2024:

È già ora di abbandonare la **chemioterapia** nella **malattia recidivata/refrattaria?**

Napoli, Hotel Paradiso • 29–30 aprile 2024

COMPLICANZE PRECOCI E TARDIVE DELLA IMMUNOTERAPIA NELLA MALATTIA RECIDIVATA/REFRATTARIA: È NECESSARIA LA PROFILASSI?

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Disclosures

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Outline

- ✓ Introduzione
- ✓ Rischio infettivo in pazienti trattati con CAR-T
  - ➢ Entro i 28 gg
  - ➢ Oltre i 28 gg
- ✓ Rischio infettivo in pazienti trattati con anticorpi bispecifici
  - ➢ BsAbs per DLBCL
  - ➢ BsAbs per MM
- ✓ Strategie di profilassi e management

Introduzione

Il linfoma diffuso a grandi cellule B (DLBCL) rappresenta la forma più comune di linfoma non-Hodgkin, con circa 60,000 nuovi casi stimati nel 2023 in US ed Europa

Nonostante le recenti innovazioni terapeutiche, la mortalità correlata è di circa il 30-40%

Kanas et al. Leuk Lymphoma 2022
Siegel et al. CA Cancer J Clin 2023

Il mieloma multiplo rappresenta il 2% di tutte le neoplasie ematologiche

Forme refrattarie a terapie di prima linea (Inibitori del proteasoma, farmaci immunomodulanti ed anticorpi anti-CD38) rappresentavano fino a non molti anni fa condizioni del tutte prive di efficaci strategie terapeutiche

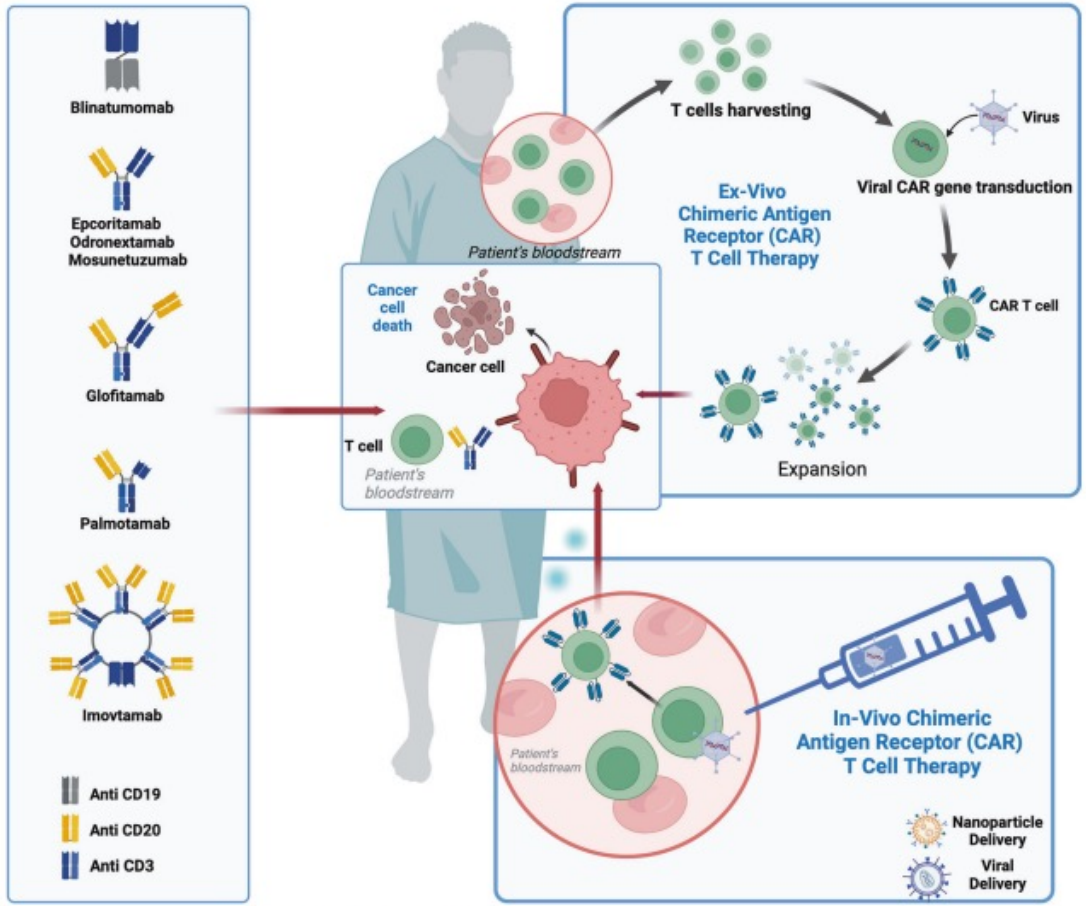
Kumar et al. Nat Rev Clin Oncol 2018
Mikkileni et al. J Natl Compr Canc Netw 2023

Introduzione

Le recenti innovazioni nel campo dell'immunoterapia, includente tra gli altri anticorpi monoclonali bispecifici e chimeric antigen receptor T cell therapy (CAR-T), ha rivoluzionato il trattamento delle forme recidivanti/remittenti di DLBCL e MM

I rischi infettivi correlati all'utilizzo di queste line terapeutiche restano però ad oggi scarsamente definiti

Trabolsi et al. Blood Cancer J 2024



Immune-therapy and infections

Patients who receive CAR-T and B-specific antibodies had elevated risk for serious infections due to the profound and prolonged immunosuppression:

- **severe hypogammaglobulinemia**
- **prolonged cytopenias (especially neutropenia)**
- **T-cell exhaustion**
- **reduced bone marrow reserves from primary disease and previous therapies**
- **severe CRS with massive releases of cytokines that can cause a form of immune paralysis which further predisposes patients to infections**

REVIEW ARTICLE OPEN

Monitoring, prophylaxis, and treatment of infections in patients with MM receiving bispecific antibody therapy: consensus recommendations from an expert panel

Noopur Raje[1✉], Kenneth Anderson[2], Hermann Einsele[3], Yvonne Efebera[4], Francesca Gay[5], Sarah P. Hammond[1,2,6], Alexander M. Lesokhin[7,8], Sagar Lonial[9], Heinz Ludwig[10], Philippe Moreau[11], Krina Patel[12], Karthik Ramasamy[13,14] and Maria-Victoria Mateos[15]

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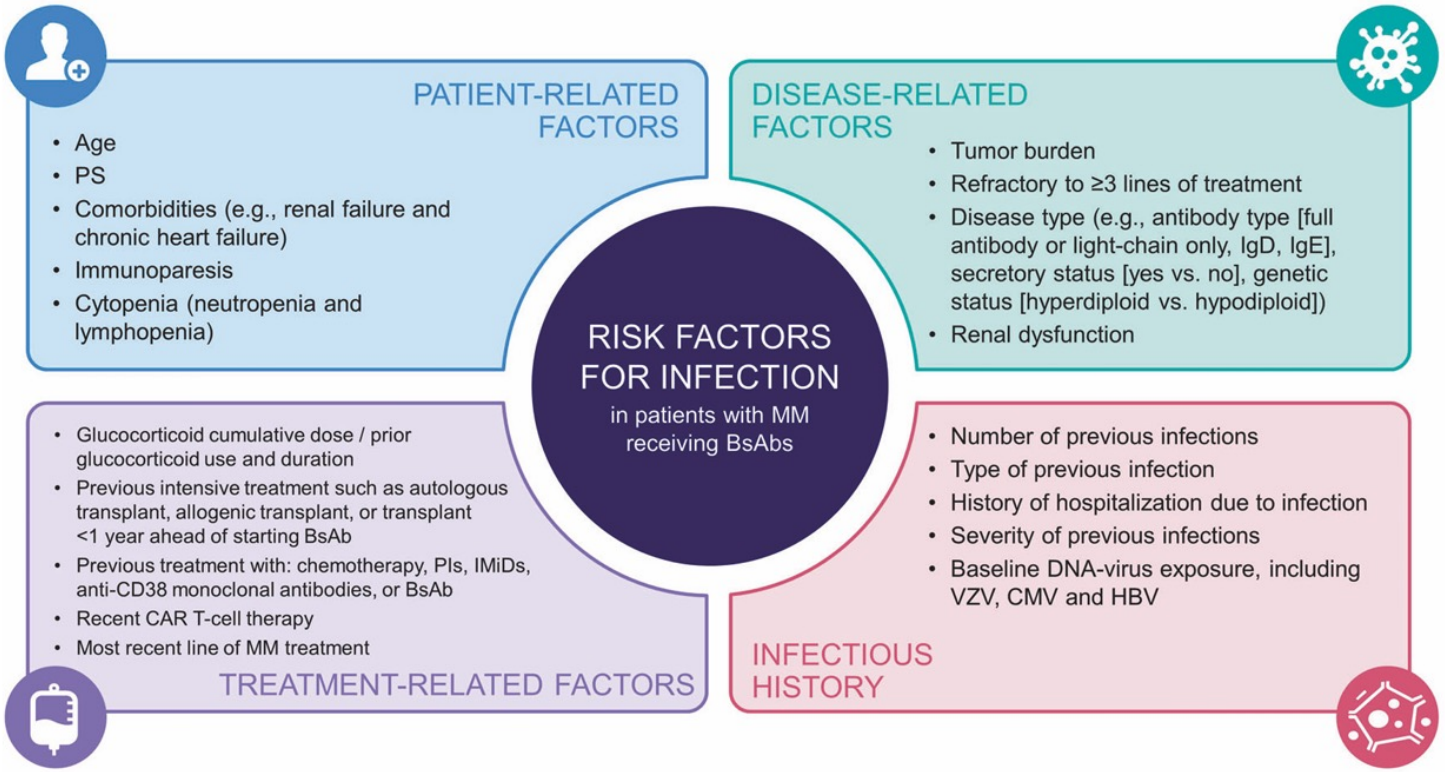

Adverse events identified in studies including at least 50 patients

CAR-T studies

	Idecabtagene vicleucel (KarMMa)[11]	Ciltacabtagene autoleucel (CARTITUDE-1)[14]	bb21217 (CRB-402)[15]	P-BCMA-101 (PRIME)[16]	Zevorcabtagene autoleucel) (LUMMICAR STUDY1)[17]	LCAR-B38M 9 (LEGEND-2)[18]	ALLO-715 (UNIVERSAL)[19]	Orvacabtagene autoleucel (EVOLVE)[20]	CT103A (FUMANBA-1)[21]
Target structure	BCMA	BCMA (two binding domains)	BCMA	BCMA	BCMA	BCMA (two binding domains)	BCMA, alloCAR T	BCMA, with fully human binder	BCMA, fully human
Number of patients	128	97	72	90	102	74	52	51	103
Median follow-up, months	13·3	27·7	9·0	..	9	47·8	14·8	5·9	12·2
Cell dose	450 × 10^6 CAR T cells (n=54)	0·51–0·95 × 10^6 CAR T cells per kg	150 × 10^6, 300 × 10^6, or 450 × 10^6 CAR T cells	Step-up doses 0·75–15 × 10^8 cells per kg, later 0·75 × 10^8 cells per kg	150 × 10^6 CAR T cells	0·07–2·10 × 10^6 CAR T cells per kg	4 dose levels (40, 160, 320, and 480 × 106); 320 × 106 selected for expansion, plus anti-CD52 antibody at 39 mg and 60 mg	300 × 10^6, 450 × 10^6, and 600 × 10^6 CAR T cells	1·0 × 10^6 CAR T cells per kg
Number of lines of therapy	5	6	6	6	4	3	8 (39 mg cohort); 6 (60 mg cohort)	6	4
Overall response rate	81%	97·9%	69% (for the dose 450 × 10^6; 74%)	73% in combination with rituximab and 71% with lenalidomide	92·2%	87·8%	64% (39 mg cohort), 67% (60 mg cohort)	91%	95%
PFS or DOR	PFS: median 12·1 months	PFS: median NR, at 27 months 54·9%	DOR: median 17 months	..	PFS: median NR, at 9 months 84·6%; DOR: median NR, at 9 months 86·1%	PFS: median 18·04 months DOR: median 23·26 months	DOR 8·3 months (39 mg cohort), 9·2 months (60 mg cohort)[1]	Median PFS not reached	Median PFS and DOR not reached
Cytokine release syndrome grade 1–4	96% (6%, grade ≥3)	95% (4%, grade ≥3)	75% (4%, grade ≥3)	25% (0%, grade ≥3)	90·2% (6·9%, grade ≥3)	At day 100: 91·9% (9·5%, grade ≥3)	52% (2%, grade ≥3)	2%, grade ≥3	93·2% (1%, grade ≥3)
Neurotoxicity grade 1–4	20% (6%, grade ≥3)	21·6% (12·3%, grade ≥3)	15% (4%, grade ≥3)	7% (2%, grade ≥3)	ICANS: 2% (0%, grade ≥3)	At day 100: 1·4% (0%, grade ≥3)	11% (0%, grade ≥3)	4%, grade ≥3	ICANS: 1·9% (0%, grade ≥3)
Infections grade 1–4	70%	58% (20%, grade ≥3; follow-up: 12·4 months)	..	..	29·4%, grade ≥3	9% (follow-up: 8 months in 5* patients)	59% (30%, grade ≥3)	14%, grade ≥3	..
Thrombocytopenia grade 1–4	65%	79·4% (59·8%, grade ≥3)	..	30%, grade ≥3	..	At day 100: 41·9% (18·9%, grade ≥3)	..	At day 29: 44%, grade ≥3	58·3%, grade ≥3
Neutropenia grade 1–4	94%	95·9% (94·8%, grade ≥3)	..	74%, grade ≥3	..	..	..	At day 29: 55%, grade ≥3	79·6%, grade ≥3
Anaemia grade 1–4	63%	81·4% (68%, grade ≥3)	..	35%, grade ≥3	..	At day 100: 29·7% (14·9%, grade ≥3)	..	At day 29: 21%, grade ≥3	46·8%, grade ≥3 (follow-up at 9·6 months in 79 patients)

(Table 2 continues on next page)

Range: 9-59%
Range grade 3: 14-29.4%

BsAbs studies

	Teclistamab (MajesTEC-1)[2]	Talquetamab (MonumenTAL-1)[3]	Elranatamab (MagnetisMM-1)[4]	Elranatamab (MagnetisMM-3)[5]	Linvoseltamab[6]	ABBV-383 (formerly TNB-383B)[7]	Alnuctamab[8]	Forimtamig (formerly RG6234)[9]	Cevostamab (NCT03275103)[10]
Target structure	BCMA and CD3	GPRC5D and CD3	BCMA and CD3	BCMA and CD3	BCMA and CD3	BCMA and CD3	BCMA and CD3	GPRC5D and CD3	FcRH5 and CD3
Number of patients	165	288	55	123 (cohort A)	167	124	68	105	160
Median follow-up, months	14·1	14·9	12·0	10·4	3·2	10·8	4·1	11·6	6·1
BsAb dose	Step-up doses of 60 µg/kg and 0·3 mg/kg, thereafter weekly subcutaneous 1·5 mg/kg	405 µg/kg sc weekly, 800 µg/kg sc every 2 weeks, and doses from 0·5 to 1600·0 µg/kg either sc or IV	Single priming dose 600 µg/kg or 44 mg followed by 1000 µg/kg or 76 mg, once weekly or once every 2 weeks	76 mg once weekly on a 28-day cycle with two step-up doses 12 mg and 32 mg during week 1	200 mg dose levels (n=87)	14 dose levels (25–120 000 µg), every 3 weeks	150–10 000 µg, with both fixed and step-up sc dosing	Intravenous dose range: 6–10 000 µg (n=51)	Single step-up dose (50–3600 µg) on C1D1, target dose (150–198 000 µg) on C1D8 ; double step-up (0·3–1·2 mg) C1D1, and C1D8 (3·6 mg), target dose (60–160 mg) on C1D15 followed by once every 3 weeks for a total of 17 cycles, unless PD or toxicity
Number of lines of therapy	5	5	5	5	5	5	4	5	6
Overall response rate	63·0%	74·1%	64·0%	61·0%	64·0%	57·0%	53·0%	71·4%	36·7%; 54·5% with tocilizumab
PFS or DOR	PFS: median 11·3 months	PFS: median 7·5 months	PFS: median 11·8 months; DOR: median 17·1 months	PFS: median NR, at 9 months 63%; DOR: median NR, at 9 months 84·4%	DOR: median NR (data from abstract)	PFS: median 10·4 months	DOR: median NR	DOR: median 10·8 months	DOR: median 15·6 months
Cytokine release syndrome									
Grade 1–2	72·0%	79·0%	87·3%	56·3%	37·0%	57·0%	53·0%	82·4%	With tocilizumab 35·3%; without tocilizumab 90·7%
Grade ≥3	0·7%	2·1%	0	0	1·0%	2·0%	0	2·0%	With tocilizumab 0·4%; without tocilizumab 0·2%
ICANS or neurotoxicity grade 1–4	3·0%, all grade 1–2; neurotoxicity: 4·5%	10·7%, grade 3: 3% with IV infusion (phase 2 patients only)	0%	3·4%, all grade 1–2; 119 patients with two step-up doses	5·6% (all grades); 1·2%, grade ≥3	1·6%	3·0%, grade 1–2; PNP: 6·0%, grade 1–2	ICANS-like adverse events: 9·8%; 2%, grade ≥3	ICANS associated with cytokine release syndrome: 13·1%
Infections grade 1–4	76·4% (44·8% grade ≥3)	57·3% (16·8%, grade ≥3)	27·3%, grade ≥3	66·7% (35·0%, grade ≥3)	54·0% (29·0%, grade ≥3)	41·0%	34·0% (9·0%, grade ≥3)	60·8% (21·5%, grade ≥3)	42·5% (18·8% grade ≥3)
Thrombocytopenia grade 1–4	40·0% (21%, grade ≥3)	27·3% (20·3%, grade ≥3)	50·9% (29·1%, grade ≥3)	30·1 % (22·0%, grade ≥3)	15·0% (10·0%, grade ≥3)	25·0% (10·0%, grade ≥3)	24·0% (9·0%, grade ≥3)	31·4% (13·7%, grade ≥3)	9·8% (5·9%, grade ≥3)
Neutropenia grade 1–4	70·9% (64·2%, grade ≥3)	34·3% (30·8%, grade ≥3)	74·5% (71·0%, grade ≥3)	48·0% (48·0%, grade ≥3)	20·0% (17·0%, grade ≥3)	41·0% (35·0%, grade ≥3)	37·0% (32·0%, grade ≥3)	23·5% (11·8%, grade ≥3)	18·1% (16·3%, grade ≥3)
Anaemia grade 1–4	52·0% (37·0%, grade ≥3)	44·8% (31·5%, grade ≥3)	67·3% (50·9%, grade ≥3)	48·0% (36·6%, grade ≥3)	28·0% (24·0%, grade ≥3)	33·0% (14·0%, grade ≥3)	38·0% (25·0%, grade ≥3)	33·3% (15·7%, grade ≥3)	31·9% (21·9%, grade ≥3)

(Table 1 continues on next page)

Range: 27.3-76.4%
Range grade 3: 9-44.8%

Ludwig H, Lancet Oncol 2023

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  - ➢ BsAbs per MM
- ✓ Strategie di management e profilassi

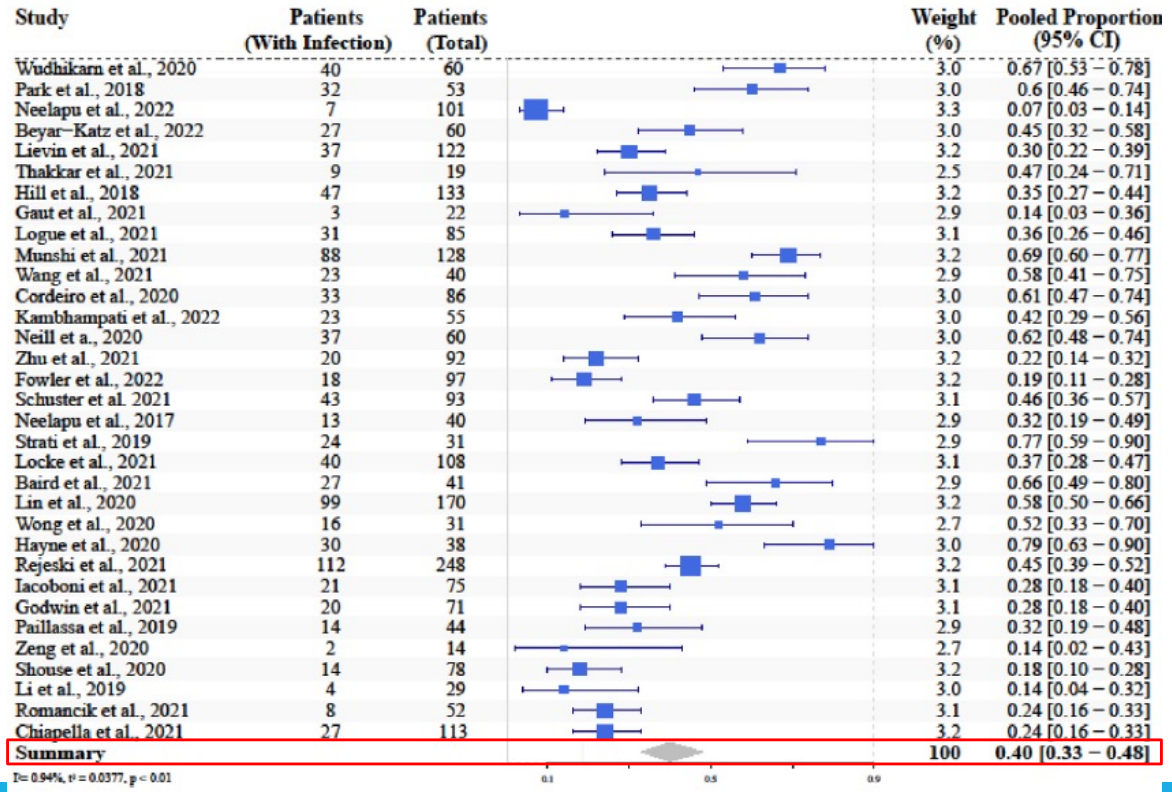
Infections in haematology patients treated with CAR-T therapies: A systematic review and meta-analysis

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]

