27es JNI 2026 PARIS
et la région Île-de-France Palais des Congrès
Journées Nationales d'infectiologie
du jeudi 18 juin au samedi 20 juin 2026
Journée Nationale de Formation des Paramédicaux en Infectiologie
Vendredi 19 juin 2026

Infections après CAR-T cells et anticorps bispécifiques

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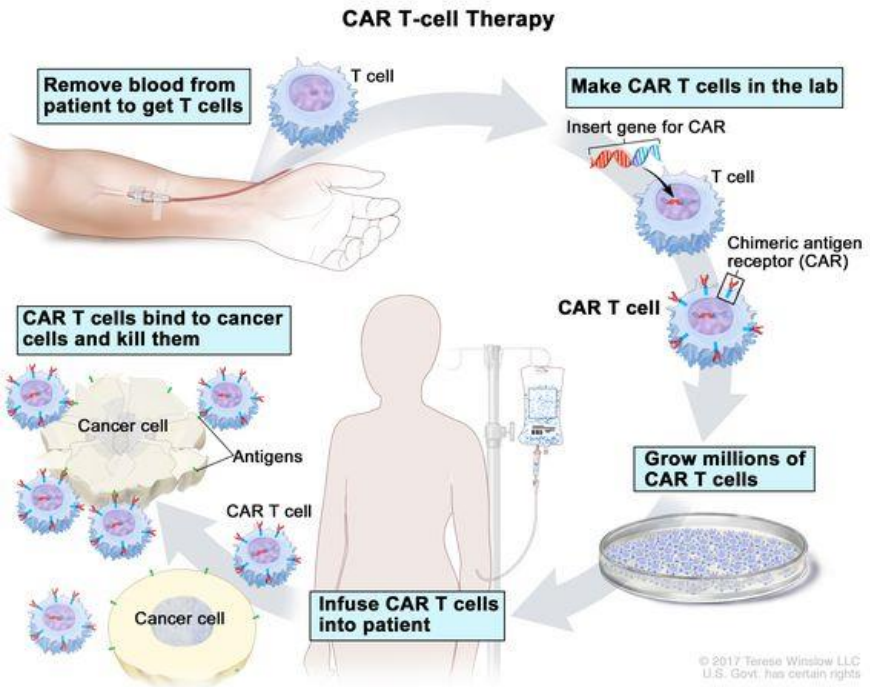
APHP, Hopital Henri Mondor

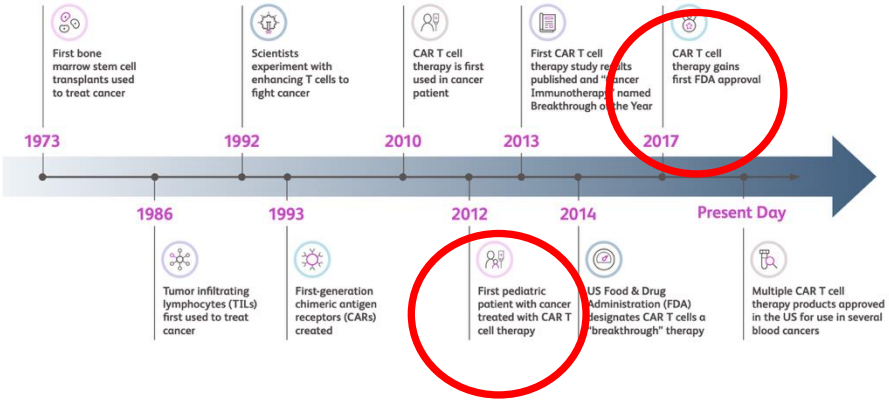
Déclaration d'intérêt de 2014 à 2025

- Intérêts financiers : non
- Liens durables ou permanents :non
- Interventions ponctuelles : AZ, MSD, Pfizer,Gilead, Moderna, GSK
- Intérêts indirects :non

