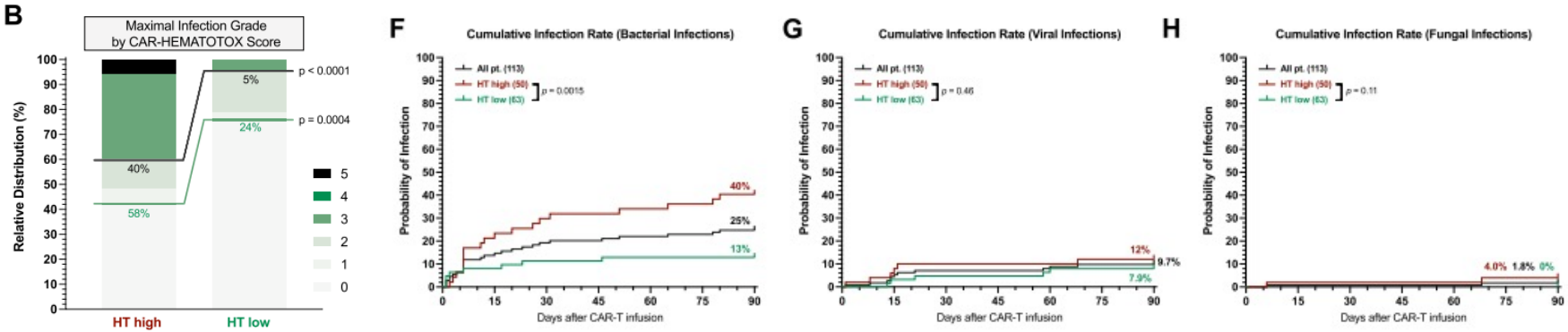
RESEARCH Open Access

The CAR-HEMATOTOX score as a prognostic model of toxicity and response in patients receiving BCMA-directed CAR-T for relapsed/refractory multiple myeloma

Kai Rejeski[1,2,3,4*†], Doris K. Hansen[5†], Radhika Bansal[6], Pierre Sesques[7], Sikander Ailawadhi[8], Jennifer M. Logue[5], Eva Bräunlein[9], David M. Cordas dos Santos[1,3], Ciara L. Freeman[5], Melissa Alsina[5], Sebastian Theurich[1,3], Yucai Wang[6], Angela M. Krackhardt[3,4,9,10], Frederick L. Locke[5], Emmanuel Bachy[7], Michael D. Jain[5], Yi Lin[6†] and Marion Subklewe[1,2,3,4†]



Compared to their HT low counterparts, HThigh patients displayed prolonged severe neutropenia (median 9 vs. 3 days, p<0.001), an increased severe infection rate (40% vs. 5%, p<0.001), and more severe ICANS (grade≥3: 16% vs. 0%, p<0.001).



RECOMMENDED VACCINATION SCHEDULE AFTER AUTOLOGOUS OR ALLOGENEIC HCT[gg]