Critical Reviews in Oncology / Hematology 192 (2023) 104134

Systematic review e metanalisi

41 studi (26 osservazionali, 12 trial di fase 2, 3 di fase 3), che hanno valutato l'incidenza di infezioni in pazienti sottoposti a trattamento con CAR-T per neoplasie ematologiche



Study	Patients (With Infection)	Patients (Total)	Weight (%)	Pooled Proportion (95% CI)
Wudhikarn et al., 2020	40	60	3.0	0.67 [0.53 – 0.78]
Park et al., 2018	32	53	3.0	0.6 [0.46 – 0.74]
Neelapu et al., 2022	7	101	3.3	0.07 [0.03 – 0.14]
Beyar–Katz et al., 2022	27	60	3.0	0.45 [0.32 – 0.58]
Lievin et al., 2021	37	122	3.2	0.30 [0.22 – 0.39]
Thakkar et al., 2021	9	19	2.5	0.47 [0.24 – 0.71]
Hill et al., 2018	47	133	3.2	0.35 [0.27 – 0.44]
Gaut et al., 2021	3	22	2.9	0.14 [0.03 – 0.36]
Logue et al., 2021	31	85	3.1	0.36 [0.26 – 0.46]
Munshi et al., 2021	88	128	3.2	0.69 [0.60 – 0.77]
Wang et al., 2021	23	40	2.9	0.58 [0.41 – 0.75]
Cordeiro et al., 2020	33	86	3.0	0.61 [0.47 – 0.74]
Kambhampati et al., 2022	23	55	3.0	0.42 [0.29 – 0.56]
Neill et a., 2020	37	60	3.0	0.62 [0.48 – 0.74]
Zhu et al., 2021	20	92	3.2	0.22 [0.14 – 0.32]
Fowler et al., 2022	18	97	3.2	0.19 [0.11 – 0.28]
Schuster et al. 2021	43	93	3.1	0.46 [0.36 – 0.57]
Neelapu et al., 2017	13	40	2.9	0.32 [0.19 – 0.49]
Strati et al., 2019	24	31	2.9	0.77 [0.59 – 0.90]
Locke et al., 2021	40	108	3.1	0.37 [0.28 – 0.47]
Baird et al., 2021	27	41	2.9	0.66 [0.49 – 0.80]
Lin et al., 2020	99	170	3.2	0.58 [0.50 – 0.66]
Wong et al., 2020	16	31	2.7	0.52 [0.33 – 0.70]
Hayne et al., 2020	30	38	3.0	0.79 [0.63 – 0.90]
Rejeski et al., 2021	112	248	3.2	0.45 [0.39 – 0.52]
Iacoboni et al., 2021	21	75	3.1	0.28 [0.18 – 0.40]
Godwin et al., 2021	20	71	3.1	0.28 [0.18 – 0.40]
Paillassa et al., 2019	14	44	2.9	0.32 [0.19 – 0.48]
Zeng et al., 2020	2	14	2.7	0.14 [0.02 – 0.43]
Shouse et al., 2020	14	78	3.2	0.18 [0.10 – 0.28]
Li et al., 2019	4	29	3.0	0.14 [0.04 – 0.32]
Romancik et al., 2021	8	52	3.1	0.24 [0.16 – 0.33]
Chiapella et al., 2021	27	113	3.2	0.24 [0.16 – 0.33]
Summary			100	**0.40 [0.33 – 0.48]**

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

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

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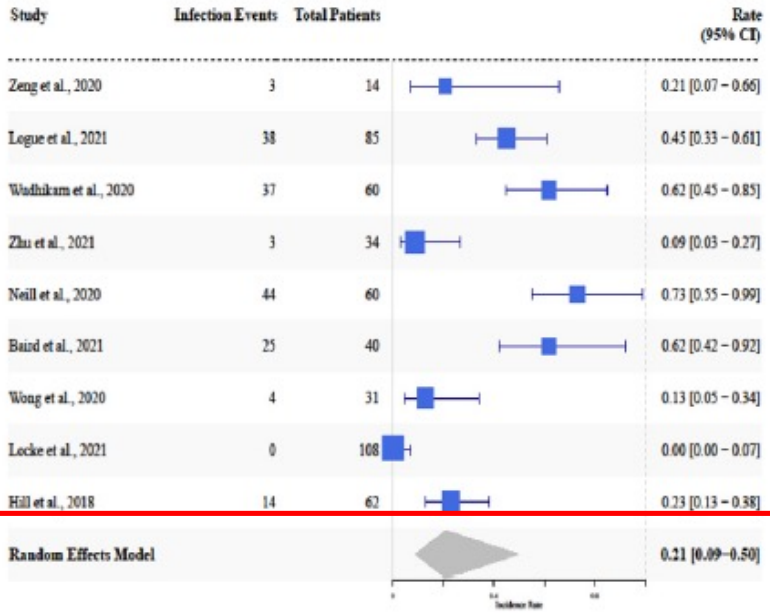
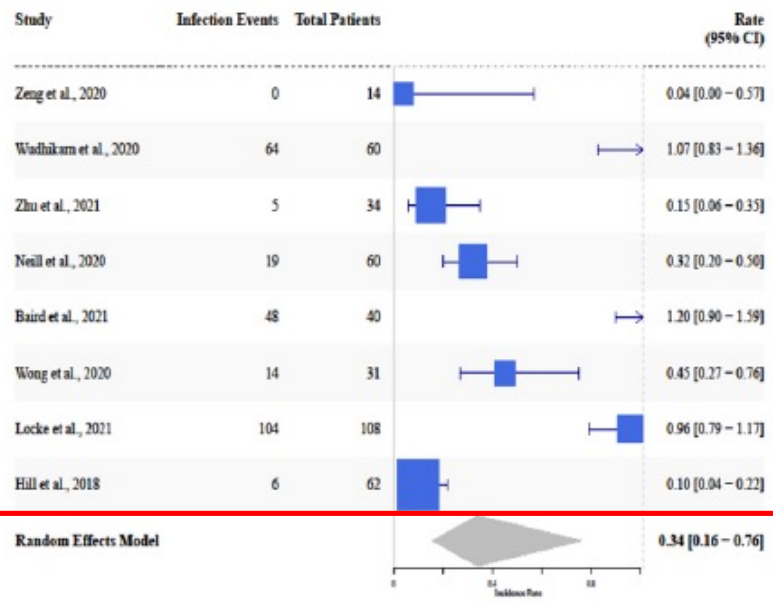
NHL – Early infections



NHL – Late infections



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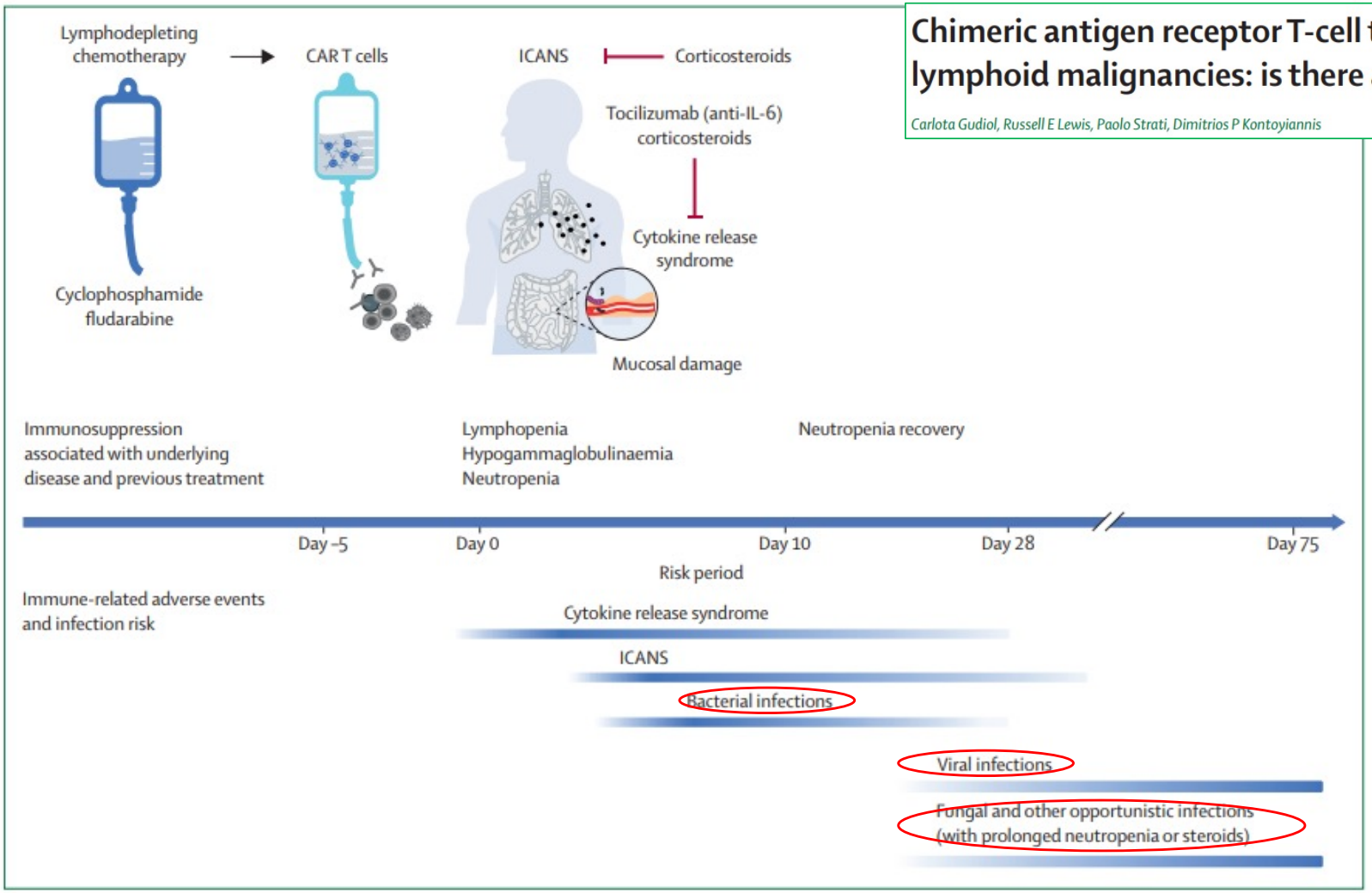
  - ➢ BsAbs per MM
- ✓ Strategie di management e profilassi

Chimeric antigen receptor T-cell therapy for the treatment of lymphoid malignancies: is there an excess risk for infection?

Carlota Gudiol, Russell E Lewis, Paolo Strati, Dimitrios P Kontoyiannis



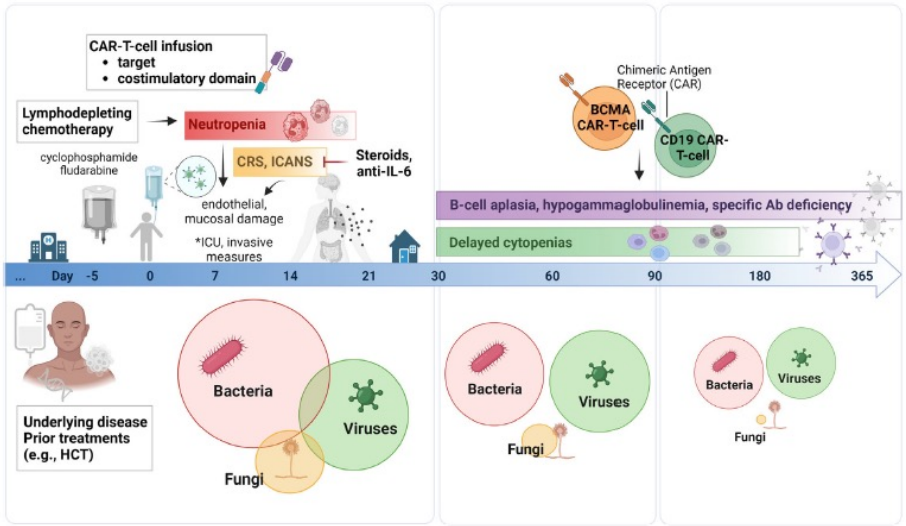
Gudiol et al. Lancet Haematol 2021

Received: 7 June 2023 | Revised: 30 August 2023 | Accepted: 10 September 2023
DOI: 10.1111/tid.14157

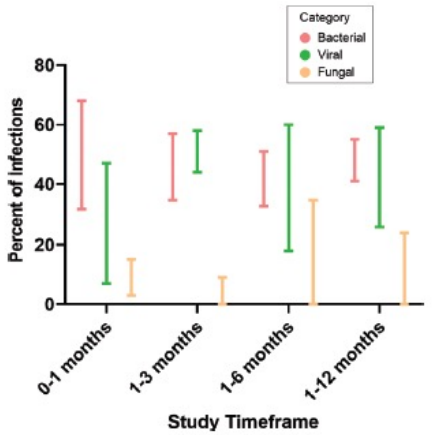
REVIEW ARTICLE

Infections after chimeric antigen receptor (CAR)-T-cell therapy for hematologic malignancies

Eleftheria Kampouri[1,2] | Jessica S. Little[3,4] | Kai Rejeski[5,6] | Oriol Manuel[2] | Sarah P. Hammond[4,7] | Joshua A. Hill[1,8,9]



Relative frequency of infection types (bacterial, viral and fungal) as percentage of all infections after CD19 CAR-T-cell therapy during different time intervals



Timeframe	Bacterial cause	Viral cause	Fungal cause	References
0–1 month	32%–68%	7%–47%	3%–15%	35-38,40,49, 50,57,59,79
1–3 months	35%–57%	44%–58%	0%–9%	35,38,59
1–6 months	33%–51%	18%–60%	0%–35%	37,46,49
1–12 months	41%–55%	26%–59%	0%–24%	40,49,59

Kampoyri E, Transpl Infect Dis 2023

blood
Regular Article

IMMUNOBIOLOGY AND IMMUNOTHERAPY

Infectious complications of CD19-targeted chimeric antigen receptor–modified T-cell immunotherapy

Joshua A. Hill,[1,2] Daniel Li,[3] Kevin A. Hay,[4,5] Margaret L. Green,[1,2] Sindhu Cherian,[6] Xueyan Chen,[6] Stanley R. Riddell,[1,4] David G. Malc
Michael Boeckh,[1,2] and Cameron J. Turtle[1,4]

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[3]Juno Therapeutics, Seattle, WA; [4]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA; [5]Department of Medicine, University o
Columbia, Vancouver, BC, Canada; and [6]Department of Laboratory Medicine, University of Washington, Seattle, WA

133 patients treated with CD19 CAR-Tcells
The cohort included patients with
- acute lymphoblastic leukemia (ALL; n° 47),
- chronic lymphocytic leukemia (n° 24)
- non-Hodgkin lymphoma (n° 62).

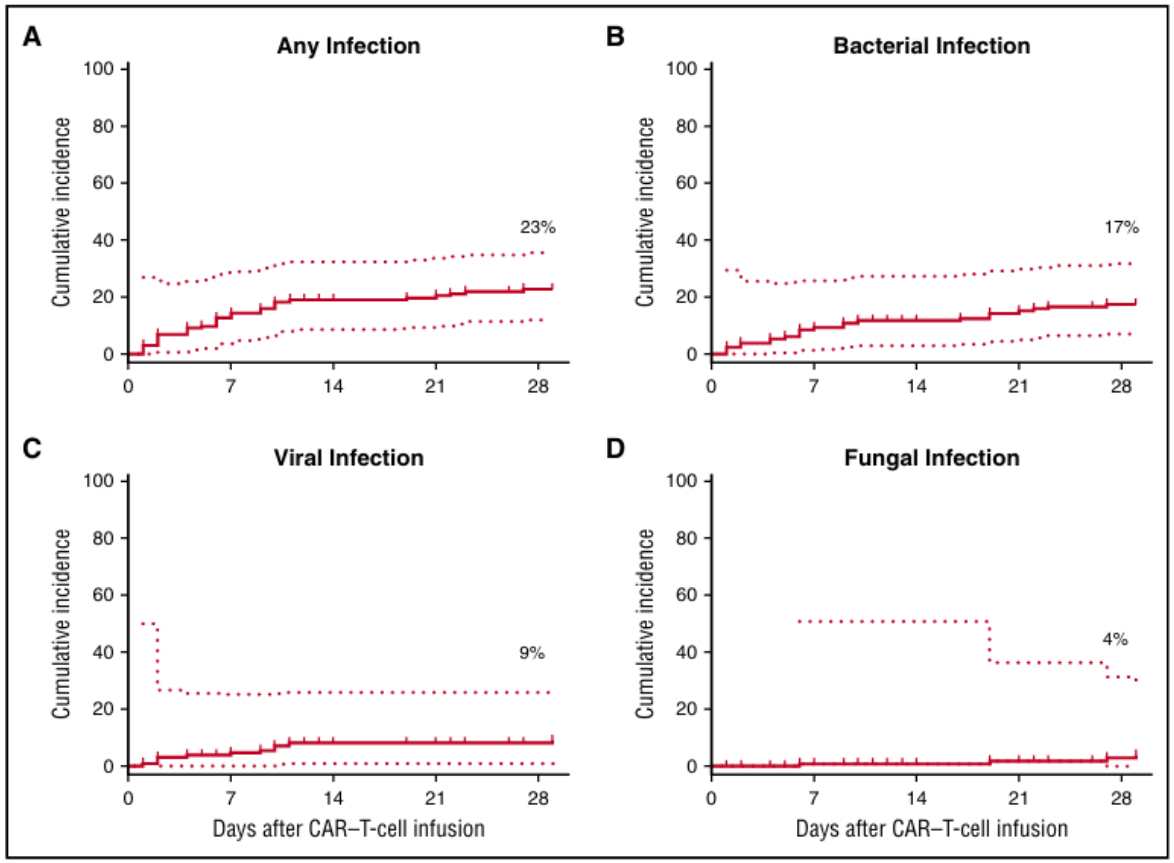

Figure 1. Cumulative-incidence curves of time-to-first infection for any infection and for specific infection categories. (A-D) Cumulative incidences among all patients (n = 133) of any (A), bacterial (B), viral (C), and fungal (D) infections within the first 28 days after CAR–T-cell infusion. Dotted lines represent 95% CIs.

Blood. 2018;131(1):121-130)

blood
Regular Article

IMMUNOBIOLOGY AND IMMUNOTHERAPY

Infectious complications of CD19-targeted chimeric antigen receptor–modified T-cell immunotherapy

Joshua A. Hill,[1,2] Daniel Li,[3] Kevin A. Hay,[4,5] Margaret L. Green,[1,2] Sindhu Cherian,[6] Xueyan Chen,[6] Stanley R. Riddell,[1,4] David G. Maloney,[1,4] Michael Boeckh,[1,2] and Cameron J. Turtle[1,4]

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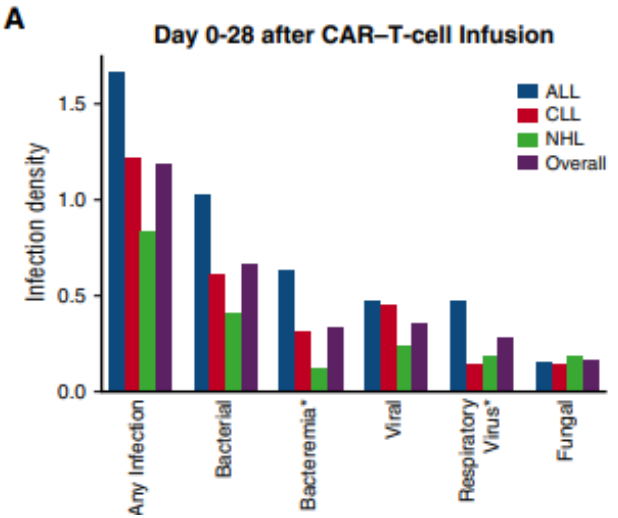


Incidence of bacterial, viral, and fungal infections in the first 28 days afterCAR–T-cell infusion

Type of infection	ALL, n = 47		CLL, n = 24		NHL, n = 62		Total, N = 133	
	Events	No. of patients (%)	Events	No. of patients (%)	Events	No. of patients (%)	Events	No. of patients (%)
Any infection	21	14 (29.8)	8	5 (20.8)	14	11 (17.7)	43	30 (22.6)
Bacterial infections	13	12 (25.5)	4	4 (16.7)	7	6 (9.7)	24	22 (16.5)
Bacteremia*	8	7 (14.9)	2	2 (8.3)	2	1 (1.6)	12	10 (7.5)
Bacterial site infections†	5	5 (10.6)	2	2 (8.3)	5	5 (8.1)	12	12 (9.0)
Viral infections	6	5 (10.6)	3	2 (8.3)	4	4 (6.5)	13	11 (8.3)
Respiratory virus‡	6	5 (10.6)	1	1 (4.2)	3	3 (4.8)	10	9 (6.8)
Other virus§	0	0 (0.0)	2	1 (4.2)	1	1 (1.6)	3	2 (1.6)
Fungal infections‖	2	2 (4.3)	1	1 (4.2)	3	1 (1.6)	6	4 (3.0)
Nonmold¶	1	1 (2.1)	0	0 (0.0)	3	2 (3.2)	4	3 (2.3)
Mold#	1	1 (2.1)	1	1 (4.2)	0	0 (0.0)	2	2 (1.5)

Blood. 2018;131(1):121-130)

Infectious complications of CD19-targeted chimeric antigen receptor–modified T-cell immunotherapy

Joshua A. Hill,[1,2] Daniel Li,[3] Kevin A. Hay,[4,5] Margaret L. Green,[1,2] Sindhu Cherian,[6] Xueyan Chen,[6] Stanley R. Riddell,[1,4] David G. Maloney,[1,4] Michael Boeckh,[1,2] and Cameron J. Turtle[1,4]

blood Regular Article

blood® 4 JANUARY 2018 | VOLUME 131, NUMBER 1

Risk factors for infections occurring within 28 days

133 patients treated with CD19 CAR-Tcells
The cohort included patients with
- acute lymphoblastic leukemia (ALL; n° 47),
- chronic lymphocytic leukemia (n° 24)
- non-Hodgkin lymphoma (n° 62).