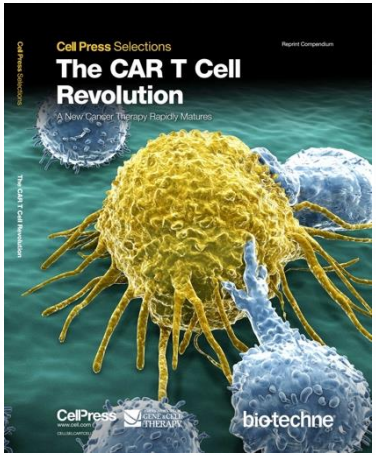
CAR-T cells

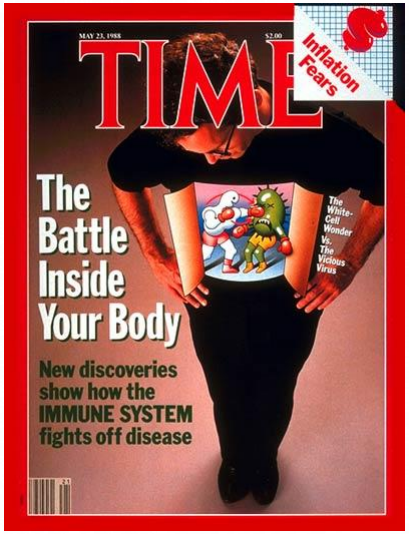


CAR-T (chimeric antigen receptor-T) cell = immunothérapie « vivante »



CAR-T cells





2016 → 2026

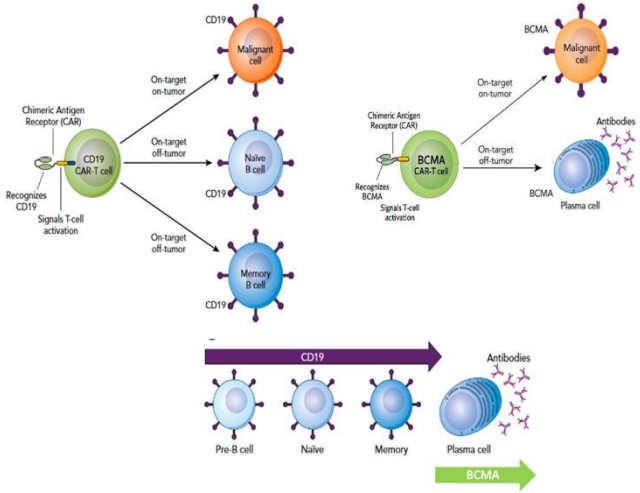
LAL, hémopathies B R/R
2eme ligne LNH B
Lymphomes indolents
Myélome multiple

Rémission complète (CR):

- 40-58% CD19 CAR
- 33-67% BCMA CAR

Immunodépression multifactorielle et dynamique

Effet on target-off tumor



[Adapted from : A. Hill et K. Seo, "How I prevent infections in patients receiving CD19-targeted chimeric antigen receptor T cells for B-cell malignancies". Blood, 2020.]