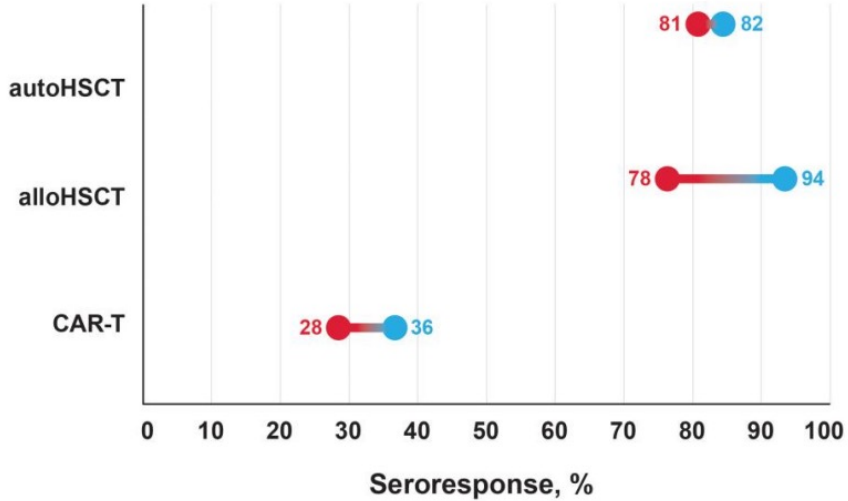
Inactivated, Subunit, or Toxoid Vaccines[hh]	Recommended Timing After HCT	Number of Doses[nn]
Tdap[ii]	6–12 months	3
Haemophilus influenzae type b (Hib)	6–12 months	3
Pneumococcal vaccination[jj]	3–6 months	3–4
Hepatitis A[kk] (Hep A)	6–12 months	2
Hepatitis B[kk] (Hep B)	6–12 months	2–3
Meningococcal conjugate vaccine[ll]	6–12 months	2–3
Influenza (injectable)	6 months	1, annually[oo]
Inactivated polio vaccine	6–12 months	3
Recombinant zoster vaccine[mm]	50–70 days after autologous HCT May be considered after allogeneic HCT	2
HPV vaccine	>6–12 months For patients ≤26 years, consider up to age 45	3
COVID-19	6 months	1 or more doses per CDC recommendations[pp]

Live Vaccines[mm]	Recommended Timing After HCT	Number of Doses[jj]
Measles/mumps/rubella (MMR)	≥24 months (may vaccinate earlier when risk:benefit ratio suggests)[qq]	1–2
Varicella vaccine	≥24 months (if no GVHD or ongoing immunosuppression and patient was seronegative for varicella pretransplant)	2

The Journal of Infectious Diseases® 2023;228(S1):S55–69

COVID-19 Vaccination in Patients With Cancer and Patients Receiving HSCT or CAR-T Therapy: Immune Response, Real-World Effectiveness, and Implications for the Future

Victoria G. Hall[1,2] and Benjamin W. Teh[1,2,©]



Cellular responses were variable with T-cell responses observed in 33% to 86% of patients with hematologic malignancies, and 42% to 72% of HSCT/ CAR-T recipients. Greater frequency of SARS-CoV-2-specific polyfunctional (interferon-γ, interleukin 2 producing) CD8+ T cells correlated with survival postinfection, highlighting their potential importance following vaccination. Furthermore, T-cell responses could be crucial for protection against new viral variants

Figure 2. Summary of the range of pooled antibody response rates after 2 doses of COVID-19 vaccines in patients who received hematopoietic stem cell transplant (HSCT) or chimeric antigen receptor T-cell therapy (CAR-T) [16, 52–54]. Seroresponse rates will vary depending on other factors including disease treatment status, type of therapy, and timing of vaccination. Red represents the lowest seroresponse rate observed and blue represents the highest seroresponse rate observed. alloHSCT, allogeneic HSCT; autoHSCT, autologous HSCT.