Table 3. Pre-CAR–T-cell infusion factors and association with infection density within 28 days after CAR–T-cell infusion using Poisson regression

Pre-CAR–T-cell infusion variables	Ratio of infection densities (95% CI)	P	Adjusted ratio of infection densities (95% CI)	P
Age	1.00 (0.97-1.02)	.69		
Sex	0.93 (0.47-1.85)	.83		
Disease type				
ALL vs CLL	1.36 (0.60-0.37)	.46	2.68 (1.16-6.19)	.021
ALL vs NHL	2.01 (1.02-3.95)	.043	4.44 (2.06, 9.55)	<.001
Prior autologous or allogeneic HCT	0.70 (0.38-1.28)	.25		
Prior antitumor treatment regimens				
≥4 vs <4	2.24 (1.10-4.54)	.017	3.53 (1.76-7.10)	<.001
IgG <400 mg/dL prelymphodepletion	1.01 (0.52-1.96)	.98		
ALC <200 cells per mm³ prelymphodepletion	0.75 (0.38-1.48)	.42		
ANC <500 cells per mm³ prelymphodepletion	1.84 (0.88-3.84)	.10		
ANC <500 cells per mm³ pre-CAR-T	2.02 (1.08-3.78)	.024		
Lymphodepletion regimen				
Cy/Flu vs Cy/other	0.64 (0.34-1.23)	.20		
CAR–T-cell dose, cells per kg				
2×10^7 vs 2×10^5	3.06 (1.36-6.90)	<.001	7.86 (3.15-19.60)	<.001
2×10^7 vs 2×10^6	4.41 (2.13-9.17)	<.001	7.25 (3.51-14.99)	<.001

Immune reconstitution and associated infections following axicabtagene ciloleucel in relapsed or refractory large B-cell lymphoma

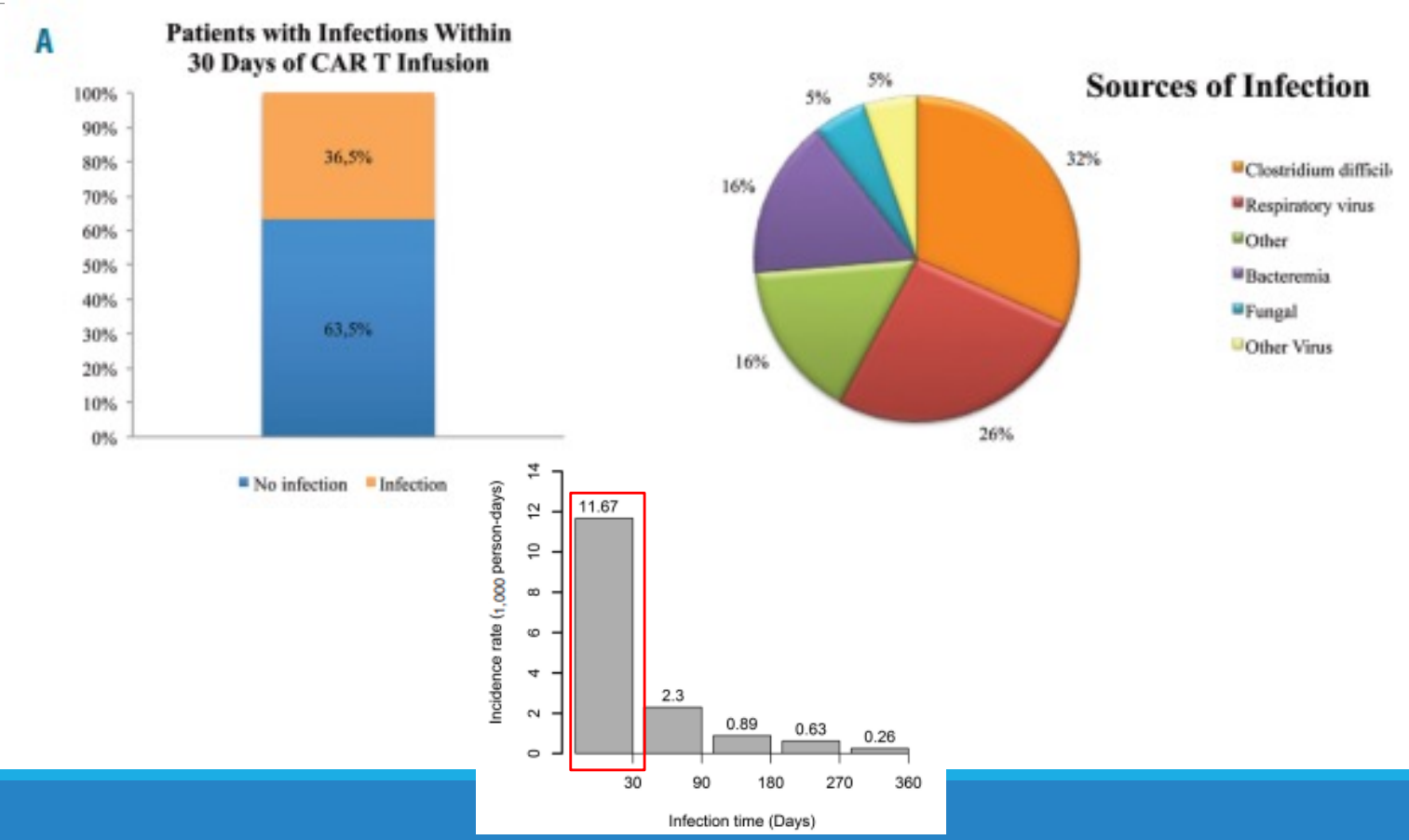
Jennifer M. Logue,[1,2*] Elisa Zucchetti,[3*] Christina A. Bachmeier,[1] Gabriel S. Krivenko,[1] Victoria Larson,[2] Daniel Ninh,[1] Giovanni Grillo,[3] Biwei Cao,[4] Jongphil Kim,[4] Julio C. Chavez,[2,5] Aliyah Baluch,[2,6] Farhad Khimani,[1,2] Aleksandr Lazaryan,[1,2] Taiga Nishihori,[1,2] Hien D. Liu,[1,2] Javier Pinilla-Ibarz,[2,5] Bijal D. Shah,[2,5] Rawan Faramand,[1,2] Anna E. Coghill,[7] Marco L. Davila,[1,2] Bhagirathbhai R. Dholaria,[1,8] Michael D. Jain[1,2#] and Frederick L. Locke[1,2#]

Haematologica 2021
Volume 106(4):978-986

Studio di coorte retrospettivo monocentrico

85 pazienti trattati con CAR-T per R/R LBCL

Outcome: incidenza di episodi infettivi nei primi 30 gg e dopo i 30 gg dall'infusione



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

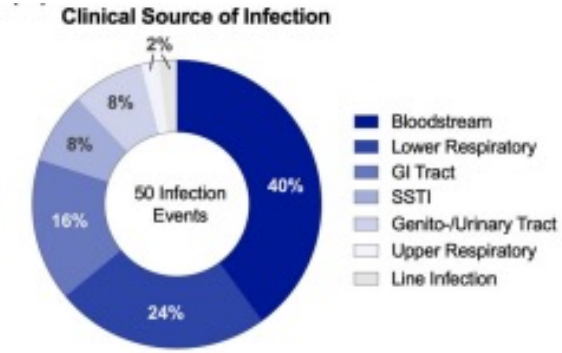
Kai Rejeski[1,2,3] | Yucai Wang[4] | Omar Albanyan[5] | Javier Munoz[6] | Pierre Sesques[7] | Gloria Iacoboni[8,9] | Lucia Lopez-Corral[10,11] | Isabelle Ries[12] | Veit L. Bücklein[1,2] | Razan Mohty[5] | Martin Dreyling[1] | Aliyah Baluch[13] | Bijal Shah[14] | Frederick L. Locke[5] | Georg Hess[12]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

AJH

Am J Hematol. 2023;98:1699–1710.

Studio di coorte multicentrico

103 pazienti con linfoma mantellare R/R sottoposti a trattamento con CAR-T dal 2015 al 2022



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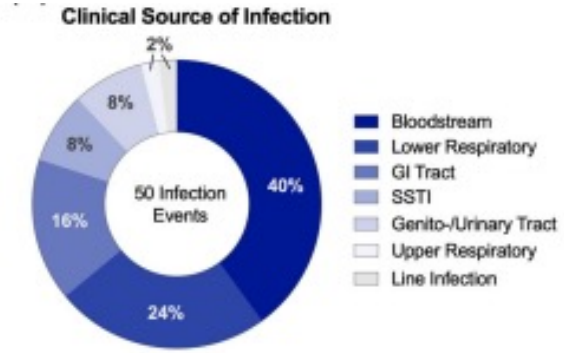
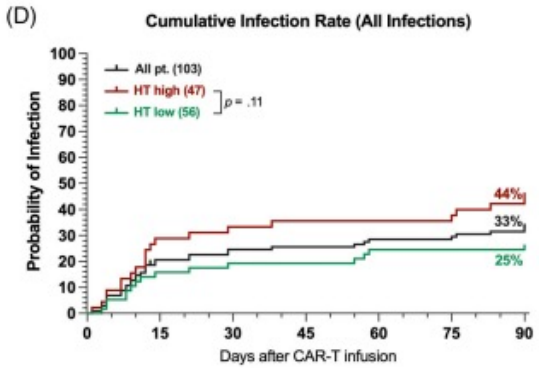
Am J Hematol. 2023;98:1699–1710.

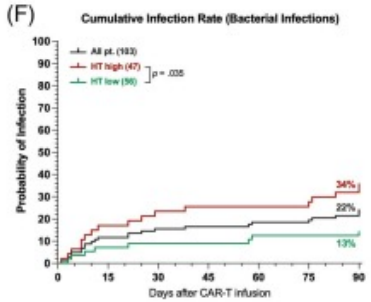
Studio di coorte multicentrico

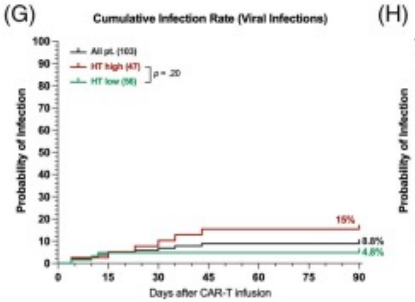
103 pazienti con linfoma mantellare R/R sottoposti a trattamento con CAR-T dal 2015 al 2022

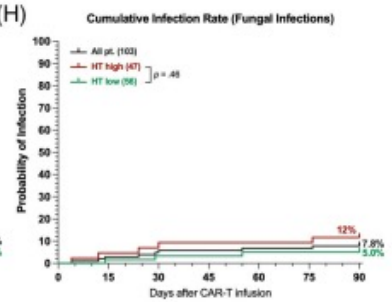
Frequenza di eventi infettivi stratificati sulla base del CAR-HEMATOTOX score includente conta neutrofili, PLT, Hb, Ferritina e PCR









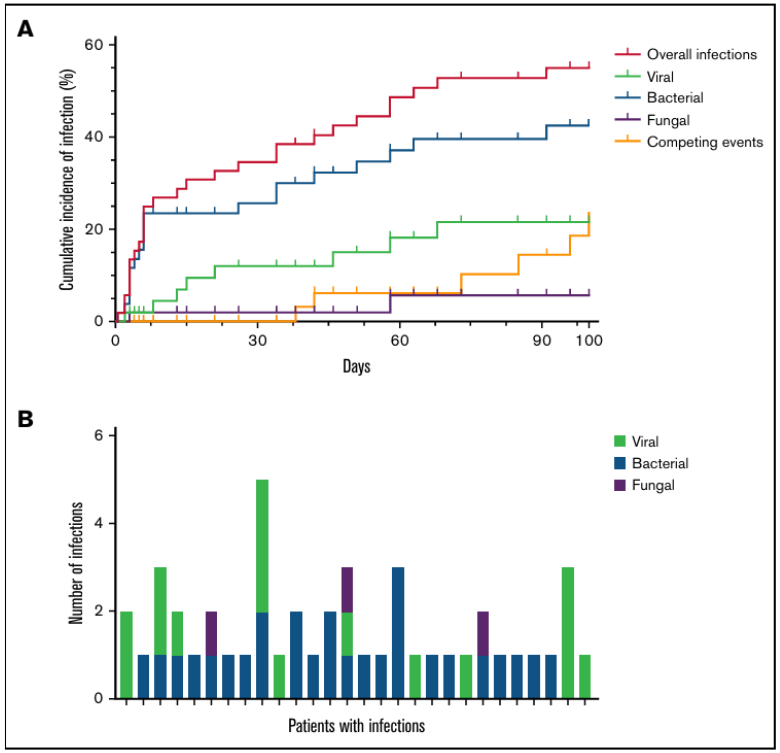


IMMUNOBIOLOGY AND IMMUNOTHERAPY | DECEMBER 14, 2022

Early cytopenias and infections after standard of care idecabtagene vicleucel in relapsed or refractory multiple myeloma

Jennifer M. Logue, Lauren C. Peres, Hamza Hashmi, Christelle M. Colin-Leitzinger, Alexandria M. Shrewsbury, Hitomi Hosoya, Rebecca M. Gonzalez, Christina Copponex, Krista H. Kottra, Vanna Hovanky, Bita Sahaf, Sunita Patil, Aleksandr Lazaryan, Michael D. Jain, Aliyah Baluch, Olga V. Klinkova, Nelli Bejanyan, Rawan G. Faramand, Hany Elmariah, Farhad Khimani, Marco L. Davila, Asmita Mishra, Brandon J. Blue, Ariel F. Grajales-Cruz, Omar A. Castaneda Puglianini, Hien D. Liu, Taiga Nishihori, Ciara L. Freeman, Jason B. Brayer, Kenneth H. Shain, Rachid C. Baz, Frederick L. Looke, Melissa Alsina, Surbhi Sidana, Doris K. Hansen

Multicenter retrospective study included 52 patients who received SOCide-cel



- Within 100 days after ide-cel infusion, 46 documented infections occurred in 28/52 patients (54%).
- 14 infections were severe and occurred in12/52 patients (23%).
- No patient died of infection in the first 100 days
- **Earlier infections in the first 30 days after ide -cel were typically bacterial (68%), and 50% were considered severe**.
- **Of these earlier bacterial infections, unspecified bacterial pneumonia, Clostridioides difficile colitis, and skin or soft tissue infections were most common.**
- **Later infections between days 31and 100 were 50% bacterial, most commonly sinusitis, and 42% viral, most commonly coronavirus disease 2019 (COVID-19, SARS CoV2).**

Blood Adv (2022) 6 (24): 6109–6119.
https://doi.org/10.1182/bloodadvances.2022008320

Outline

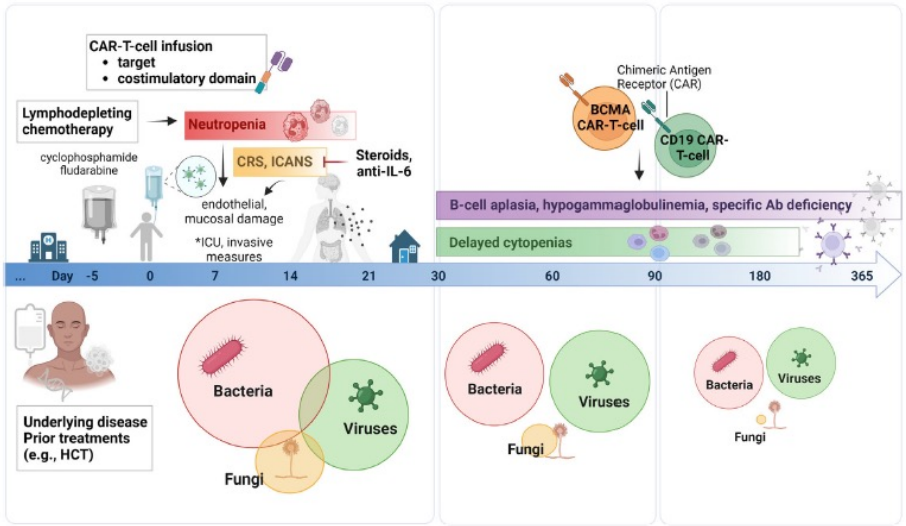
- ✓ Introduzione
- ✓ **Rischio infettivo in pazienti trattati con CAR-T**
  - ➢ Entro i 28 gg
  - ➢ **Oltre i 28 gg**
- ✓ Rischio infettivo in pazienti trattati con anticorpi bispecifici
  - ➢ BsAbs per DLBCL
  - ➢ BsAbs per MM
- ✓ Strategie di management e profilassi

Received: 7 June 2023 | Revised: 30 August 2023 | Accepted: 10 September 2023
DOI: 10.1111/tid.14157

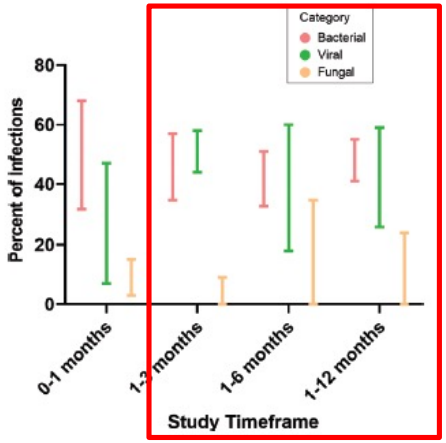
REVIEW ARTICLE

Infections after chimeric antigen receptor (CAR)-T-cell therapy for hematologic malignancies

Eleftheria Kampouri[1,2] | Jessica S. Little[3,4] | Kai Rejeski[5,6] | Oriol Manuel[2] | Sarah P. Hammond[4,7] | Joshua A. Hill[1,8,9]



Relative frequency of infection types (bacterial, viral and fungal) as percentage of all infections after CD19 CAR-T-cell therapy during different time intervals



Timeframe	Bacterial cause	Viral cause	Fungal cause	References
0–1 month	32%–68%	7%–47%	3%–15%	35-38,40,49, 50,57,59,79
1–3 months	35%–57%	44%–58%	0%–9%	35,38,59
1–6 months	33%–51%	18%–60%	0%–35%	37,46,49
1–12 months	41%–55%	26%–59%	0%–24%	40,49,59

Kampoyri E, Transpl Infect Dis 2023

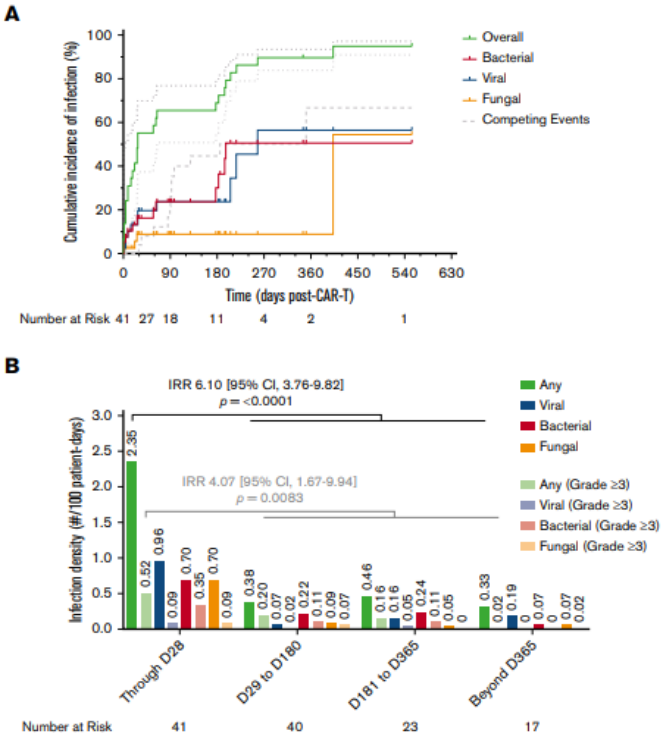
Immune reconstitution and infectious complications following axicabtagene ciloleucel therapy for large B-cell lymphoma

Studio di coorte prospettico monocentrico
41 pazienti con LBCL trattati con axi-cel tra il 2017 e il 2019
Outcome: incidenza e caratterizzazione degli episodi infettivi nel corso del follow-up

blood advances

John H. Baird,[1,2] David J. Epstein,[3] John S. Tamaresis,[4] Zachary Ehlinger,[2] Jay Y. Spiegel,[1,2] Juliana Craig,[1,2] Gursharan K. Claire,[1,2] Matthew J. Frank,[1,2] Lori Muffly,[1,2] Parveen Shiraz,[1,2] Everett Meyer,[1,2] Sally Arai,[1] Janice (Wes) Brown,[1,3] Laura Johnston,[1] Robert Lowsky,[1] Robert S. Negrin,[1] Andrew R. Rezvani,[1] Wen-Kai Weng,[1] Theresa Latchford,[1] Bita Sahaf,[2] Crystal L. Mackall,[1,2,5] David B. Miklos,[1,2,*] and Surbhi Sidana[1,2,*]

12 JANUARY 2021 · VOLUME 5, NUMBER 1



	Through D28		D29 To D180		D181 To D365		Beyond D365		Total Follow Up	
Number at Risk	*n = 41*		*n = 40*		*n = 23*		*n = 17*		*n = 41*	
	Events (Severe)*	*Patients (%)*	*Events (Severe*)*	*Patients (%)*	*Events (Severe*)*	*Patients (%)*	*Events (Severe*)*	*Patients (%)*	*Events (Severe*)*	*Patients (%)*
Any Infection	25 (6)	19 (46.3)	17 (9)	16 (40)	17 (6)	10 (52.6)	14 (1)	8 (47.1)	73 (22)	27 (65.9)
Viral Infections	11 (1)	8 (19.5)	3 (1)	3 (7.5)	6 (2)	4 (21.1)	8 (0)	7 (41.2)	28 (4)	18 (43.9)
Respiratory virus **	4 (0)	4 (9.8)	3 (1)	3 (7.5)	5 (2)	3 (15.8)	2 (0)	2 (11.8)	14 (3)	11 (26.8)
Herpes zoster	1 (0)	1 (2.4)	0 (0)	0 (0)	1 (0)	1 (5.3)	5 (0)	5 (29.4)	7 (0)	7 (17.1)
Other ***	6 (1)	3 (7.3)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	1 (5.9)	7 (1)	5 (12.2)
Bacterial Infections	8 (4)	7 (17.1)	10 (5)	9 (22.5)	9 (4)	6 (26.1)	3 (0)	1 (5.9)	30 (13)	17 (41.5)
Site infection †	7 (3)	6 (14.6)	6 (1)	6 (15)	3 (1)	2 (8.7)	2 (0)	2 (11.8)	18 (5)	12 (29.3)
Lower respiratory tract	1 (1)	1 (2.4)	4 (4)	3 (7.5)	5 (2)	3 (13)	1 (0)	1 (5.9)	11 (7)	8 (19.5)
Bacteremia	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (4.3)	0 (0)	0 (0)	1 (1)	1 (2.4)
Fungal Infections	6 (1)	4 (9.8)	4 (3)	4 (10)	2 (0)	2 (8.7)	3 (1)	3 (17.6)	17 (5)	13 (31.7)
Yeast ‡	6 (1)	4 (9.8)	1 (0)	1 (2.5)	0 (0)	0 (0)	1 (0)	1 (5.9)	8 (1)	6 (14.6)
Mold	0 (0)	0 (0)	1 (1)	1 (2.5)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (2.4)
Pulmonary infection §	0 (0)	0 (0)	0 (0)	0 (0)	2 (0)	2 (8.7)	1 (0)	1 (5.9)	3 (0)	3 (7.3)
Pneumocystis jirovecii ‖	0 (0)	0 (0)	2 (2)	2 (5)	0 (0)	0 (0)	1 (1)	1 (5.9)	3 (3)	3 (7.3)

Immune reconstitution and infectious complications following axicabtagene ciloleucel therapy for large B-cell lymphoma

Studio di coorte prospettico monocentrico
41 pazienti con LBCL trattati con axi-cel tra il 2017 e il 2019
Outcome: incidenza e caratterizzazione degli episodi infettivi nel corso del follow-up

blood advances

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12 JANUARY 2021 · VOLUME 5, NUMBER 1

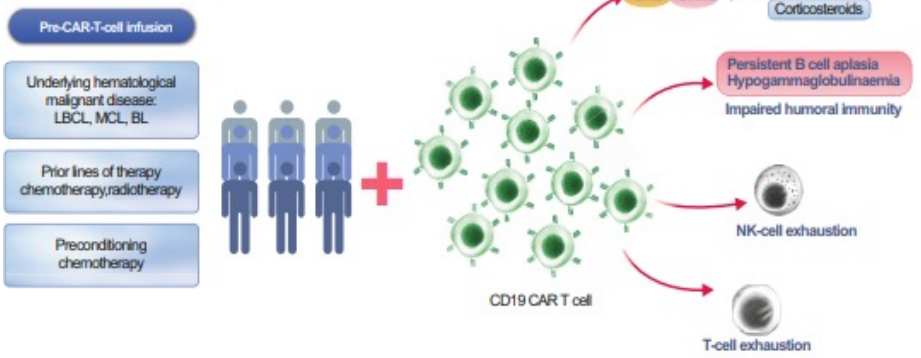
Table S8: Risk factors for infection density beyond day 28 post-infusion.

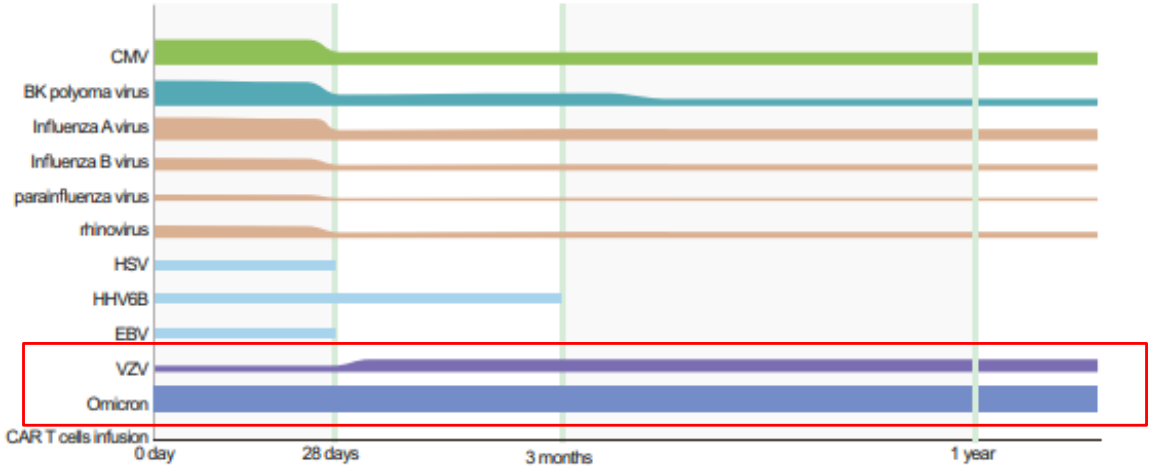
Risk Factor	IRR* (95% CI)	*P*
Ongoing Severe Neutropenia		
G-CSF Use >D+28 vs. ≤D+28	1.47 (0.88-2.41)	0.149
Delayed CD4+ T-cell Recovery		
CD4+ count <200 vs. >200 at M+6	1.42 (0.86-2.37)	0.199
Hypogammaglobulinemia		
Any IVIG Use vs. None	1.56 (0.96-2.52)	0.079
Clinical Response to Axi-cel		
Response vs. Relapse/PD	0.89 (0.51-1.63)	0.645
Lines of Prior Therapy		
>3 vs. ≤3	1.81 (1.13-2.91)	0.020

Improving the safety of CAR-T-cell therapy: The risk and prevention of viral infection for patients with relapsed or refractory B-cell lymphoma undergoing CAR-T-cell therapy

Hu Qian[1,2] | Xingcheng Yang[1,2] | Tingting Zhang[3,4,5] | Ping Zou[6]
Yicheng Zhang[1,2] | Weiwei Tian[4,5] | Zekai Mao[1,2] | Jia Wei[1,2,4,5]

Am J Hematol. 2024;99:662–678.





COVID-19 and CAR T cells: a report on current challenges and future directions from the EPICOVIDEHA survey by EHA-IDWP

blood advances
12 APRIL 2022 • VOLUME 6, NUMBER 7

Alessandro Busca,[1,*] Jon Salmanton-García,[2,3,*] Paolo Corradini,[4] Francesco Marchesi,[5] Alba Cabirta,[6,7] Roberta Di Blasi,[8] Remy Dulery,[9] Sylvain Lamure,[10] Francesca Farina,[11] Barbora Weinbergerová,[12] Josip Batinić,[13-15] Anna Nordlander,[16] Alberto López-García,[17] Ľuboš Drgoňa,[18] Ildefonso Espigado-Tocino,[19] Iker Falces-Romero,[20] Ramón García-Sanz,[21] Carolina García-Vidal,[22] Anna Guidetti,[23] Nina Khanna,[24] Austin Kulasekararaj,[25] Johan Maertens,[26] Martin Hoenigl,[27-29] Nikolai Klimko,[30] Philipp Koehler,[2,3] Antonio Pagliuca,[31] Francesco Passamonti,[32] Oliver A. Cornely,[2,3,33,34] and Livio Pagano[35,36]

Studio di coorte retrospettivo multicentrico

459 pz sottoposti a trattamento con CAR-T

30 pazienti con diagnosi di infezione da SARS-COV-2 da Gennaio 2020 a Febbraio 2021

Outcome: 15 pazienti (50%) deceduti nel corso del follow-up (mediana di FU 71 gg), di cui 10 per COVID-19

Table 2. Univariable and multivariable analyses of factors associated with mortality of patients with COVID-19 receiving CAR T cells

	All patients						Time between CAR T-cell therapy and COVID-19, mo					
							≤6			>6		
	Univariable			Multivariable			Univariable			Univariable		
	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P	HR	95% CI	P
Sex												
Female	–	–	–	–	–	–	–	–	–	–	–	–
Male	2.682	0.849-8.474	.093	2.742	0.848-8.861	.092	4.897	0.591-40.604	.141	1.928	0.417-8.908	.401
Age, y												
<50	–	–	–	–	–	–	–	–	–	–	–	–
≥50	5.119	0.673-38.955	.115	–	–	–	1.809	0.222-14.742	.580	42.159	0.068-26 050.639	.254
Comorbidities, n												
None	–	–	–	–	–	–	–	–	–	–	–	–
1	3.093	0.772-12.393	.111	–	–	–	3.093	0.772-12.393	.111	3.438	0.482-24.537	.218
2	3.021	0.498-18.328	.229	–	–	–	3.021	0.498-18.328	.229	2.055	0.185-22.871	.558
≥3	1.880	0.413-8.562	.414	–	–	–	1.880	0.413-8.562	.414	6.111	0.820-45.529	.077
Malignancy status at COVID-19 diagnosis												
Controlled disease	–	–	–	–	–	–	–	–	–	–	–	–
Active disease	2.707	0.931-7.870	.067	2.652	0.907-7.754	.075	2.707	0.931-7.870	.944	1.121	0.133-9.446	.916
Unknown	1.579	0.188-13.238	.674	1.059	0.123-9.132	.958	–	–	.947	–	–	–
CAR T-cell construct												
Axi-cel	–	–	–	–	–	–	–	–	–	–	–	–
Tisa-cel	0.888	0.321-2.458	.820	–	–	–	0.479	0.092-2.494	.382	1.552	0.296-8.132	.603
Other	–	–	.986	–	–	–	–	–	.991	–	–	–
ICU stay	1.529	0.554-4.225	.413	–	–	–	0.887	0.211-3.729	.870	3.331	0.643-17.247	.152
Tocilizumab/steroids after CAR T cells	1.437	0.520-3.972	.484	–	–	–						
Time from CAR T cells to COVID-19, mo												
≤6	–	–	–	–	–	–						
>6	0.998	0.359-2.770	.996	–	–	–						
Neutrophils at COVID-19 diagnosis, n per mm³												
≤500	–	–	–	–	–	–	–	–	–	–	–	–
>500	0.611	0.161-2.321	.469	–	–	–	0.761	0.167-3.472	.724	–	–	–
Lymphocytes at COVID-19 diagnosis, n per mm³												
≤200	–	–	–	–	–	–	–	–	–	–	–	–
>200	0.551	0.164-1.846	.334	–	–	–	0.568	0.133-2.419	.444	0.872	0.089-8.511	.907

Axi-cel, axicabtagene ciloleucel; CI, confidence interval; HR, hazard ratio; tisa-cel, tisagenlecleucel.

Impact of SARS-CoV-2 vaccination and monoclonal antibodies on outcome post–CD19-directed CAR T-cell therapy: an EPICOVIDEHA survey

blood advances

13 JUNE 2023 • VOLUME 7, NUMBER 11

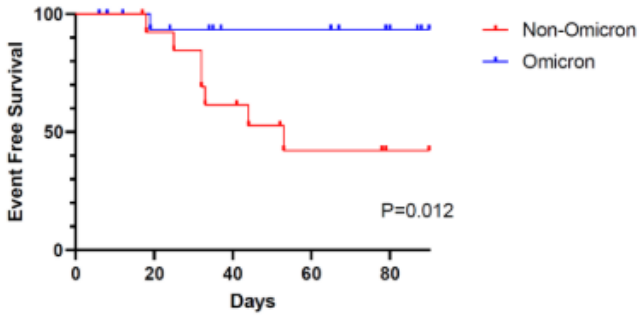
Jaap A. van Doesum,[1,*] Jon Salmanton-García,[2-4,*] Francesco Marchesi,[5] Roberta Di Blasi,[6,7] Iker Falces-Romero,[8,9] Alba Cabirta,[10,11] Francesca Farina,[12] Caroline Besson,[13,14] Barbora Weinbergerová,[15] Jens Van Praet,[16] Martin Schönlein,[17] Alberto López-García,[18] Sylvain Lamure,[19] Anna Guidetti,[20] Cristina De Ramón-Sánchez,[21,22] Josip Batinić,[23,24] Eleni Gavriilaki,[25] Athanasios Tragiannidis,[25] Maria Chiara Tisi,[26] Gaëtan Plantefeve,[27] Verena Petzer,[28] Irati Ormazabal-Vélez,[29] Joyce Marques de Almeida,[30] Monia Marchetti,[31] Johan Maertens,[32,33] Marina Machado,[34] Austin Kulasekararaj,[35] José-Ángel Hernández-Rivas,[36] Maria Gomes da Silva,[37] Noemí Fernández,[38] Ildefonso Espigado,[39] Ľuboš Drgoňa,[40] Giulia Dragonetti,[41] Elisabetta Metafuni,[41] Maria Calbacho,[42] Ola Blennow,[43] Dominik Wolf,[28] Bjorn van Anrooij,[1] Raquel Nunes Rodrigues,[37] Anna Nordlander,[43] Juan-Alberto Martín-González,[44] Raphaël Liévin,[6,7] Moraima Jiménez,[10] Stefanie K. Gräfe,[3,45,46] Ramón García-Sanz,[21,22] Raúl Córdoba,[18] Laman Rahimli,[2-4] Tom van Meerten,[1] Oliver A. Cornely,[2-4,47,48] and Livio Pagano[41]

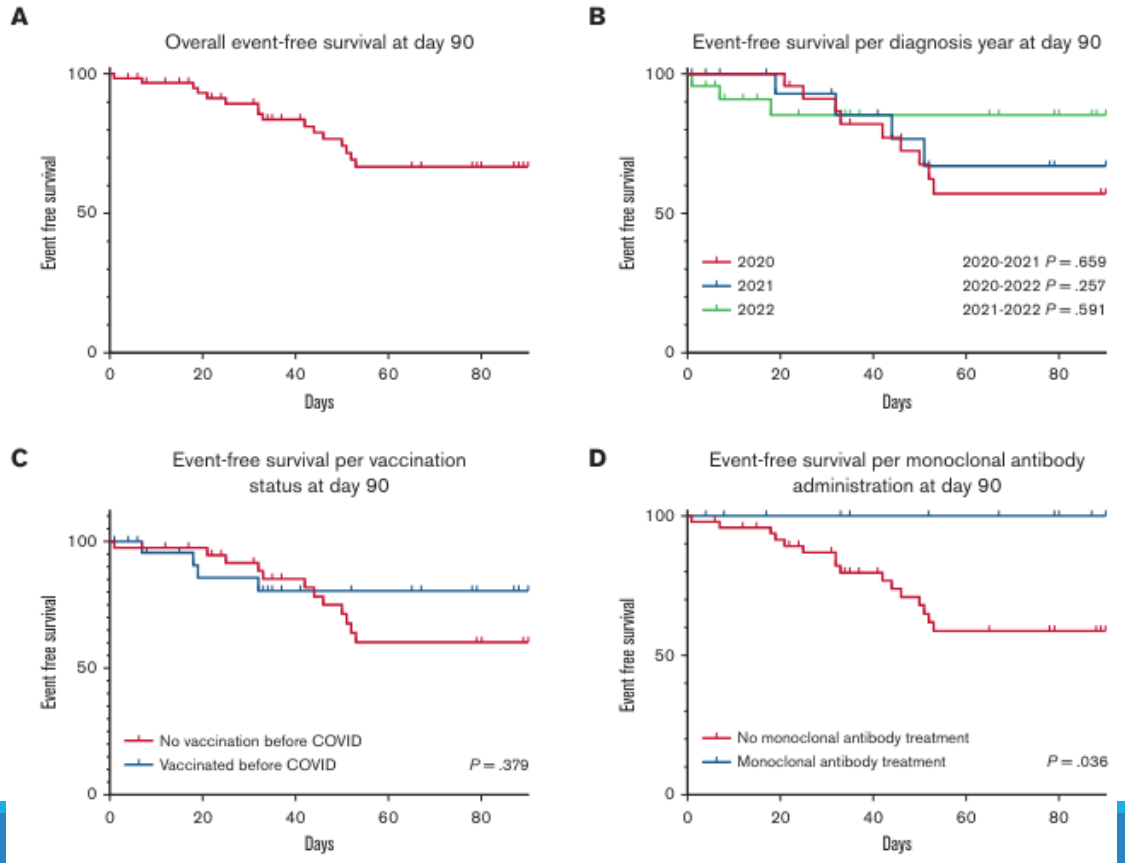
Studio retrospettivo multicentrico

64 pazienti sottoposti a trattamento con CAR-T per BCL (62) o B-ALL (2) con diagnosi di COVID-19 fino a Giugno 2022

Outcome: mortalità a 90 giorni in relazione allo stato vaccinale e all'utilizzo di terapie precoci con monoclonali

Supplement figure 3. Event Free survival Omicron vs other variants (Wildtype, Alpha, Delta)





Low incidence of invasive fungal disease following CD19 chimeric antigen receptor T-cell therapy for non-Hodgkin lymphoma

Jessica S. Little,[1-3] Muneerah M. Aleissa,[1,3,4] Katherine Beluch,[1,3] Isabel H. Gonzalez-Bocco,[1-3] Francisco M. Marty,[1-3] Jennifer Manne-Goehler,[1,2,5] Sophia Koo,[1-3] Sarah P. Hammond,[2,3,5,6,*] and Caron A. Jacobson[2,3,*]

blood advances

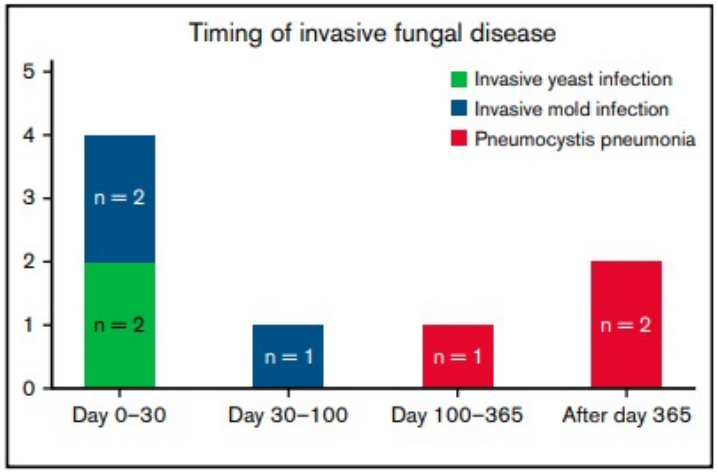
23 AUGUST 2022 • VOLUME 6, NUMBER 16

Studio retrospettivo monocentrico

280 pazienti sottoposti a CAR-T per LNH

Outcome: Incidenza e caratterizzazione delle Infezioni fungine invasive

Characteristics	CAR T-cell patients N = 280
Demographics	
Age, median (range)	64 (19-82)
Sex n (%)	
Male	185 (66)
Female	95 (34)
Underlying disease, n (%)	
Diffuse large B-cell lymphoma	158 (56)
Transformed follicular lymphoma	57 (20)
High-grade B-cell lymphoma	13 (5)
Transformed marginal cell lymphoma	10 (4)
Primary mediastinal B-cell lymphoma	10 (4)
Follicular lymphoma	9 (3)
Mantle cell lymphoma	8 (3)
Other non-Hodgkin lymphomas*	8 (3)
Transformed chronic lymphocytic leukemia	7 (2.5)
Prior lines of chemotherapy, median (range)	3 (2-10)
Prior HCT, n (%)	
Allogeneic	9 (3)
Autologous	82 (29)
CAR T-cell product, n (%)	
Axicabtagene ciloleucel	244 (87)
Tisagenlecleucel	22 (8)
Brexucabtagene autoleucel	8 (3)
Lisocabtagene maraleucel	6 (2)

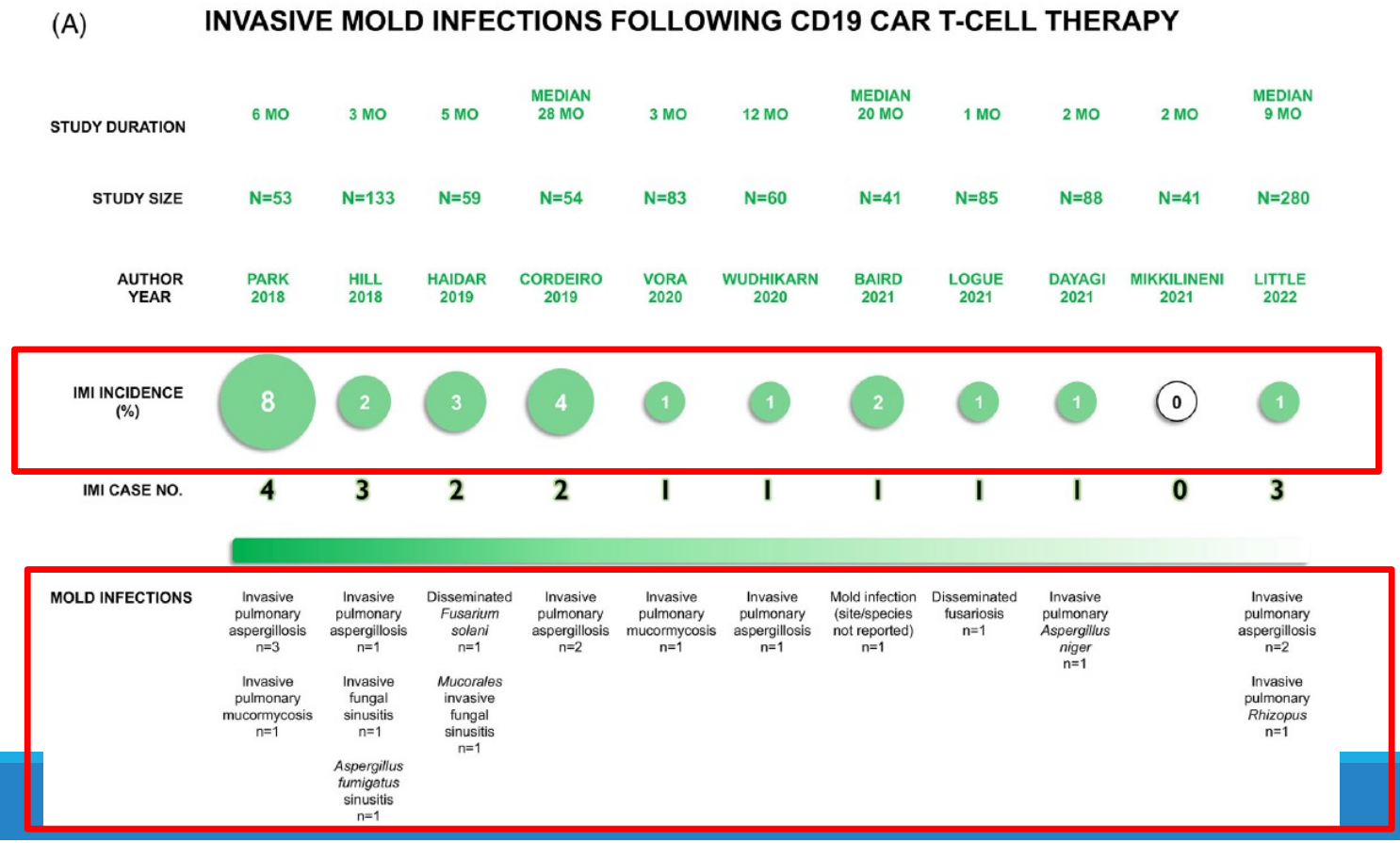


Infections after chimeric antigen receptor (CAR)-T-cell therapy for hematologic malignancies