Transplantation and Cellular Therapy 29 (2023) 277.e1–277.e9

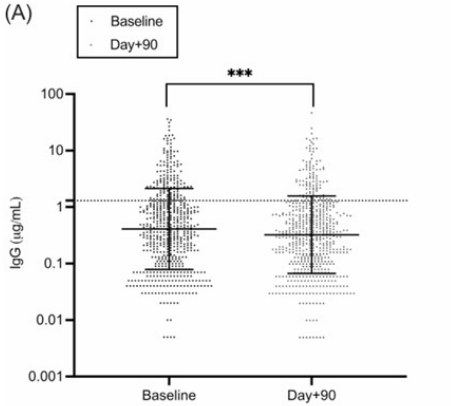
Transplantation and Cellular Therapy

journal homepage: www.tctjournal.org

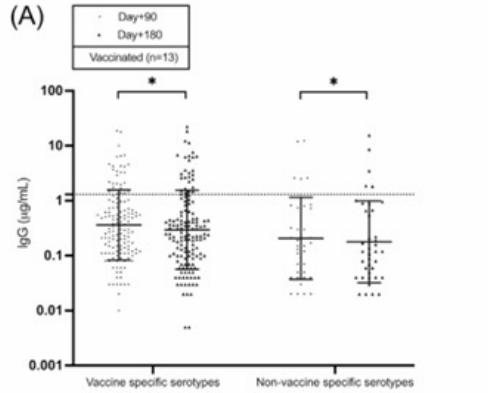
Full Length Article
Infectious Disease

Pneumococcal Conjugate Vaccine Does Not Induce Humoral Response When Administrated Within the Six Months After CD19 CAR T-Cell Therapy

Dasom Lee[1], Aryanna I Jordan[1], Meghan A. Menges[2], Aleksandr Lazaryan[2], Taiga Nishihori[2], Sameh R. Gaballa[3], Bijal D Shah[3], Javier Pinilla-Ibarz[3], Aliyah Baluch[4], Olga V. Klinkova[4], Julio C. Chavez[3], Michael D. Jain[2], Frederick L. Locke[2,*]



Before vaccination



After vaccination

(B)

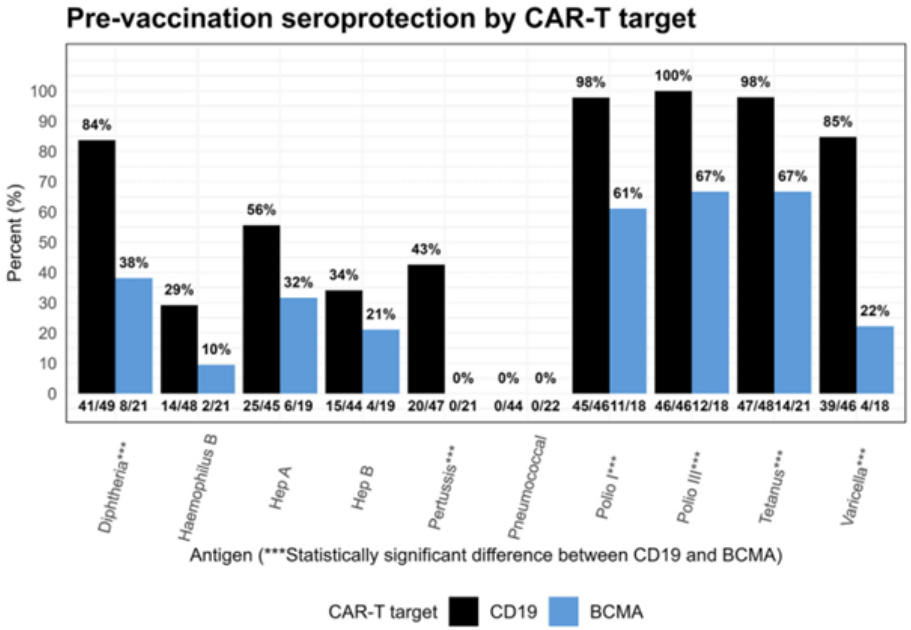
	Vaccinated (n=13)		Unvaccinated (n=17)	
Number of vaccine specific serotypes at protective level	Day+90	Day+180	Day+90	Day+180
0-2	8 (62%)	8 (62%)	6 (35%)	8 (47%)
3-5	2 (15%)	2 (15%)	8 (47%)	6 (35%)
6+	3 (23%)	3 (23%)	3 (18%)	3 (18%)

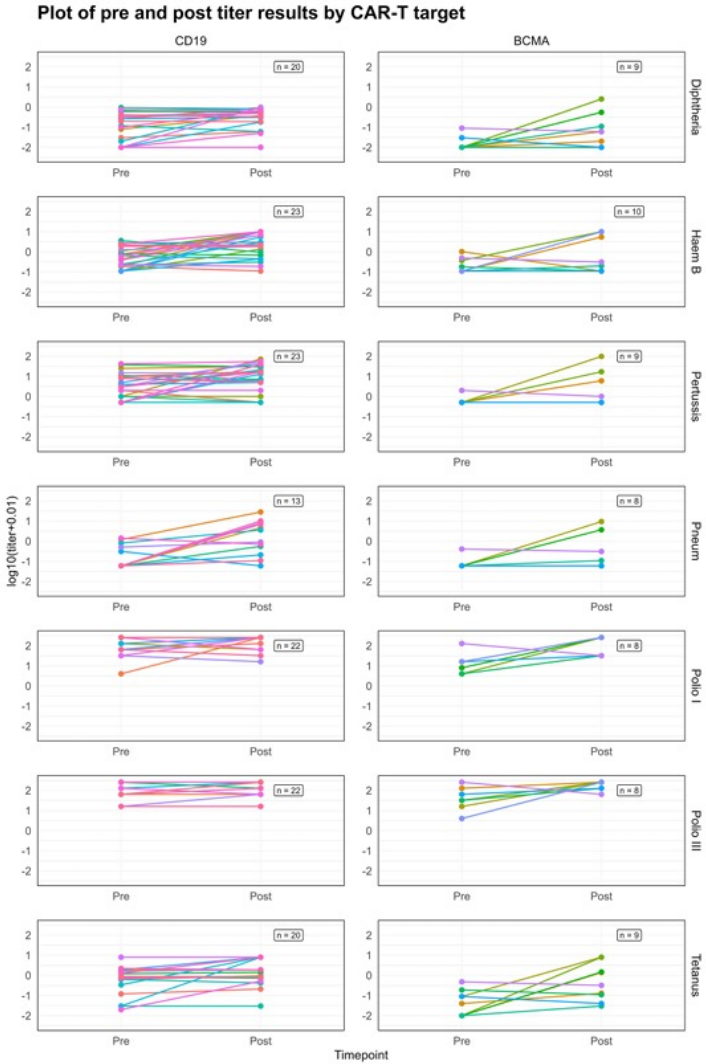
PCV13 vaccination at day+90 or day+180 after CAR-T did not increase humoral protection against pneumococcus. Only at day+540 was there evidence of humoral protection against pneumococcus in a modest proportion of patients.

Blood Cancer Journal (2025)15:114;

Humoral vaccine responses following Chimeric Antigen Receptor T-cell therapy for hematological malignancies

Sigrun Einarsdottir[1,2], Stephanie Lobaugh[3], Danny Luan[1], Marina Gomez-Llobell[1], Padmapriya Subramanian[4], Sean Devlin[3], David Chung[1,5], Parastoo B. Dahi[1,5,6], Lorenzo Falchi[5,6,7], Sergio Giralt[1,5,6], Heather Landau[1,5,6], Alexander M. Lesokhin[5,6], Richard Lin[1,5,6], Jennifer Lue[5,7], Sham Mailankody[5,6,7], M. Lia Palomba[5,6,8], Jae H. Park[5,6,8], Gilles Salles[5,6,8], Michael Scordo[1,5,6], Silvia Escribano-Serrat[1], Jaime Sanz[1], Kai Rejeski[1,9], Roni Shouval[1,5], Saad Usmani[5,6,7], Miguel-Angel Perales[1,5,6], Gunjan Shah[1,5,6,11] and Zainab Shahid[10,11]✉