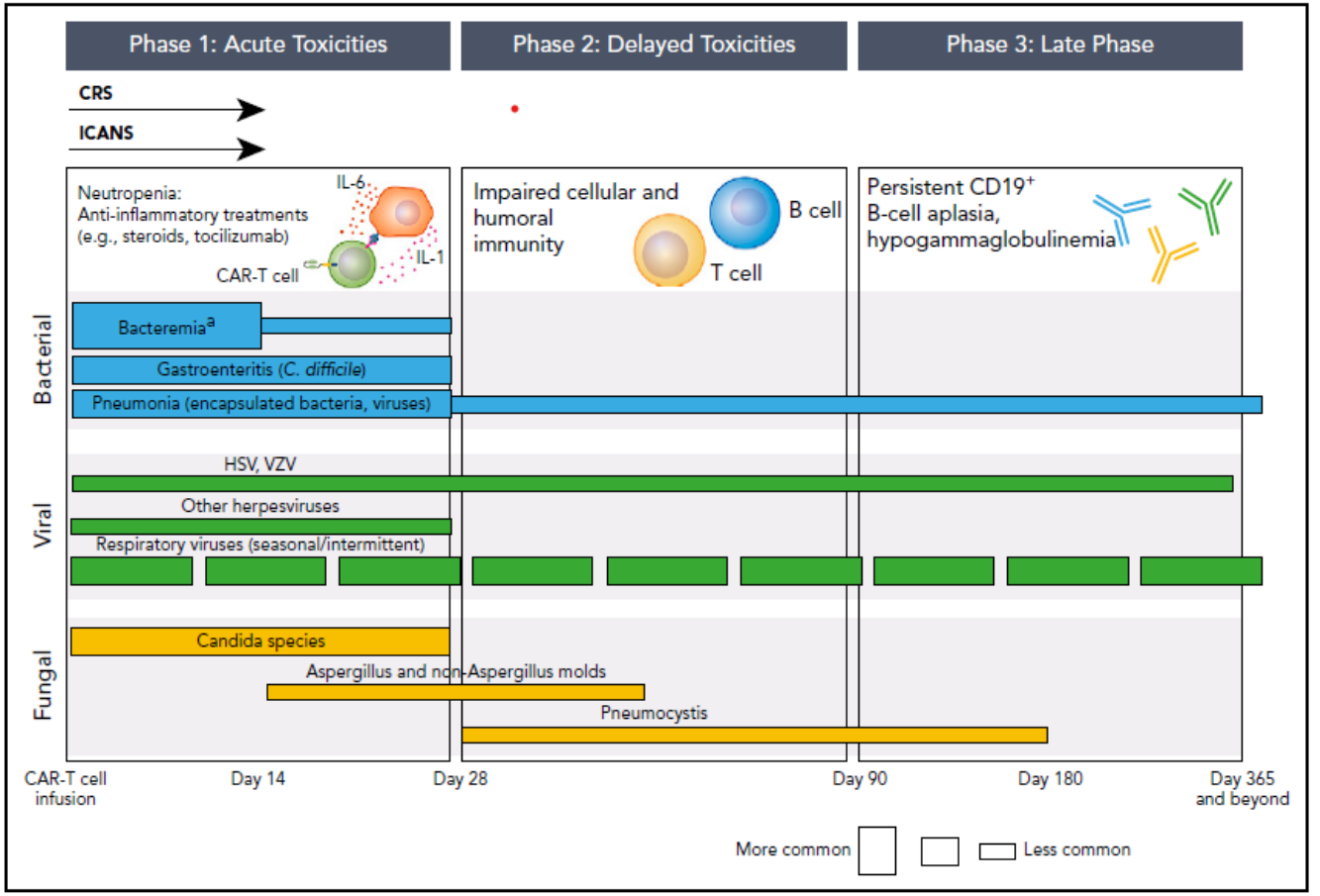
Eleftheria Kampouri[1,2] | Jessica S. Little[3,4] | Kai Rejeski[5,6] | Oriol Manuel[2] | Sarah P. Hammond[4,7] | Joshua A. Hill[1,8,9]

TRANSPLANT INFECTIOUS DISEASE

Transpl Infect Dis. 2023:25(Suppl. 1):e14157.



Phases of opportunistic infections in CD19-targeted CAR–T-cell therapy recipients



Hill JA, Blood 2020

Outline

- ✓ Introduzione
- ✓ Rischio infettivo in pazienti trattati con CAR-T
  - ➢ Entro i 28 gg
  - ➢ Oltre i 28 gg
- ✓ **Rischio infettivo in pazienti trattati con anticorpi bispecifici**
  - ➢ **BsAbs per DLBCL**
  - ➢ BsAbs per MM
- ✓ Strategie di management e profilassi

Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell–Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

Martin Hutchings, PhD[1]; Franck Morschhauser, MD, PhD[2]; Gloria Iacoboni, MD[3,4]; Carmelo Carlo-Stella, MD[5]; Fritz C. Offner, MD, PhD[6]; Anna Sureda, MD, PhD[7]; Gilles Salles, MD[8]; Joaquín Martínez-Lopez, MD, PhD, MBA[9]; Michael Crump, MD[10]; Denise N. Thomas, MSc[11]; Peter N. Morcos, PharmD[11]; Cristiano Ferlini, MD[11]; Ann-Marie E. Bröske, PhD[12]; Anton Belousov, PhD[13]; Marina Bacac, PhD[13]; Natalie Dimier, PhD[14]; David J. Carlile, PhD[14]; Linda Lundberg, PhD[15]; David Perez-Callejo, MD, PhD[15]; Pablo Umaña, PhD[13]; Tom Moore, MD[12]; Martin Weisser, MD[12]; and Michael J. Dickinson, MBBS, DMedSci[16]

Journal of Clinical Oncology®
2021 Volume 39, Issue 18 **1959**

Trial di fase 1

171 pazienti con LNH sottoposti ad 1 o più linee di trattamento e senza opzioni di trattamento efficaci, trattati con glofitamab

Outcome: efficacia (tempo alla progressione o morte) e tollerabilità (incidenza di AEs di grado 1-5)

No. of Patients (%)	All Glofitamab Cohorts (N = 171)	RP2D Glofitamab Cohort 2.5/10/30 mg (n = 35)
Any AE	168 (98.2)	34 (97.1)
Common (≥ 5% of patients) grade ≥ 3 AEs by preferred term		
Neutropenia[a]	43 (25.1)	9 (25.7)
Thrombocytopenia	14 (8.2)	3 (8.6)
Anemia	13 (7.6)	0
CRS	6 (3.5)	2 (5.7)
Gamma-glutamyltransferase increased	5 (2.9)	2 (5.7)
Pneumonia	5 (2.9)	2 (5.7)
Febrile neutropenia	5 (2.9)	2 (5.7)
SAE	100 (58.5)	21 (60.0)
SAE related to glofitamab	77 (45.0)	18 (51.4)
Adverse events of special interest (all grades)		
CRS	86 (50.3)	25 (71.4)
Infections and infestations	88 (51.5)	15 (42.9)
Neurologic adverse event	74 (43.3)	11 (31.4)
ICANS-like event	9 (5.3)	2 (5.7)
Febrile neutropenia	5 (2.9)	2 (5.7)
Grade 5 (fatal) adverse event	2 (1.2)	0

Grade ≥3 Infections: 30 (17.5%)

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

Michael J. Dickinson, M.B., B.S., D.Med.Sc., Carmelo Carlo-Stella, M.D., Franck Morschhauser, M.D., Ph.D., Emmanuel Bachy, M.D., Ph.D., Paolo Corradini, M.D., Gloria Iacoboni, M.D., Cyrus Khan, M.D., Tomasz Wróbel, M.D., Fritz Offner, M.D., Ph.D., Marek Trněný, M.D., Shang-Ju Wu, M.D., Ph.D., Guillaume Cartron, M.D., Ph.D., Mark Hertzberg, M.B., B.S., Ph.D., Anna Sureda, M.D., Ph.D., David Perez-Callejo, Ph.D., Linda Lundberg, Ph.D., James Relf, M.D., Mark Dixon, M.Sc., Emma Clark, M.Sc., Kathryn Humphrey, B.Sc., and Martin Hutchings, M.D., Ph.D.

N Engl J Med 2022;387:2220-31.

Trial di fase 2

155 pazienti (Gennaio 2020-Settembre 2021) con RR DLBCL sottoposti ad almeno 2 linee precedenti di trattamento, trattati con glofitamab (con pretrattamento con obinutuzumab per ridurre il rischio di CRS)

Outcome primario: tasso di risposta completa; secondari: tempo alla risposta, sopravvivenza libera da progressione, tasso di AEs

7/8 (87.5%) AEs fatali dovuti ad episodi infettivi: COVID-19 (5 pz), sepsi (2 pz)

Table 3. Adverse Events in All the Patients Treated at the Phase 2 Dose (Safety Population).*

Event	Patients (N=154)
	no. (%)
Any adverse event	152 (99)
Any serious adverse event	73 (47)
Most common serious adverse events‡	
Cytokine release syndrome, per ASTCT	32 (21)
Sepsis	6 (4)
Tumor flare	5 (3)
Covid-19–related pneumonia	5 (3)
Covid-19	4 (3)
Adverse events of special interest	
Cytokine release syndrome, grade ≥2 per ASTCT	24 (16)
Cytokine release syndrome, grade ≥2 per Lee et al.[28]	28 (18)
Infection, any grade	59 (38)
Neurologic event, grade ≥2	23 (15)
Event grade consistent with ICANS, any grade§	12 (8)
Tumor flare, grade ≥2	11 (7)
AST, ALT, or total bilirubin elevation, grade ≥2	11 (7)
Febrile neutropenia, grade ≥3	4 (3)
Tumor lysis syndrome, grade ≥3	2 (1)

Elif Birtas Atesoglu[1] | Zafer Gulbas[2] | Ant Uzay[3] | Muhit Ozcan[4] | Fahir Ozkalemkas[5] | Mehmet Sinan Dal[6] | Hakan Kalyon[1] | Olga Meltem Akay[1] | Burak Deveci[7] | Huseyin Bekoz[8] | Omur Gokmen Sevindik[8] | Tayfur Toptas[9] | Fergun Yilmaz[9] | Derya Koyun[4] | Nihan Alkis[10] | Inci Alacacioglu[11] | Mehmet Sonmez[12] | Irfan Yavasoglu[13] | Anil Tombak[14] | Ozgur Mehtap[15] | Fatih Kurnaz[16] | Orhan Kemal Yuce[17] | Volkan Karakus[18] | Mehmet Turgut[19] | Derya Deniz Kurekci[19] | Mesut Ayer[20] | Muzaffer Keklik[21] | Deram Buyuktas[22] | Murat Ozbalak[20] | Burhan Ferhanoglu[1]

Hematological Oncology. 2023;41:663–673.

Glofitamab in relapsed/refractory diffuse large B-cell lymphoma: Real-world data

Studio retrospettivo multicentrico

46 pz con RR DLBCL sottoposti ad almeno 3 precedenti linee di trattamento, trattati con glofitamab (Marzo 2021-Settembre 2022) in uso compassionevole

Outcome primario Tasso di risposta; secondari: sopravvivenza complessiva e sopravvivenza libera da progressione, tollerabilità

TABLE 3 Adverse events that occurred in patients treated with glofitamab.

	All grades	≥Grade 3	Grade 5
Anemia	16 (37.2%)	8 (18.6%)	
Neutropenia	17 (39.5%)	10 (23.2%)	
Thrombocytopenia	12 (27.9%)	8 (18.6%)	
Fatigue	14 (32.6%)		
Nausea	9 (20.9%)		
Diarrhea	3 (7%)		
Fever	16 (37.2%)		
Febrile neutropenia	8 (18.6%)		2
COVID-19 infection	9 (20.9%)		4
Tumor flare	2 (4.7%)		
CRS	12 (27.9%)	4 (9.3%)	1
Neurologic adverse event	3 (7%)		

Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial

Catherine Thieblemont, MD, PhD[1]; Tycel Phillips, MD[2]; Herve Ghesquieres, MD, PhD[3]; Chan Y. Cheah, MBBS, DMSc[4,5]; Michael Roost Clausen, MD, PhD[6]; David Cunningham, MD[7]; Young Rok Do, MD, PhD[8]; Tatyana Feldman, MD[9]; Robin Gasiorowski, MBBS, PhD[10]; Wojciech Jurczak, MD, PhD[11]; Tae Min Kim, MD, PhD[12]; David John Lewis, MD[13]; Marjolein van der Poel, MD, PhD[14]; Michelle Limei Poon, MD[15]; Mariana Cota Stirner, MD, PhD[16]; Nurgul Kilavuz, MSc[17]; Christopher Chiu, PhD[17]; Menghui Chen, PhD[17]; Mariana Sacchi, MD[17]; Brian Elliott, MD[17]; Tahamtan Ahmadi, MD, PhD[17]; Martin Hutchings, MD, PhD[18]; and Pieternella J. Lugtenburg, MD, PhD[19]

J Clin Oncol 41:2238-2247. © 2022

Trial di fase 1/2

157 pazienti con RR DLBCL sottoposti ad almeno2 linee di trattamento, trattati con epcoritamab (Giugno 2020-Gennaio 2022)

Outcome primario: tasso di risposta complessiva; secondari: durata della risposta, risposta completa, durata della risposta completa, sopravvivenza libera da progressione, tasso di AEs

Patient	Any Grade (N = 157), No. (%)	Grade ≥ 3 (N = 157), No. (%)
Any AE	156 (99.4)	96 (61.1)
Any treatment-related AE	130 (82.8)	42 (26.8)
SAE	89 (56.7)	—
Serious treatment-related AE	55 (35.0)	—
Treatment-emergent AE leading to treatment discontinuation	12 (7.6)	11 (7.0)
Treatment-emergent AE in ≥ 10% of patients[a]		
CRS	78 (49.7)	4 (2.5)
Pyrexia[b]	37 (23.6)	0
Fatigue	36 (22.9)	3 (1.9)
Neutropenia	34 (21.7)	23 (14.6)
AEs of special interest		
CRS[c]	78 (49.7)	4 (2.5)
ICANS[d]	10 (6.4)	1 (0.6)
Clinical tumor lysis syndrome	2 (1.3)	2 (1.3)

3/9 (33.3%) AEs fatali dovuti ad episodi infettivi: COVID-19 (2 pz), PML (1 pz)

Outline

- ✓ Introduzione
- ✓ Rischio infettivo in pazienti trattati con CAR-T
  - ➢ Entro i 28 gg
  - ➢ Oltre i 28 gg
- ✓ **Rischio infettivo in pazienti trattati con anticorpi bispecifici**
  - ➢ BsAbs per DLBCL
  - ➢ **BsAbs per MM**
- ✓ Strategie di management e profilassi

Teclistamab in relapsed refractory multiple myeloma: multi-institutional real-world study

Meera Mohan[1,8], Jorge Monge[2,8], Nishi Shah[3,8], Danny Luan[2], Mark Forsberg[3], Vineel Bhatlapenumarthi[1], Metodi Balev[4], Anannya Patwari[1], Heloise Cheruvalath[5], Divaya Bhutani[4], Sharmilan Thanendrarajan[6], Binod Dhakal[1], Maurizio Zangari[6], Samer Al-Hadidi[6], Dennis Cooper[3], Suzanne Lentzsch[4], Frits van Rhee[7], Anita D'Souza[1], Aniko Szabo[7], Carolina Schinke[6,9] and Rajshekhar Chakraborty[4,9]✉

Blood Cancer Journal

Blood Cancer Journal (2024)14:35;

Studio retrospettivo multicentrico

110 pazienti con RR-MM che hanno ricevuto almeno 1 dose di teclistamab (Gennaio-Agosto 2023)

Outcome: sopravvivenza complessiva e libera da progressione; incidenza di episodi infettivi

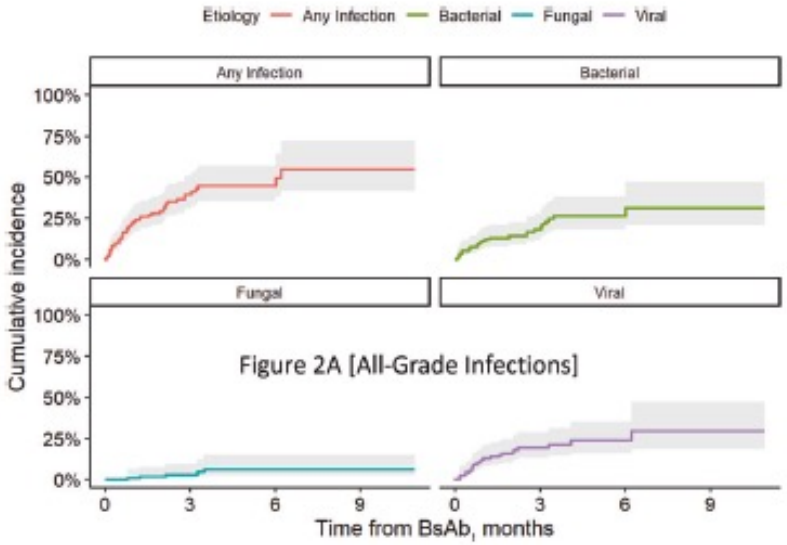


Figure 2A [All-Grade Infections]

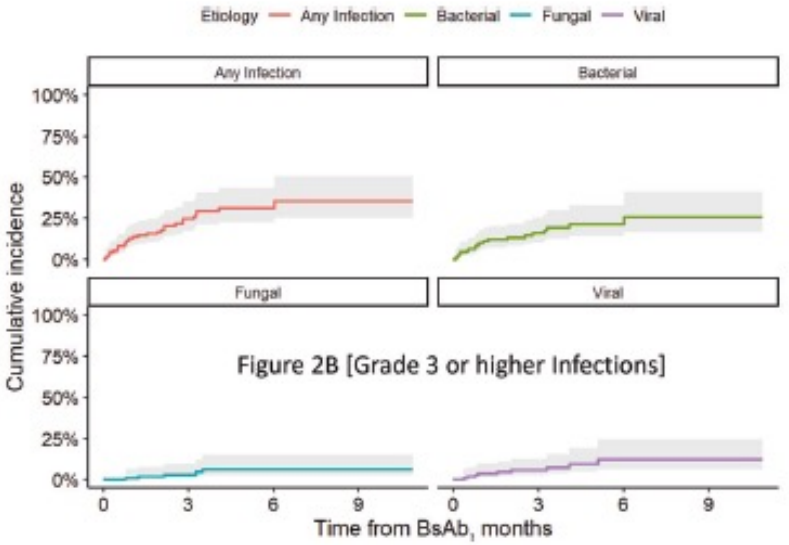


Figure 2B [Grade 3 or higher Infections]

Infezioni batteriche
LRTI: 12
UTI: 10
BSI: 9
Altro: 5

Infezioni Fungine invasive
PJP: 3
Candidiasi invasiva: 2

Infezioni virali
COVID-19: 7
Altro: 27

Incidence, timing, and management of infections in patients receiving teclistamab for the treatment of relapsed/refractory multiple myeloma in the MajesTEC-1 study

Ajay K. Nooka MD[1] | Cesar Rodriguez MD[2] | María Victoria Mateos MD, PhD[3] | Salomon Manier MD, PhD[4] | Katherine Chastain MD[5] | Arnob Banerjee MD, PhD[6] | Rachel Kobos MD[5] | Keqin Qi PhD[7] | Raluca Verona PhD[6] | Margaret Doyle MSc[8] | Thomas G. Martin MD[9] | Niels W. C. J. van de Donk MD, PhD[10]

Cancer. 2024;130:886–900.

Sottoanalisi del MajesTEC-1, trial di fase 1/2

165 pazienti con RR-MM (Marzo 2020-Agosto 2021) esposti a 3 precedenti linee di trattamento, trattati con teclistamab 1.5 mg/kg/wk

Outcomes: incidenza e caratterizzazione degli episodi infettivi

Infezioni virali

Patients, No. (%)[a]	Total (*N* = 165)	Maximum toxicity grade 1	2	3	4	5
Key viral infections (excluding COVID-19)[b]	20 (12.1)	3 (1.8)	10 (6.1)	5 (3.0)	1 (0.6)	1 (0.6)
Adenovirus infection	5 (3.0)	1 (0.6)	1 (0.6)	3 (1.8)	0	0
Parvovirus B19 infection	5 (3.0)	0	4 (2.4)	0	1 (0.6)	0
Oral herpes[c]	4 (2.4)	1 (0.6)	3 (1.8)	0	0	0
Herpes zoster	3 (1.8)	1 (0.6)	2 (1.2)	0	0	0
Adenovirus reactivation	1 (0.6)	0	1 (0.6)	0	0	0
Adenoviral pneumonia	1 (0.6)	0	0	1 (0.6)	0	0
CMV viremia[d]	2 (1.2)	0	1 (0.6)	1 (0.6)	0	0
BK virus infection	1 (0.6)	0	1 (0.6)	0	0	0
CMV infection reactivation	1 (0.6)	0	0	1 (0.6)	0	0
PML	1 (0.6)	0	0	0	0	1 (0.6)
HBV	1 (0.6)	0	0	1 (0.6)	0	0
HBV reactivation	1 (0.6)	0	0	1 (0.6)	0	0
COVID-19 infections	48 (29.1)	3 (1.8)	9 (5.5)	17 (10.3)	1 (0.6)	18 (10.9)
COVID-19	46 (27.9)	2 (1.2)	9 (5.5)	16 (9.7)	1 (0.6)	18 (10.9)
Asymptomatic COVID-19	3 (1.8)	2 (1.2)	0	1 (0.6)	0	0

Incidence, timing, and management of infections in patients receiving teclistamab for the treatment of relapsed/ refractory multiple myeloma in the MajesTEC-1 study

Ajay K. Nooka MD[1] | Cesar Rodriguez MD[2] | María Victoria Mateos MD, PhD[3] | Salomon Manier MD, PhD[4] | Katherine Chastain MD[5] | Arnob Banerjee MD, PhD[6] | Rachel Kobos MD[5] | Keqin Qi PhD[7] | Raluca Verona PhD[6] | Margaret Doyle MSc[8] | Thomas G. Martin MD[9] | Niels W. C. J. van de Donk MD, PhD[10]

Cancer. 2024;130:886–900.