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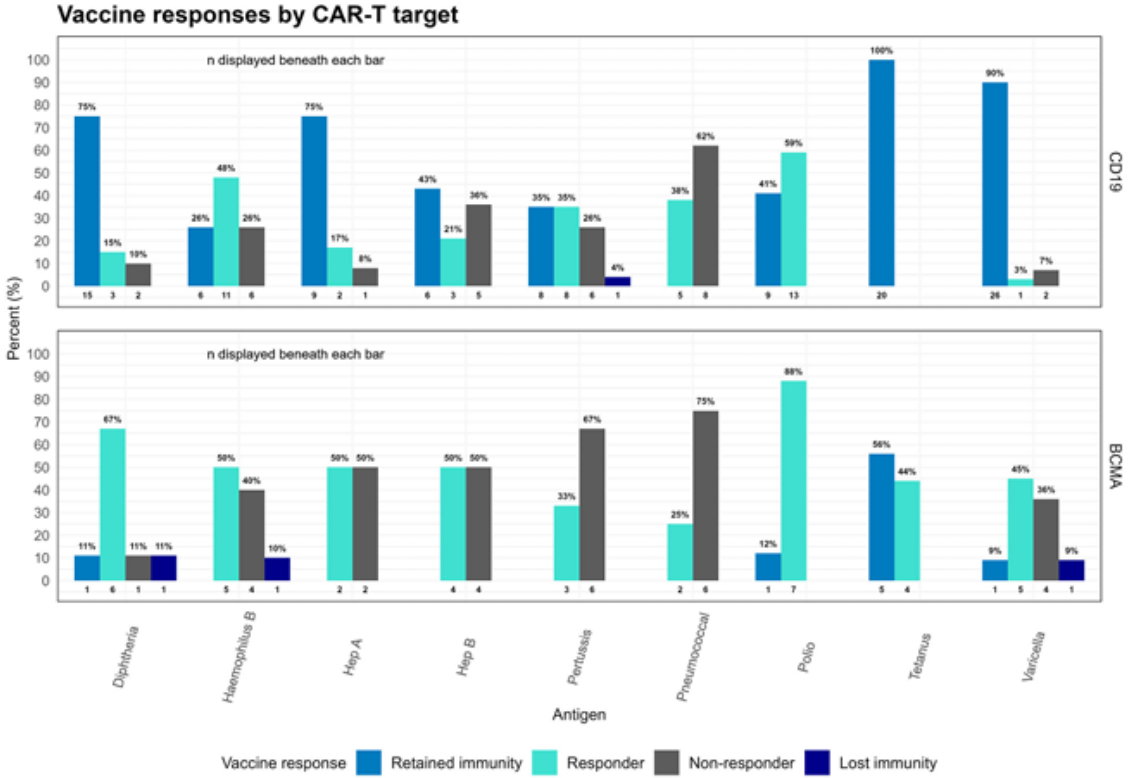

Fig. 3 Vaccine responses by CAR T target.

Transplantation and Cellular Therapy 30 (2024) 955–969

Transplantation and Cellular Therapy

journal homepage: www.astctjournal.org

Guideline

Best Practice Considerations by The American Society of Transplant and Cellular Therapy: Infection Prevention and Management After Chimeric Antigen Receptor T Cell Therapy for Hematological Malignancies

Zainab Shahid[1,*], Tania Jain[2], Veronica Dioverti[3], Martini Pennisi[4], Lekha Mikkilineni[5], Swetha Kambhampati Thiruvengadam[6], Nirali N Shah[7], Sanjeet Dadwal[8], Genovefa Papanicolaou[1], Mehdi Hamadani[9], Paul A. Carpenter[10], Gabriela Maron Alfaro[11], Susan K. Seo[1], Joshua A. Hill[12]

Vaccination Recommendations for CAR T Recipients

Killed/Inactivated Vaccines*	Pre-CAR	>3m	> 6m	>6m	>8m	>10m	>12	>18	Interval Between Vaccinations
Influenza†	Flu	Flu							Yearly
RSV†		RSV							ACIP guidance
SARS-Cov†	SARS-CoV-2	SARS-CoV-2							ACIP guidance for immuno-compromised patients
Pneumococus‡			PCV20	titers	PCV20	PCV20			1-2 mo
Diphtheria, tetanus, and acellular pertussis (DTap) §,‖			DTap	titers	Td	Td			1-2 mo
Hepatitis A ¶,#			HAV	titers			HAV		6 mo
Hepatitis B #,**			HAB	titers	HBV		HBV		2 mo
Shingrix††							VZV	VZV	