Patients, No. (%)[a]	Total (*N* = 165)	Maximum toxicity grade 1	2	3	4	5
Fungal infections (excluding PJP)	9 (5.5)	1 (0.6)	8 (4.8)	0	0	0
Oral candidiasis	3 (1.8)	0	3 (1.8)	0	0	0
Oral fungal infection	3 (1.8)	1 (0.6)	2 (1.2)	0	0	0
Aspergillus infection	1 (0.6)	0	1 (0.6)	0	0	0
Fungal skin infection	1 (0.6)	0	1 (0.6)	0	0	0
Skin *Candida*	1 (0.6)	0	1 (0.6)	0	0	0
PJP infections	7 (4.2)	0	0	5 (3.0)	2 (1.2)	0
PJP	7 (4.2)	0	0	5 (3.0)	2 (1.2)	0

Infezioni fungine

Patients, No. (%)[a]	Total (*N* = 165)	Maximum toxicity grade 1	2	3	4	5
GI infections	15 (9.1)	4 (2.4)	9 (5.5)	2 (1.2)	0	0
Clostridium difficile colitis	5 (3.0)	1 (0.6)	4 (2.4)	0	0	0
Gastroenteritis	5 (3.0)	2 (1.2)	3 (1.8)	0	0	0
Infectious enterocolitis	3 (1.8)	0	2 (1.2)	1 (0.6)	0	0
Bacterial diarrhea	1 (0.6)	0	1 (0.6)	0	0	0
Diverticulitis	1 (0.6)	0	0	1 (0.6)	0	0
GI infection (unknown etiology)	1 (0.6)	1 (0.6)	0	0	0	0

Infezioni del tratto gastroenterico

Patients, No. (%)[a]	Total (*N* = 165)	Maximum toxicity grade 1	2	3	4	5
Respiratory infections (excluding PJP and COVID-19)	95 (57.6)	4 (2.4)	59 (35.8)	30 (18.2)	0	2 (1.2)
Pneumonia						
No pathogen specified	34 (20.6)	0	10 (6.1)	23 (13.9)	0	1 (0.6)
Pseudomonal pneumonia	4 (2.4)	0	1 (0.6)	3 (1.8)	0	0
Pneumococcal pneumonia	3 (1.8)	0	2 (1.2)	0	0	1 (0.6)
Staphylococcal pneumonia	2 (1.2)	0	0	2 (1.2)	0	0
Enterobacter pneumonia	1 (0.6)	0	0	1 (0.6)	0	0
Klebsiella pneumonia	1 (0.6)	0	0	1 (0.6)	0	0
Metapneumovirus pneumonia	1 (0.6)	0	0	1 (0.6)	0	0
Moraxella pneumonia	1 (0.6)	0	0	1 (0.6)	0	0
RSV pneumonia	1 (0.6)	0	1 (0.6)	0	0	0

Polmoniti batteriche

Characteristics and incidence of infections in patients with multiple myeloma treated by bispecific antibodies: a national retrospective study on the behalf of G2I and Intergroupe Francophone du Myélome

Aurélie Jourdes [1], Elise Cellerin [2], Cyrille Touzeau [3], Stéphanie Harel [4], Blandine Denis [5], Guillaume Escure [6], Emmanuel Faure [6,7], Simon Jamard [8], Francois Danion [9,10], Cécile Sonntag [11], Florence Ader [12,13], Lionel Karlin [14], Sarah Soueges [12], Clarisse Cazelles [15,16], Clémentine de La Porte des Vaux [17], Laurent Frenzel [15,18], Fanny Lanternier [17,19], Xavier Brousse [20], Titouan Cazaubiel [21,22], Pierre Berger [23], Aude Collignon [24], Mathieu Blot [25,26,27], Andrea Pieragostini [28], Morgane Charles [29], Carine Chaleteix [30], Alexis Redor [31], Virginie Roland [32], Tom Cartau [33], Margaret Macro [34], Thomas Chalopin [2], Nicolas Vallet [2,35], Aurore Perrot [20,36], Guillaume Martin-Blondel [1,37,*], on behalf of the G2I and the IFM networks

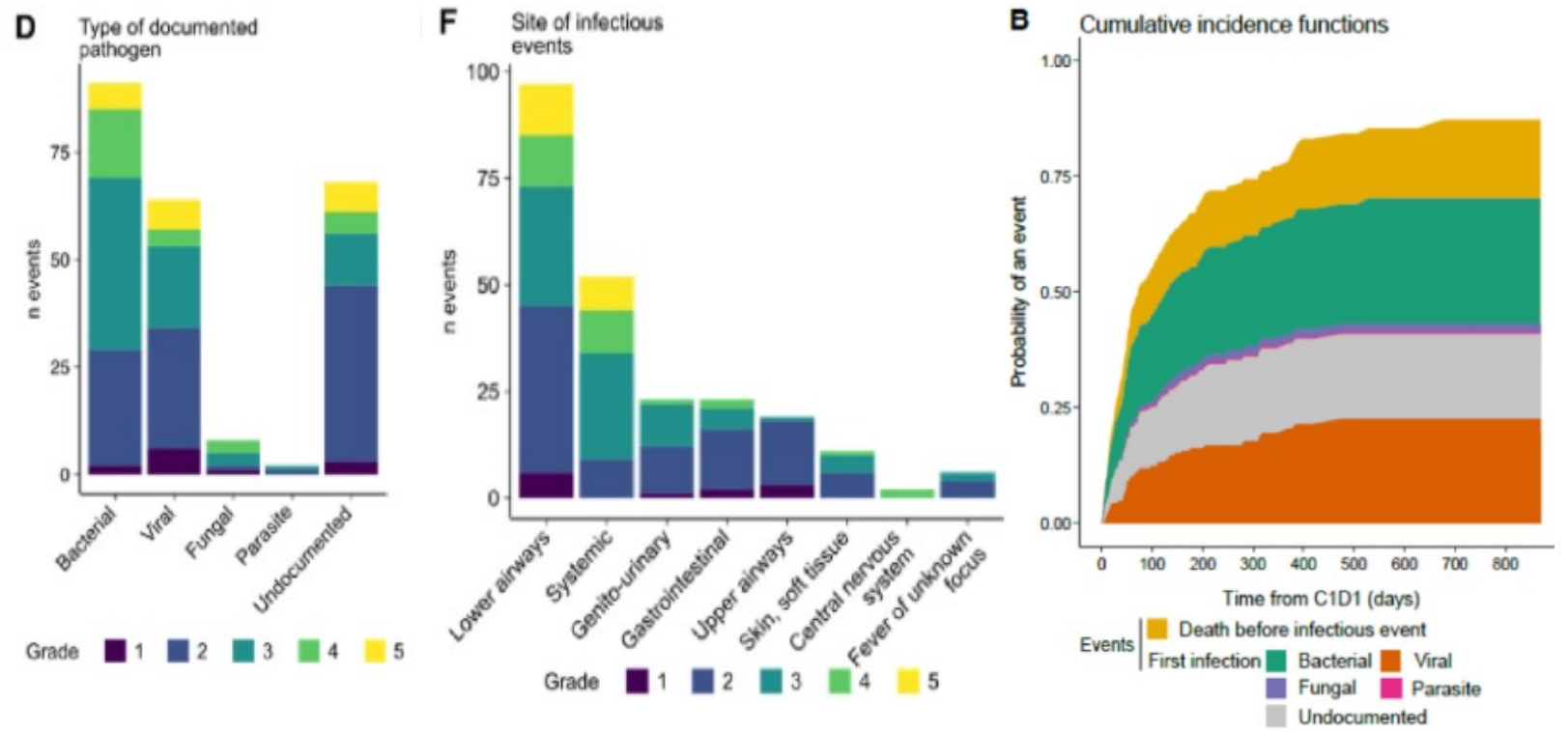
CMI CLINICAL MICROBIOLOGY AND INFECTION
ESCMID

Jourdes, CMI 2024 [in press]

Studio retrospettivo multicentrico

229 pazienti (Dicembre 2020- Febbraio 2023) trattati con BsAb per RR-MM (teclistamab: 152, elranatamab: 47; talquetamab: 29)

Outcome: incidenza e caratteristiche degli episodi infettivi che hanno richiesto ospedalizzazione



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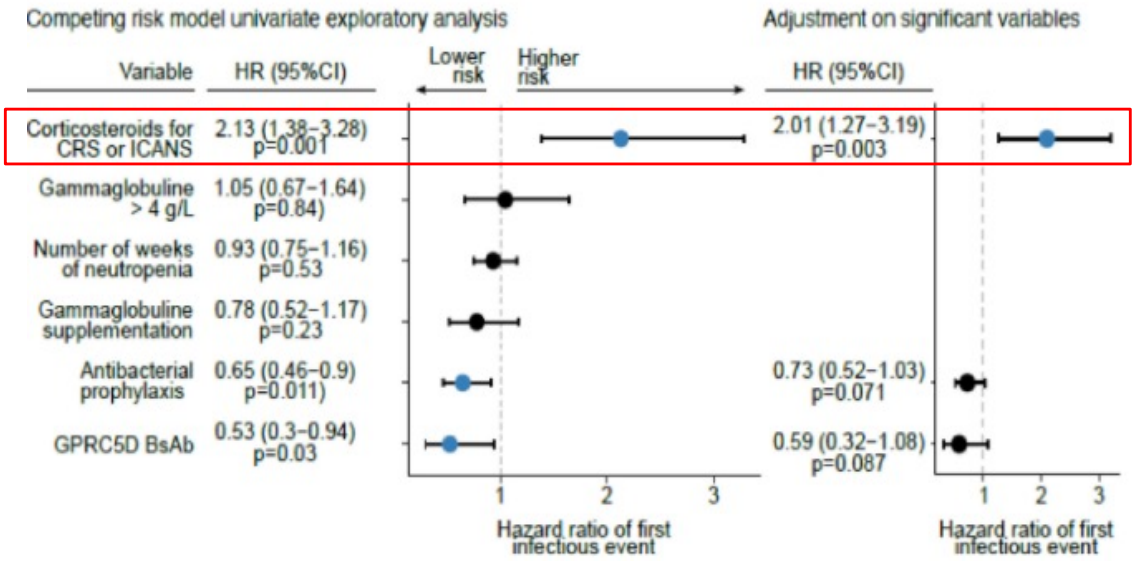
Jourdes, CMI 2024 [in press]

Table 2
Characteristics and grades of infections impacting patient management

Variables	Total (n = 234)
Site of infection, n (%)	
Systemic	52 (22)
Upper respiratory tract	19 (8)
Lower respiratory tract	97 (41)
Gastrointestinal tract	23 (10)
Genitourinary tract	23 (10)
Skin and soft tissue	11 (5)
CNS	2 (1)
Pathogens isolated[a], n (%)	n = 165
Bacterial	92/165 (56)
Enterobacteriaceae	48/165 (29)
Pseudomonas aeruginosa and other non-fermentative gram-negative bacteria	13/165 (7)
Anaerobic bacteria	11/165 (6)
Enterococci	6/165 (4)
Staphylococci	5/165 (3)
Streptococci[b]	4/165 (2)
Haemophilus influenzae	4/165 (2)
Neisseria	1/165 (1)
Viral	63/165 (38)
Respiratory viruses[c]	40/165 (24)
CMV	8/165 (5)
Enterovirus	3/165 (2)
HSV	2/165 (1)
VZV	2/165 (1)
Parvovirus B19	2/165 (1)
HBV	2/165 (1)
JC virus	2/165 (1)
Sapovirus	1/165 (1)
Adenovirus	1/165 (1)
Fungi	8/165 (5)
Aspergillus spp	6/165 (4)
Scedosporium spp	1/165 (1)
Pneumocystis jirovecii	1/165 (1)
Parasites	2/165 (1)
Toxoplasmosis	1/165 (1)
Giardiasis	1/165 (1)
Undocumented	69 (29)



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- ✓ Introduzione
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  - ➢ Entro i 28 gg
  - ➢ Oltre i 28 gg
- ✓ Rischio infettivo in pazienti trattati con anticorpi bispecifici
  - ➢ BsAbs per DLBCL
  - ➢ BsAbs per MM
- ✓ **Strategie di profilassi e management**

Infection (2021) 49:215–231
https://doi.org/10.1007/s15010-020-01521-5

REVIEW

Recommendations for screening, monitoring, prevention, and prophylaxis of infections in adult and pediatric patients receiving CAR T-cell therapy: a position paper

Ibai Los-Arcos[1,2] · Gloria Iacoboni[3,4] · Manuela Aguilar-Guisado[5] · Laia Alsina-Manrique[6] · Cristina Díaz de Heredia[7] · Claudia Fortuny-Guasch[8] · Irene García-Cadenas[9] · Carolina García-Vidal[10] · Marta González-Vicent[11] · Rafael Hernani[12] · Mi Kwon[13] · Marina Machado[14] · Xavier Martínez-Gómez[15] · Valentín Ortiz Maldonado[16,17] · Carolina Pinto Pla[18] · José Luis Piñana[19] · Virginia Pomar[20] · Juan Luis Reguera-Ortega[21] · Miguel Salavert[22] · Pere Soler-Palacín[23] · Lourdes Vázquez-López[24] · Pere Barba[3,4] · Isabel Ruiz-Camps[1,2]

Vaccination program

Antigens (vaccines)	Time after HSCT	Recommended interval between doses	Number of doses
Diphteria, tetanus and pertussis (DTPa-dTpa/tD)	6 months (dose 1) 7 months (dose 2) 8 months (dose 3) 18 months (dose 4)	1–2 months	4
Poliomielitis (PI)	6 months (dose 1) 7 months (dose 2) 8 months (dose 3) 18 months (dose 4)	1 month	4
Haemophilus influenza b (Hib)	6 months (dose 1) 7 months (dose 2) 8 months (dose 3) 18 months (dose 4)	1 month	4
Hepatitis B (HB)	6 months (dose 1) 7 months (dose 2) 8 months (dose 3) 18 months (dose 4)	1–2 months	4
Meningococcus (MACWY) (MB)	12 months (dose 1) 18 months (dose 2)	12 months (12 and 18 months)	2
Pneumococcus (PN13)	Sequential schedule:		
	PN13:	1–2 months	3
	3 months (dose 1) 4 months (dose 2) 5 months (dose 3)		1
(PN23)	PN23:	2 months after PN13	2
	12–24 months (dose 1) 5 years after first dose of PN23 (dose 2)		
Hepatitis A (HA)	6 months (dose 1) 12 months (dose 2)	6 months	2
Influenza	4–6 months (influenza season)	1 month in first time vaccination of patients younger than 9 years	1 (2 in first-time vaccination of patients younger than 9 years)
Papilloma virus (HPV)	12 months (dose 1) 13–14 months (dose 2) 18 months (dose 3)	1–2 months (between dose 1 and 2) 4 months (between dose 2 and 3)	3
Measles, mumps and rubella (MMR)	24 months (only if no immunosu-pression or graft versus host dis-ease are present and cell immunity is reconstituted) 24 months (dose 1) 25 months (dose 2)	1 month	2
Varicella (VZ)	24 months (only if no immunosu-pression or graft versus host dis-ease are present and cell immunity is reconstituted) 24 months (dose 1) 25 months (dose 2)	1 month	2

Spanish position paper, Infection 2021

DOI: 10.1002/cncr.35107

ORIGINAL ARTICLE

Incidence, timing, and management of infections in patients receiving teclistamab for the treatment of relapsed/refractory multiple myeloma in the MajesTEC-1 study

Ajay K. Nooka MD[1] | Cesar Rodriguez MD[2] | María Victoria Mateos MD, PhD[3] | Salomon Manier MD, PhD[4] | Katherine Chastain MD[5] | Arnob Banerjee MD, PhD[6] | Rachel Kobos MD[5] | Keqin Qi PhD[7] | Raluca Verona PhD[6] | Margaret Doyle MSc[8] | Thomas G. Martin MD[9] | Niels W. C. J. van de Donk MD, PhD[10]

Patients (*N* = 165) received subcutaneous teclistamab 1.5 mg/kg weekly
after a step-up dosing schedule (0.06 mg/kg and 0.3 mg/kg, each separated by 2–4 days).

Patients were enrolled between March 2020 and August 2021, and had RRMM (International Myeloma Working Group criteria)

Patients were monitored frequently for infections; prophylaxis and management were per institutional guidelines.

	Incidence	Timing	Prophylaxis and management	Recommendations
Infections in the overall MajesTEC-1 population	• 80.0% all grades • 55.2% grade 3/4 • 9.1% opportunistic • 3.0% discontinuations • 12.7% deaths	• Median time to first onset, 1.7 months (range, 0.0–24.7) for any-grade infections and 4.2 months (range, 0.0–34.6) for grade 3–5 infections • Highest incidence of grade 3/4 infections within first 2 months of starting teclistamab; infections of all grades occurred throughout	Baseline prophylaxis: • 68.5% antiviral (40.0% acyclovir, 29.1% valacyclovir, 0.6% entecavir, 0.6% ribavirin) • 32.1% PJP (29.1% sulfamethoxazole/trimethoprim, 1.8% atovaquone, 1.2% pentamidine) • 6.1% IgG replacement • 0.6% G-CSF (filgrastim) • 1.2% steroids (0.6% hydrocortisone, 0.6% prednisone)	• Before starting teclistamab, patients should be screened for HBV (HBsAg, anti-HBs, anti-HBc, HBV DNA), HCV (HCV RNA), and HIV. Follow local guidelines for baseline viral screening (e.g., CMV, EBV) • All patients initiating teclistamab should be up to date with vaccinations (i.e., COVID-19, influenza, VZV, and pneumococcal) • Teclistamab should not be given in patients with any active infections • Patients should be closely monitored across a range of infection types throughout teclistamab treatment and encouraged to actively report signs of infection and unexpected symptoms to facilitate prompt investigation and intervention, which may include temporary teclistamab interruption, to ensure infections fully resolve

Cancer 2024

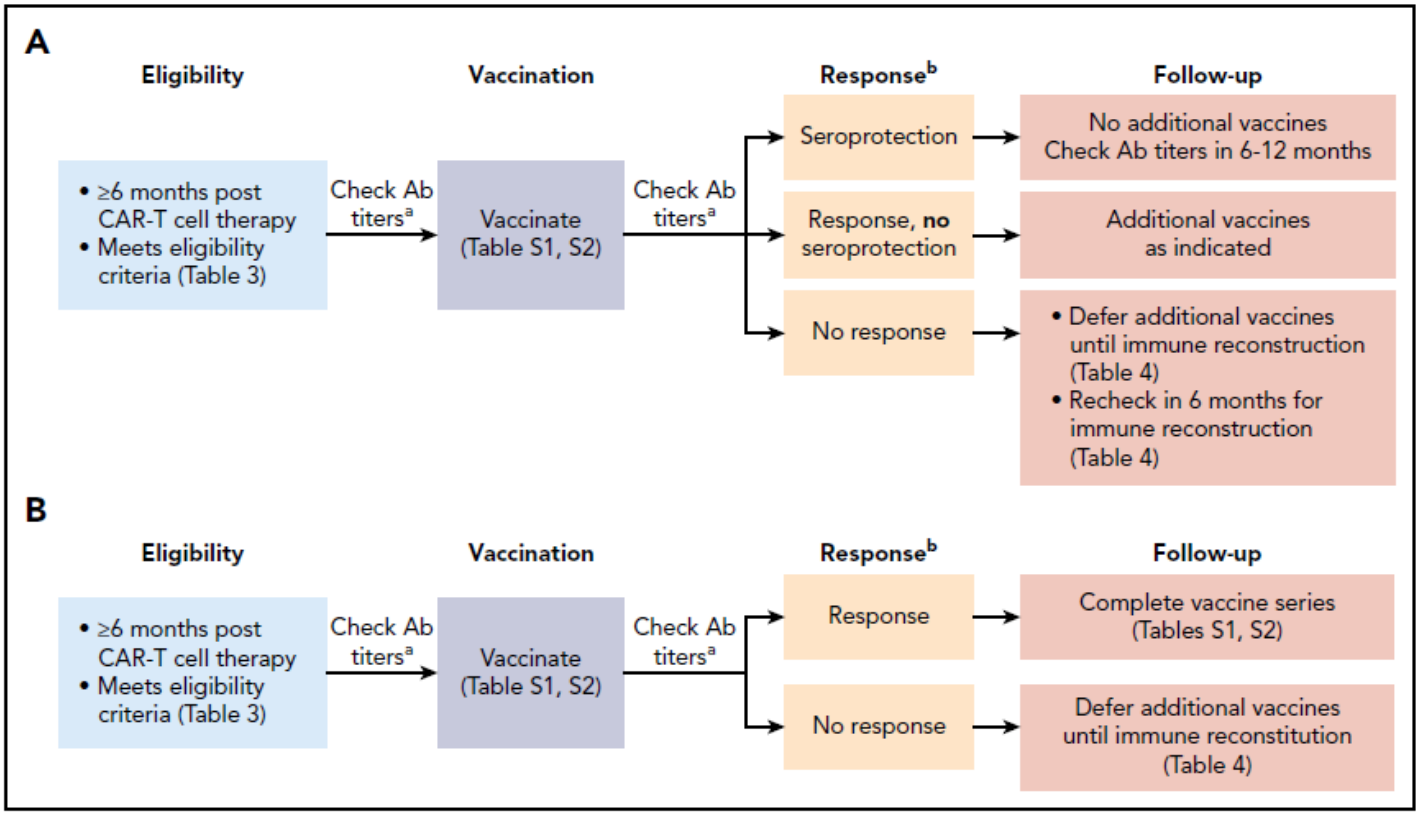
blood
How I Treat

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

Joshua A. Hill[1-4] and Susan K. Seo[5,6]

Table 3. Eligibility criteria for vaccinations after CD19-targeted CAR–T-cell therapy

Criteria for vaccinations
Indications*
Killed/inactivated vaccines†
• ≥6 mo post CD19-targeted CAR–T-cell therapy
• ≥2 mo since last immunoglobulin treatment; a trial off of supplemental immunoglobulins can be considered in patients without chronic or serious bacterial infections in the preceding 6 mo
Live and nonlive adjuvant vaccines
• ≥1 y post CD19-targeted CAR–T-cell therapy
Contraindications*
Killed/inactivated vaccines†
• Supplemental immunoglobulins within the past 2 mo
• Receiving immunosuppressive therapy that reduces T-cell or B-cell function or active symptoms of graft-versus-host disease that requires treatment
• Administration of an anti-CD20 or anti-CD19 agent within the past 6 mo
• Actively receiving chemotherapy‡
Live and nonlive adjuvant vaccines
• Administration of an anti-CD20 or anti-CD19 agent within the past 6 mo
• ≤1 y post CD19-targeted CAR–T-cell therapy
• ≤2 y post autologous or allogeneic HCT
• ≤1 y off all systemic immunosuppressive therapy
• ≤8 mo after last dose of supplemental immunoglobulins
• Absolute $CD4^+$ T-cell count ≤200 cells/mm^3
• Absolute $CD19^+$ or $CD20^+$ B-cell count ≤20 cells/mm^3
• Actively receiving chemotherapy‡



A: Possible vaccination approach in CD19-targeted CAR–T-cell therapy recipients who have no history of prior HCT or who completed post-HCT vaccines.
B: Possible vaccination approach in CD19-targeted CAR–T-cell therapy recipients who have a history of prior HCT and did not complete post-HCT vaccines

Hill JA, Blood 2020

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  - ➢ BsAbs per MM
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  - ✓ **Batteri**

Prevention and management of adverse events during treatment with bispecific antibodies and CAR T cells in multiple myeloma: a consensus report of the European Myeloma Network

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Bacterial infections

Prophylaxis
In patients with **high risk for infections** (eg, history of recurrent bacterial infections, prolonged neutropenia, or hypogammaglobinaemia): levofloxacin 250 mg twice a day or co-trimoxazole 800 mg/160 mg twice a day
In **patients with low IgG** (≤400 mg/dL) or history of recurrent bacterial infections intravenous IgG (400 mg/kg, every 2–4 weeks)

Treatment
Dependent on infectious agent, if identified **without neutropenia:** levofloxacin, amoxicillin calvulamate
Concomitant neutropenia: broad spectrum antibiotics, third generation cephalosporin (eg, ceftriaxone, cefotaxime, ceftazidime, or carbopenem [meropenem, imipenem-cilastatin]); vancomycin should be reserved for specific indications (MRSA, catheter infections, and others)

Lancet Oncol 2023; 24: e255–69

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Type of infection	Indication	Drugs and dosages (adults)	Drugs and dosages (children)	Duration
Bacterial infections	Routine prophylaxis not recommended			
Viral infections	HSV seropositive patients	Acyclovir 400-800 mg every 12 h po (or 5 mg/kg every 12 h iv)	Acyclovir OR: 20 mg/kg every 8 h (MD 800 mg every 12 h) IV: 250 mg/m^2 every 8 h;	At least 60–100 days after CAR T-cell infusion and even longer in high-risk patients (recent allogenic HSCT, steroid/tocilizumab therapy…)
Invasive fungal infections	Fluconazole in all cases and prophylaxis of filamentous fungi if two or more risk factors are present: 1. ≥ 4 prior treatment lines 2. Neutropenia (< 500mm^3) prior to the infusion 3. CAR-T doses > 2 × 10^7/kg 4. Previous IFI 5. Tocilizumab and/or steroids	Fluconazole 400 mg every 24 h For filamentous fungi: Posaconazole (tablets) 300 mg every 12 h on first day and then 300 mg once daily po Nebulized liposomal amphotericin B 24 mg once a week Micafungin 100 mg once daily	Fluconazole: 3–6 mg/kg (single daily dose) orally/iv (MD 400 mg) For filamentous fungi: Posaconazole oral solution: < 34 kg: 4 mg/kg every 6 h (first day) and 4 mg/kg every 8 h thereafter ≥ 34 kg: 200 mg every 6 h (first day) and 200 mg every 8 h thereafter ≥ 13 years (tablets) 300 mg every 12 h (first day) and 300 mg once daily thereafter Nebulized liposomal amphotericin B 24 mg once a week Micafungin—3–4 mg/kg 2 days a week (MD: 300 mg)	Until neutrophil recovery
Pneumocystis jirovecii	All cases	Trimethoprim sulfamethoxazole 800/160 mg three times pw or aerosolized pentamidine (300 mg) every 3–4 weeks	Cotrimoxazole 5 mg TMP/kg/day every 12–24 h 3 days a week orally (MD:160/800 mg) Pentamidine IV:4 mg/kg every 28 days (MD:300 mg)	1 week before the infusion and until CD4 count > than 200 cells/μL

Spanish position paper, Infection 2021

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  - ✓ **Batteri: no routine prophylaxis**

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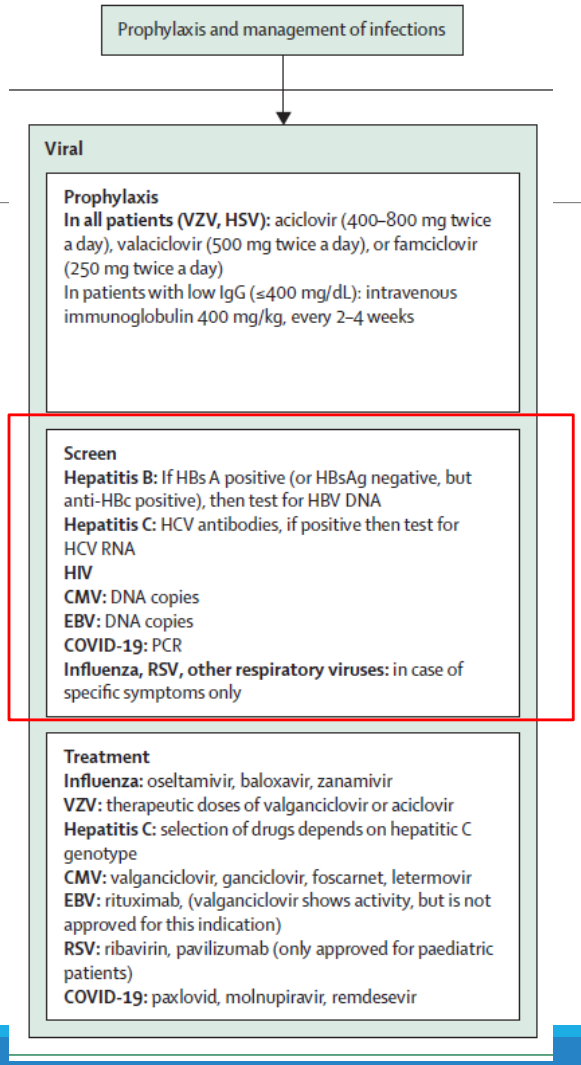

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Cancer 2024

HBV reactivation in HBsAg-positive patients treated with CAR-T-cell therapy

Studies evaluating HBV reactivation in HBsAg-positive patients treated with Chimeric antigen receptor–engineered (CAR) T-cell therapy

Reference	Study design	Country	Number of patients	NUC	Duration of ppx after CHT	Incidence HBV	Hepatitis flare	Death due to HBV reactivation	Median Follow-up
Cao, Blood 2020	Retrospective single-center study	China	ETV in 19	ETV in all	15.6 months	1 (5.3%)	1	0	NA
Fu, 2023	Retrospective single-center study	China	6 ETV 1 TDF	ETV in 6 TDF in 1	NA	1 (14.2%) in ETV	NA	NA	15.1 months (7.2-.24.8)
Wang 2020	Retrospective multi-center study	China	12	NUC not specified	NA	2 (16.7%)	0	0	10 months (3-24)
Liu, 2020	Retrospective single-center study	China	6	ETV in all	NA	0	0	0	NA
Yang C, 2020	Retrospective multi-center study	China	15	ETV in 11 TDF in 2 ADF in 1 LAM in 1	NA	3 (20%), 2 in ETV e 1 in TDF	0	0	NA
Cui, 2020	Retrospective single-center study	China	5	ETV in 3 TDF in 2	NA	0	0	0	NA

LMV: lamivudine; ETV: entecavir; TDF: tenofovir; ADF: adefovir; N.A. not available; CHT: chemotherapy; ppx: prophylaxis

AISF/SIMIT guidelines, In preparation

World Journal of Gastroenterology

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REVIEW

Prevention and management of hepatitis B virus reactivation in patients with hematological malignancies in the targeted therapy era

Joyce Wing Yan Mak, Alvin Wing Hin Law, Kimmy Wan Tung Law, Rita Ho, Carmen Ka Man Cheung, Man Fai Law

- Since there are a lack of prospective or retrospective studies on the risk of HBV reactivation in patients receiving **bispecific antibodies**, the real incidence of HBV reactivation is unclear.
- However, bispecific antibodies will profoundly suppress B-cell activity. These drugs are highly potent and the effect on B-cell depletion is expected to be significant.
- Therefore, we recommend antiviral prophylaxis against HBV in patients with either CHB and past resolved HBV infection.

Ref.	Indication for CAR-T	*N*	CHB, *n*	Past resolved HBV infection, *n*	Antiviral prophylaxis, % patients	Definition of HBV reactivation	Rate of HBV reactivation	HBV-related death
Prospective studies								
Liu *et al*[87], 2020	B-cell lymphoma	17	6	11	100% for CHB, and 45.5% for past infection (entecavir)	Elevation of HBV DNA levels to > 1000 IU/mL and/or HBsAg reverse seroconversion in HBsAg-negative patients	0	0
Yang *et al* [89], 2020	DLBCL	15	15	0	100% (lamivudine, entecavir, tenofovir, or adefovir dipivoxil)	Positive follow-up HBV-DNA test if the baseline HBV-DNA is undetectable/negative or > 10-fold increase from baseline	20%	0
Li *et al* [86], 2021	ALL, B-cell lymphoma	30	0	30	No prophylaxis	Elevation of HBV DNA ≥ 100 IU/mL for two consecutive measurements	6.6%	0
Wang *et al* [88], 2020	ALL, B-cell lymphoma, PCM	70	12	29	100% for CHB (entecavir, tenofovir disoproxil, or lamivudine). Nil for patients with past HBV infection	> 1 log increase in HBV DNA, HBV DNA-positive when previously negative, HBV DNA > 2000 IU/mL if no baseline level was available, or reverse sero-conversion from HBsAg-negative to positive	16.7% with chronic infection and 34.4 % with past infection	0
Retrospective studies								
Cao *et al*[83], 2020	ALL, NHL	89	19	37	100% for chronic infection, and 5.4% for past infection	100-fold increase in HBV DNA when compared with baseline or HBV DNA ≥ 10^3 IU/mL in a patient with a previously undetectable level or reverse seroconversion from HBsAg negative to HBsAg positive	5.3% for CHB	0
Han *et al*[85], 2020	Multiple myeloma	9	1	8	100% for CHB, 25% for past infection (lamivudine/entecavir)	HBsAg seroconversion or increase in HBV DNA levels by at least 10-fold or 1 × 10^9 copies/mL	12.5% for past infection	0
Cui *et al*[84], 2021	DLBCL, B-ALL	20	5	15	100% for CHB (entecavir or tenofovir), 13.3% for past HBV infection (entecavir)	For CHB: (1) ≥ 2 log increase in HBV DNA compared to the baseline level; (2) HBV DNA ≥ 3 log IU/mL in a patient with previously undetectable level; and (3) HBV DNA ≥ 4 log IU/mL if the baseline level is not available. For resolved HBV infection: HBV DNA is detectable; reverse HBsAg seroconversion	6.2% for past infection	0

WJG, 2023

HBV, HCV, HIV

- HBsAg-positive, patients with detectable HBV DNA load and patients: entecavir or tenofovir
- Patients with previous infection (HBsAg negative but anti-HBc-positive): Entecavir prophylaxis should be maintained for at least 6–12 months post-CAR T-cell infusion, or as long as the patient is on bsAbs
- Patients with HCV infection should be considered for DAA therapy
- There are no data for patients with HIV, as these were excluded from all trials

CMV, EBV

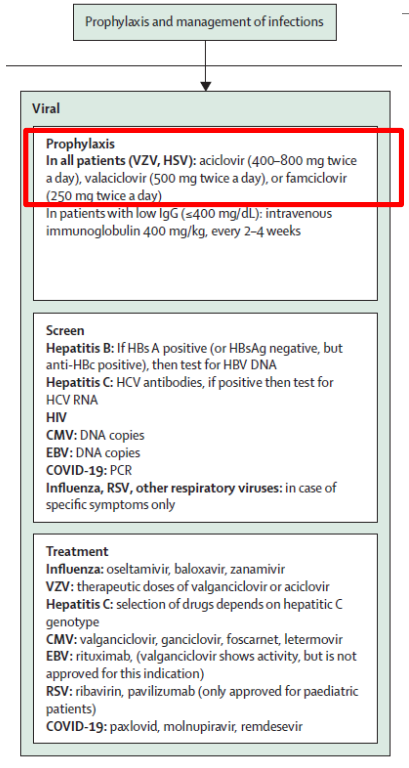
- Cytomegalovirus, Epstein-Barr virus reactivation might occur after and during treatment exposure, and testing for these pathogens should be considered depending on the patient's individual situation.
- For the diagnosis of viral infections, PCR testing of the sample in question should be used rather than serum antibody testing because many patients are unable to develop an antibody response.
- C-reactive protein and procalcitonin concentrations are also elevated in individuals with non-infectious causes of inflammation.

Outline

- ✓ Introduzione
- ✓ Rischio infettivo in pazienti trattati con CAR-T
  - ➢ Entro i 28 gg
  - ➢ Oltre i 28 gg
- ✓ Rischio infettivo in pazienti trattati con anticorpi bispecifici
  - ➢ BsAbs per DLBCL
  - ➢ BsAbs per MM
- ✓ **Strategie di profilassi e management**
  - ✓ Batteri
  - ✓ **Virus:** screening**, profilassi e trattamento**

Prevention and management of adverse events during treatment with bispecific antibodies and CAR T cells in multiple myeloma: a consensus report of the European Myeloma Network

Heinz Ludwig, Evangelos Terpos, Niels van de Donk, Maria-Victoria Mateos, Philippe Moreau, Melitios-Athanasios Dimopoulos, Michel Delforge, Paula Rodriguez-Otero, Jesús San-Miguel, Kwee Yong, Francesca Gay, Hermann Einsele, Roberto Mina, Jo Caers, Christoph Driessen, Pellegrino Musto, Sonja Zweegman, Monika Engelhardt, Gordon Cook, Katja Weisel, Annemiek Broijl, Meral Beksac, Jelena Bila, Fredrik Schjesvold, Michele Cavo, Roman Hajek, Cyrille Touzeau, Mario Boccadoro, Pieter Sonneveld



Lancet Oncol 2023; 24: e255–69

Infection (2021) 49:215–231
https://doi.org/10.1007/s15010-020-01521-5

REVIEW

Recommendations for screening, monitoring, prevention, and prophylaxis of infections in adult and pediatric patients receiving CAR T-cell therapy: a position paper

Ibai Los-Arcos[1,2] · Gloria Iacoboni[3,4] · Manuela Aguilar-Guisado[5] · Laia Alsina-Manrique[6] · Cristina Díaz de Heredia[7] · Claudia Fortuny-Guasch[8] · Irene García-Cadenas[9] · Carolina García-Vidal[10] · Marta González-Vicent[11] · Rafael Hernani[12] · Mi Kwon[13] · Marina Machado[14] · Xavier Martínez-Gómez[15] · Valentín Ortiz Maldonado[16,17] · Carolina Pinto Pla[18] · José Luis Piñana[19] · Virginia Pomar[20] · Juan Luis Reguera-Ortega[21] · Miguel Salavert[22] · Pere Soler-Palacín[23] · Lourdes Vázquez-López[24] · Pere Barba[3,4] · Isabel Ruiz-Camps[1,2]

Type of infection	Indication	Drugs and dosages (adults)	Drugs and dosages (children)	Duration
Bacterial infections	Routine prophylaxis not recommended			
Viral infections	HSV seropositive patients	Acyclovir 400-800 mg every 12 h po (or 5 mg/kg every 12 h iv)	Acyclovir OR: 20 mg/kg every 8 h (MD 800 mg every 12 h) IV: 250 mg/m^2 every 8 h;	At least 60–100 days after CAR T-cell infusion and even longer in high-risk patients (recent allogenic HSCT, steroid/tocilizumab therapy…)
Invasive fungal infections	Fluconazole in all cases and prophylaxis of filamentous fungi if two or more risk factors are present: 1. ≥ 4 prior treatment lines 2. Neutropenia (< 500mm^3) prior to the infusion 3. CAR-T doses > 2 × 10^7/kg 4. Previous IFI 5. Tocilizumab and/or steroids	Fluconazole 400 mg every 24 h For filamentous fungi: Posaconazole (tablets) 300 mg every 12 h on first day and then 300 mg once daily po Nebulized liposomal amphotericin B 24 mg once a week Micafungin 100 mg once daily	Fluconazole: 3–6 mg/kg (single daily dose) orally/iv (MD 400 mg) For filamentous fungi: Posaconazole oral solution: < 34 kg: 4 mg/kg every 6 h (first day) and 4 mg/kg every 8 h thereafter ≥ 34 kg: 200 mg every 6 h (first day) and 200 mg every 8 h thereafter ≥ 13 years (tablets) 300 mg every 12 h (first day) and 300 mg once daily thereafter Nebulized liposomal amphotericin B 24 mg once a week Micafungin—3–4 mg/kg 2 days a week (MD: 300 mg)	Until neutrophil recovery
Pneumocystis jirovecii	All cases	Trimethoprim sulfamethoxazole 800/160 mg three times pw or aerosolized pentamidine (300 mg) every 3–4 weeks	Cotrimoxazole 5 mg TMP/kg/day every 12–24 h 3 days a week orally (MD:160/800 mg) Pentamidine IV:4 mg/kg every 28 days (MD:300 mg)	1 week before the infusion and until CD4 count > than 200 cells/μL

Spanish position paper, Infection 2021

DOI: 10.1002/cncr.35107

ORIGINAL ARTICLE

Incidence, timing, and management of infections in patients receiving teclistamab for the treatment of relapsed/refractory multiple myeloma in the MajesTEC-1 study

Ajay K. Nooka MD[1] | Cesar Rodriguez MD[2] | María Victoria Mateos MD, PhD[3] | Salomon Manier MD, PhD[4] | Katherine Chastain MD[5] | Arnob Banerjee MD, PhD[6] | Rachel Kobos MD[5] | Keqin Qi PhD[7] | Raluca Verona PhD[6] | Margaret Doyle MSc[8] | Thomas G. Martin MD[9] | Niels W. C. J. van de Donk MD, PhD[10]

Patients (*N* = 165) received subcutaneous teclistamab 1.5 mg/kg weekly
after a step-up dosing schedule (0.06 mg/kg and 0.3 mg/kg, each separated by 2–4 days).

Patients were enrolled between March 2020 and August 2021, and had RRMM (International Myeloma Working Group criteria)

Patients were monitored frequently for infections; prophylaxis and management were per institutional guidelines.

	Incidence	Timing	Prophylaxis and management	Recommendations
Key viral infections (excluding COVID-19)[a]	• 12.1% overall[b] • 4.2% grade 3/4[b,c] • 0.6% deaths • 1.2% discontinuations	• Approximately half occurred within 6.6 months of starting teclistamab; continued to occur throughout (all grades) • Viral reactivation: - Adenoviral: 2.4 months - HBV: 3.5 months - CMV: 4.2 months • CMV viremia:[d] 1.2 and 10.7 months • Discontinuations: - Concurrent grade 3 adenoviral pneumonia and grade 3 PJP: 2.5 months - Grade 4 PML: 13.6 months • Death: - PML: 16.1 months	Antiviral use overall (prophylaxis and management): • 95.2% received ≥1 antiviral drug - Valacyclovir in 52.1%, acyclovir in 50.3% • Prophylaxis: • 93.3% received herpes prophylaxis overall (valacyclovir in 50.9%, acyclovir in 47.3%; most common doses [≥10% of patients] were valacyclovir 500 mg BID [32.1%], acyclovir 400 mg BID [26.1%], and valacyclovir 500 mg QD [12.7%]) - 3/3 HSV infections - 1/3 herpes zoster infections • 2/11 patients at risk of HBV reactivation (entecavir) - 0/1 patients with HBV reactivation on-study • Teclistamab interruption: • 2/5 parvovirus B19 infections • 2/5 adenovirus infections	• Prophylaxis for HSV/VZV is recommended in all patients during teclistamab treatment • Individual decisions on prophylaxis and management should be made in line with institutional guidelines and recommendations from other working groups[1,28,30–32] • May require teclistamab interruption[23,24] • Parvovirus B19, EBV and HHV6 may also need to be considered during teclistamab treatment (no cases of EBV or HHV6 observed in MajesTEC-1) • Monitor for CMV and adenovirus only in the presence of suspected symptoms or unexplained fever[32]
COVID-19 infections	• 29.1% overall • 21.2% grade 3/4[c] • 10.9% deaths • 1.2% discontinuations	• Occurred throughout teclistamab treatment (all grades) • Discontinuations: - Grade 3 COVID-19: 20.7 months - Grade 4 COVID-19: 16.4 months	Teclistamab interruption: • 29/48 COVID-19 infections • Supportive management: • 24.2% overall - 15.8% glucocorticoids - 10.3% monoclonal antibodies - 5.5% hyperimmune plasma	• All patients should be up to date with COVID-19 vaccinations, including booster doses • Management per institutional guidelines • May require teclistamab interruption[23,24]

Cancer 2024

Open Forum Infectious Diseases

REVIEW ARTICLE

Respiratory Viral Infections in Recipients of Cellular Therapies: A Review of Incidence, Outcomes, Treatment, and Prevention

Rita Wilson Dib,[1,2] Ella Ariza-Heredia,[2] Amy Spallone,[2] and Roy F. Chemaly[2]

[1]Department of Internal Medicine, Division of Infectious Diseases, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, Texas, USA, and [2]Department of Infectious Diseases, Infection Control and Employee Health, The University of Texas MD Anderson Cancer Center, Houston, Texas, USA

	EBMT/EHA (Europe)	Spanish group (Spain)	SFGM-TC (France)	Fred Hutch (US)	Dana Farber (US)	CHUV Lausanne (Switzerland)	LMU Munich (Germany)
Antibacterial prophylaxis	NR	NR	NR	FQ during neutropenia[a]	Levofloxacin 500 mg/day during neutropenia[a]	NR	Risk adapted[b]; FQ during neutropenia[a]
Antifungal prophylaxis	Consider fluconazole, posaconazole,[c] or micafungin if severe or prolonged >14 days neutropenia,[a] and/or long-term or high dose (>3 days) of steroids or post-allo-HCT	Fluconazole (400 mg/day) during neutropenia[a]	Consider fluconazole or micafungin if severe neutropenia[a] >14 days, steroids >3 days, post-allo-HCT	Fluconazole (200 mg/day) during neutropenia[a]	No antifungal prophylaxis	Fluconazole (200 mg/day) during neutropenia[a]	No antifungal prophylaxis
Anti-mold prophylaxis	See above	Posaconazole 300 mg/day,[c] nebulized liposomal amphotericin B or micafungin if ≥4 lines of prior treatment, pre-CAR-T-cell infusion severe neutropenia[a], higher dose of CAR-T-cells ($>2 \times 10^7$), previous IFI, tocilizumab, and/or steroids	Posaconazole (300 mg/day[c]) if post-allo-HCT or steroids or previous IFI	Posaconazole (300 mg/day[c]) if neutropenia[a] >20 days or steroids >3 days for at least 4 weeks after last dose of steroid (and after neutropenia resolution[a])	No anti-mold prophylaxis	Posaconazole (300 mg/day[c]) if post-allo-HCT or steroids or previous IFI	Risk-adapted[b] (posaconazole[c] or micafungin during neutropenia[a] or extended steroid exposure)
Anti-PjP prophylaxis	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for 1-year and until CD4 >200 cells/mm^3	TMP/SMX DS 3×/week Start 1 week pre-infusion (pause during neutropenia), continue until CD4 >200 cells/mm^3	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for 1-year and until CD4 >200 cells/mm^3	TMP/SMX DS 2×/day on 2 consecutive days/week Start 21–28 days post-infusion, continue for at least 6 months	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3	TMP/SMX 1DS 3×/week Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3
Antiviral prophylaxis	Acyclovir 800 mg 2×/day or valacyclovir 500 mg 2×/day Start at LD chemotherapy, continue for 1 year and until CD4 >200 cells/mm^3	Acyclovir 400–800 mg 2×/day At least 60–100 days after infusion	Acyclovir 800 mg 2×/day or valacyclovir 500 mg 2×/day Start at LD chemotherapy, continue for 1-year and until CD4 >200 cells/mm^3	Acyclovir 800 mg 2×/day or valacyclovir 500 mg 2×/day Start at lymphodepleting chemotherapy, continue for at least 1 year	Acyclovir 400 mg 3×/day or valacyclovir 500 mg 2×/day Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3	Valacyclovir 500 mg 2×/day for 6–12 months	Acyclovir 400 mg 2×/day Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3
CMV monitoring	As clinically indicated	NR	Consider in CMV seropositive patients at high risk Weekly monitoring	Patients treated with >3 days of steroids Weekly until 1 month after last dose of steroid	Strongly consider monitoring for patients receiving >5 doses dexamethasone	Consider in CMV seropositive patients at high risk Weekly/biweekly monitoring	NR
Preemptive threshold	–	NR		150 IU/mL (plasma)	None	None	None

Dib RW, Open Forum Infect Dis 2023

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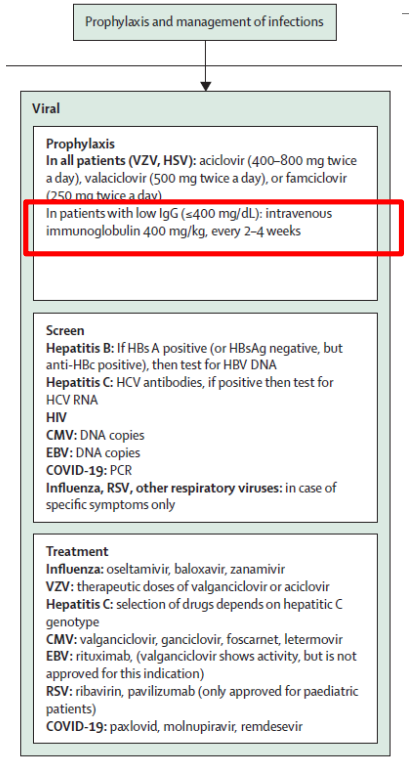

Lancet Oncol 2023; 24: e255–69

Infection (2021) 49:215–231
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REVIEW

Recommendations for screening, monitoring, prevention, and prophylaxis of infections in adult and pediatric patients receiving CAR T-cell therapy: a position paper

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Bacterial infections	Routine prophylaxis not recommended			
Viral infections	HSV seropositive patients	Acyclovir 400-800 mg every 12 h po (or 5 mg/kg every 12 h iv)	Acyclovir OR: 20 mg/kg every 8 h (MD 800 mg every 12 h) IV: 250 mg/m^2 every 8 h;	At least 60–100 days after CAR T-cell infusion and even longer in high-risk patients (recent allogenic HSCT, steroid/tocilizumab therapy…)
Invasive fungal infections	Fluconazole in all cases and prophylaxis of filamentous fungi if two or more risk factors are present: 1. ≥ 4 prior treatment lines 2. Neutropenia (< 500mm^3) prior to the infusion 3. CAR-T doses > 2 × 10^7/kg 4. Previous IFI 5. Tocilizumab and/or steroids	Fluconazole 400 mg every 24 h For filamentous fungi: Posaconazole (tablets) 300 mg every 12 h on first day and then 300 mg once daily po Nebulized liposomal amphotericin B 24 mg once a week Micafungin 100 mg once daily	Fluconazole: 3–6 mg/kg (single daily dose) orally/iv (MD 400 mg) For filamentous fungi: Posaconazole oral solution: < 34 kg: 4 mg/kg every 6 h (first day) and 4 mg/kg every 8 h thereafter ≥ 34 kg: 200 mg every 6 h (first day) and 200 mg every 8 h thereafter ≥ 13 years (tablets) 300 mg every 12 h (first day) and 300 mg once daily thereafter Nebulized liposomal amphotericin B 24 mg once a week Micafungin—3–4 mg/kg 2 days a week (MD: 300 mg)	Until neutrophil recovery
Pneumocystis jirovecii	All cases	Trimethoprim sulfamethoxazole 800/160 mg three times pw or aerosolized pentamidine (300 mg) every 3–4 weeks	Cotrimoxazole 5 mg TMP/kg/day every 12–24 h 3 days a week orally (MD:160/800 mg) Pentamidine IV:4 mg/kg every 28 days (MD:300 mg)	1 week before the infusion and until CD4 count > than 200 cells/μL

Spanish position paper, Infection 2021

blood
How I Treat

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

Joshua A. Hill[1-4] and Susan K. Seo[5,6]

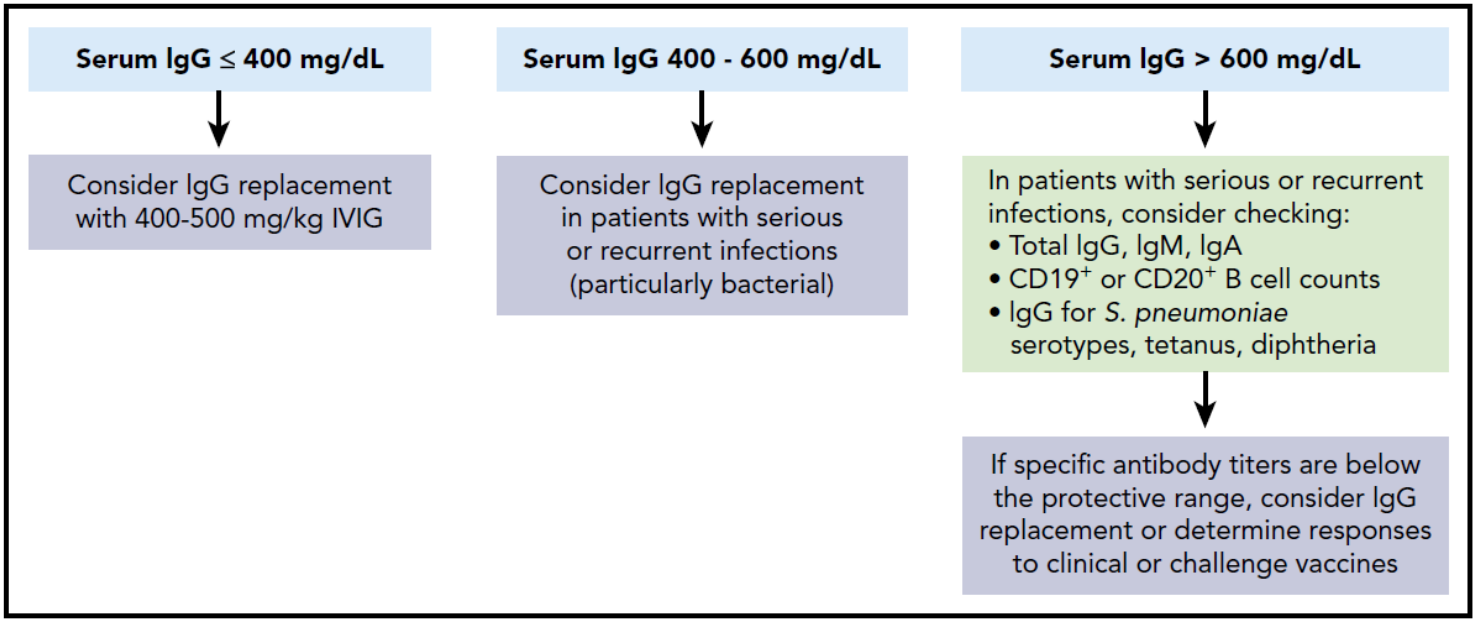

Figure 3. Indications for immunoglobulin replacement immediately prior to and for the first 3 months after CD19-targeted CAR–T-cell therapy. We suggest con-

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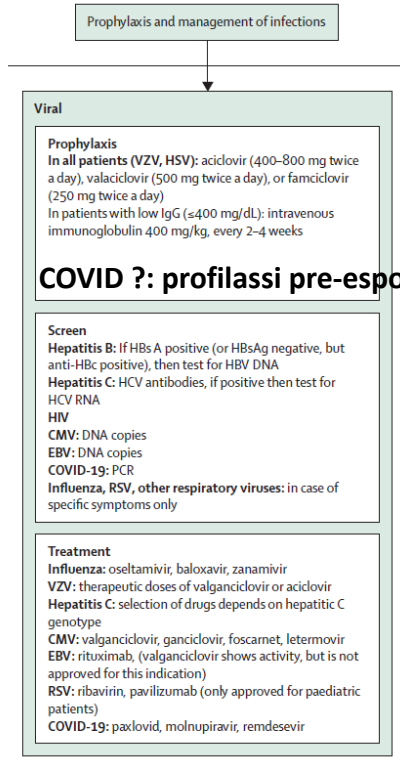

COVID ?: profilassi pre-esposizione

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Patients were enrolled between March 2020 and August 2021, and had RRMM (International Myeloma Working Group criteria)

Patients were monitored frequently for infections; prophylaxis and management were per institutional guidelines.

	Incidence	Timing	Prophylaxis and management	Recommendations
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Cancer 2024

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  - ✓ Batteri
  - ✓ Virus: screening, profilassi e trattamento
  - ✓ **miceti**

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Fungal infections

Prophylaxis
In patients with a **previous history of fungal infection, prolonged neutropenia, or glucocorticoid therapy**

Candidiasis: fluconazole 200–400 mg daily
Aspergillus: itraconazole or voriconazol 200 mg twice a day
***Pneumocystis jirovecii*:** co-trimoxazole 800 mg/160 mg once daily or three times per week

Treatment
Localised candidiasis: fluconazole
Invasive candidiasis: an echinocandin—eg, caspofungin
Aspergillosis: voriconazole, itraconazole
Pneumocystis pneumonia: co-trimoxazole, atovaquone, primaquine plus clindamycin

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REVIEW

Recommendations for screening, monitoring, prevention, and prophylaxis of infections in adult and pediatric patients receiving CAR T-cell therapy: a position paper

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Type of infection	Indication	Drugs and dosages (adults)	Drugs and dosages (children)	Duration
Bacterial infections	Routine prophylaxis not recommended			
Viral infections	HSV seropositive patients	Acyclovir 400-800 mg every 12 h po (or 5 mg/kg every 12 h iv)	Acyclovir OR: 20 mg/kg every 8 h (MD 800 mg every 12 h) IV: 250 mg/m^2 every 8 h	At least 60–100 days after CAR T-cell infusion and even longer in high-risk patients (recent allogenic HSCT, steroid/tocilizumab therapy…)
Invasive fungal infections	Fluconazole in all cases and prophylaxis of filamentous fungi if two or more risk factors are present: 1. ≥ 4 prior treatment lines 2. Neutropenia (< 500mm^3) prior to the infusion 3. CAR-T doses > 2 × 10^7/kg 4. Previous IFI 5. Tocilizumab and/or steroids	Fluconazole 400 mg every 24 h For filamentous fungi: Posaconazole (tablets) 300 mg every 12 h on first day and then 300 mg once daily po Nebulized liposomal amphotericin B 24 mg once a week Micafungin 100 mg once daily	Fluconazole: 3–6 mg/kg (single daily dose) orally/iv (MD 400 mg) For filamentous fungi: Posaconazole oral solution: < 34 kg: 4 mg/kg every 6 h (first day) and 4 mg/kg every 8 h thereafter ≥ 34 kg: 200 mg every 6 h (first day) and 200 mg every 8 h thereafter ≥ 13 years (tablets) 300 mg every 12 h (first day) and 300 mg once daily thereafter Nebulized liposomal amphotericin B 24 mg once a week Micafungin—3–4 mg/kg 2 days a week (MD: 300 mg)	Until neutrophil recovery
Pneumocystis jirovecii	All cases	Trimethoprim sulfamethoxazole 800/160 mg three times pw or aerosolized pentamidine (300 mg) every 3–4 weeks	Cotrimoxazole 5 mg TMP/kg/day every 12–24 h 3 days a week orally (MD:160/800 mg) Pentamidine IV:4 mg/kg every 28 days (MD:300 mg)	1 week before the infusion and until CD4 count > than 200 cells/μL

Spanish position paper, Infection 2021

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ORIGINAL ARTICLE

Incidence, timing, and management of infections in patients receiving teclistamab for the treatment of relapsed/refractory multiple myeloma in the MajesTEC-1 study

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Patients (*N* = 165) received subcutaneous teclistamab 1.5 mg/kg weekly
after a step-up dosing schedule (0.06 mg/kg and 0.3 mg/kg, each separated by 2–4 days).

Patients were enrolled between March 2020 and August 2021, and had RRMM (International Myeloma Working Group criteria)

Patients were monitored frequently for infections; prophylaxis and management were per institutional guidelines.

	Incidence	Timing	Prophylaxis and management	Recommendations
Fungal infections (excluding PJP)	• 5.5% overall • 0 grade 3/4[c] • 0 deaths • 0 discontinuations	• Most tended to occur with the first ~3 months	Most common antifungal medications overall (prophylaxis and management): • 7.9% fluconazole • 5.5% amphotericin B • 5.5% nystatin Teclistamab interruption: • 0/4 *Candida* infections • 1/1 *Aspergillus* infection	• Individual risk factors should be used to identify patients who may benefit from antifungal prophylaxis (steroid medication, elderly, frail, previous fungal infections, during neutropenia) • Individual decisions on prophylaxis and management should be made in line with institutional guidelines and recommendations from other working groups[1,28,30–32]
PJP infections	• 4.2% overall • 4.2% grade 3/4[c] • 0 deaths • 0.6% discontinuations	• Occurred between 2.5 and 7.8 months • Duration 8–60 days • Discontinuation: - Concurrent grade 3 adenoviral pneumonia and grade 3 PJP: 2.5 months	Most common PJP medications overall (prophylaxis and management): • 60.0% sulfamethoxazole/trimethoprim • 6.7% atovaquone • 3.6% pentamidine Prophylaxis: • 1/7 sulfamethoxazole/trimethoprim at time of infection • 2/7 atovaquone at time of infection • 2/7 stopped sulfamethoxazole/trimethoprim before infection	• Prophylaxis for PJP is recommended in all patients during teclistamab treatment. Alternatives to sulfamethoxazole/trimethoprim may need to be considered based on the potential risk of cytopenias or allergy • Individual decisions on prophylaxis and management should be made in line with institutional guidelines and recommendations from other working groups[1,28,30–32]

Cancer 2024

Open Forum Infectious Diseases

REVIEW ARTICLE

Respiratory Viral Infections in Recipients of Cellular Therapies: A Review of Incidence, Outcomes, Treatment, and Prevention

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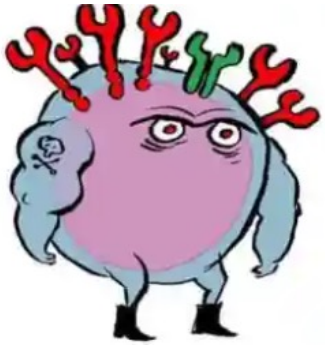
	EBMT/EHA (Europe)	Spanish group (Spain)	SFGM-TC (France)	Fred Hutch (US)	Dana Farber (US)	CHUV Lausanne (Switzerland)	LMU Munich (Germany)
Antibacterial prophylaxis	NR	NR	NR	FQ during neutropenia[a]	Levofloxacin 500 mg/day during neutropenia[a]	NR	Risk adapted[b]; FQ during neutropenia[a]
Antifungal prophylaxis	Consider fluconazole, posaconazole,[c] or micafungin if severe or prolonged >14 days neutropenia,[a] and/or long-term or high dose (>3 days) of steroids or post-allo-HCT	Fluconazole (400 mg/day) during neutropenia[a]	Consider fluconazole or micafungin if severe neutropenia[a] >14 days, steroids >3 days, post-allo-HCT	Fluconazole (200 mg/day) during neutropenia[a]	No antifungal prophylaxis	Fluconazole (200 mg/day) during neutropenia[a]	No antifungal prophylaxis
Anti-mold prophylaxis	See above	Posaconazole 300 mg/day,[c] nebulized liposomal amphotericin B or micafungin if ≥4 lines of prior treatment, pre-CAR-T-cell infusion severe neutropenia[a], higher dose of CAR-T-cells (>2 × 10^7), previous IFI, tocilizumab, and/or steroids	Posaconazole (300 mg/day[c]) if post-allo-HCT or steroids or previous IFI	Posaconazole (300 mg/day[c]) if neutropenia[a] >20 days or steroids >3 days for at least 4 weeks after last dose of steroid (and after neutropenia resolution[a])	No anti-mold prophylaxis	Posaconazole (300 mg/day[c]) if post-allo-HCT or steroids or previous IFI	Risk-adapted[b] (posaconazole[c] or micafungin during neutropenia[a] or extended steroid exposure)
Anti-PjP prophylaxis	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for 1-year and until CD4 >200 cells/mm^3	TMP/SMX DS 3×/week Start 1 week pre-infusion (pause during neutropenia), continue until CD4 >200 cells/mm^3	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for 1-year and until CD4 >200 cells/mm^3	TMP/SMX DS 2×/day on 2 consecutive days/week Start 21–28 days post-infusion, continue for at least 6 months	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3	TMP/SMX 1DS 3×/week (or SS 1×/day) Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3	TMP/SMX 1DS 3×/week Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3
Antiviral prophylaxis	Acyclovir 800 mg 2×/day or valacyclovir 500 mg 2×/day Start at LD chemotherapy, continue for 1 year and until CD4 >200 cells/mm^3	Acyclovir 400–800 mg 2×/day At least 60–100 days after infusion	Acyclovir 800 mg 2×/day or valacyclovir 500 mg 2×/day Start at LD chemotherapy, continue for 1-year and until CD4 >200 cells/mm^3	Acyclovir 800 mg 2×/day or valacyclovir 500 mg 2×/day Start at lymphodepleting chemotherapy, continue for at least 1 year	Acyclovir 400 mg 3×/day or valacyclovir 500 mg 2×/day Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3	Valacyclovir 500 mg 2×/day for 6–12 months	Acyclovir 400 mg 2×/day Start at LD chemotherapy, continue for at least 6 months or until CD4 >200 cells/mm^3
CMV monitoring	As clinically indicated	NR	Consider in CMV seropositive patients at high risk Weekly monitoring	Patients treated with >3 days of steroids Weekly until 1 month after last dose of steroid	Strongly consider monitoring for patients receiving >5 doses dexamethasone	Consider in CMV seropositive patients at high risk Weekly/biweekly monitoring	NR
Preemptive threshold	–	NR		150 IU/mL (plasma)	None	None	None

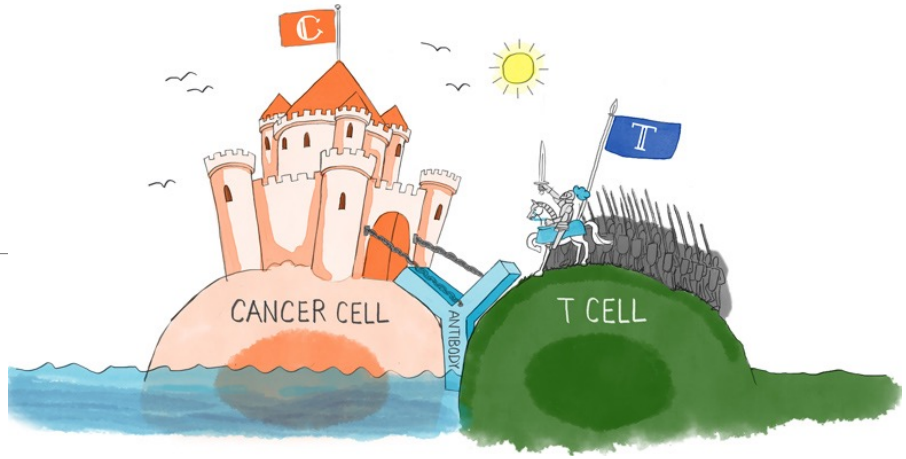
Dib RW, Open Forum Infect Dis 2023

Conclusions

- CAR-T therapy and bispecific antibody offers remarkable benefits
- Close monitoring, preventive measures, and timely management of infections are critical components of patient care during and after treatment
- Today, very few cornerstones are available:
  - screening for viral infections (HSV, HBV, HCV, HIV)
  - acyclovir prophylaxis
  - Pneumocystis jirovecii prophylaxis
- A lot of issues are again open
  - the time of vaccination
  - bacteria prophylaxis
  - acyclovir prophylaxis: in all or only in HSV positive subjects? Duration, for at least 2-3 months?
  - Duration of PJP prophylaxis, until CD4>200cells/ml?
  - fungal prophylaxis in none or in the presence of risk factors? Which?
  - COVID management
  - the role of immunoglobulin replacement



CAR-T cell



new challenges for old friends