Chimiothérapie de lymphodepletion: **neutropénie**

Toxicité propre aux CART: CRS, ICANS

↓ Hematotoxicité retardée

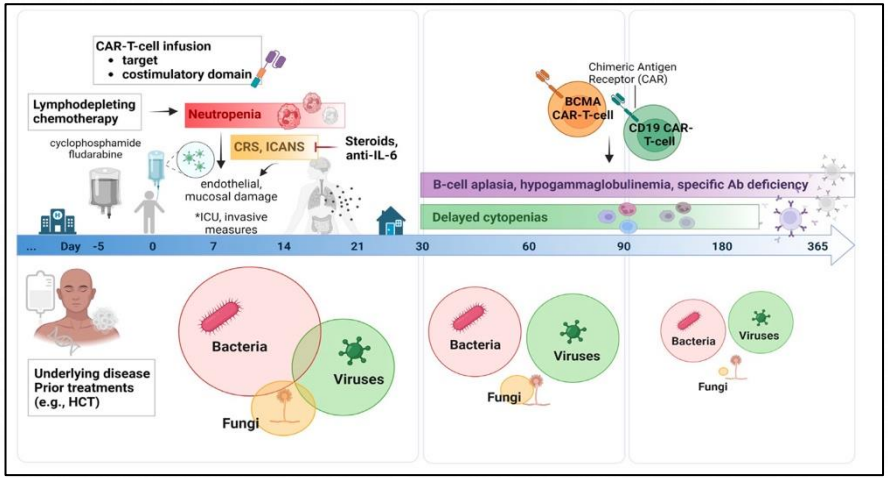
Tocilizumab, stéroïdes

↓

Neutropénie tardive

↑ risque infectieux

Timeline du risque infectieux

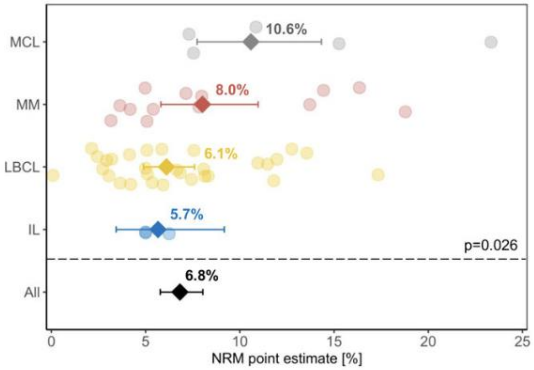


- ***Hemopathies B***
  - Incidence 30-60%
  - Infections précoces (< 30 j)
  - Infections bactériennes++
  - Peu d'IFI (4-7%), mortalité ↑

- ***Myelome multiple***
  - Incidence 58-69%
  - Infections bactériennes et virales++
  - Voies aériennes supérieures/inferieures
  - Peu d'IFI < 5%

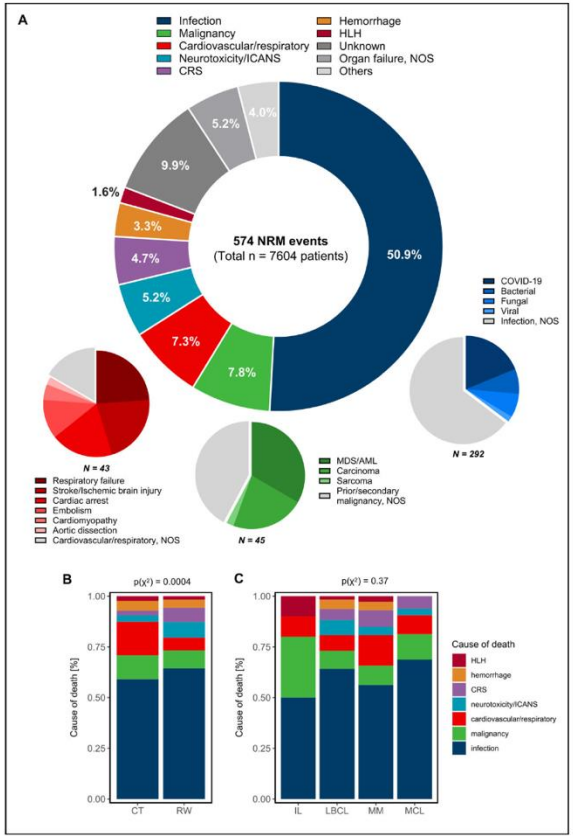
Dizman JTExpert Rev Anti Infect Ther 2022 Nov;20(11):1455-1476; Kambhampati S, Blood Adv 2022; Reynolds GK, Crit Rev Oncol Hematol. 2023;

Infection: principale cause de la mortalité non liée à la rechute après CART



7600 patients
18 CT
28 études vie réelle

NRM dépends du type de produit/maladie de fond

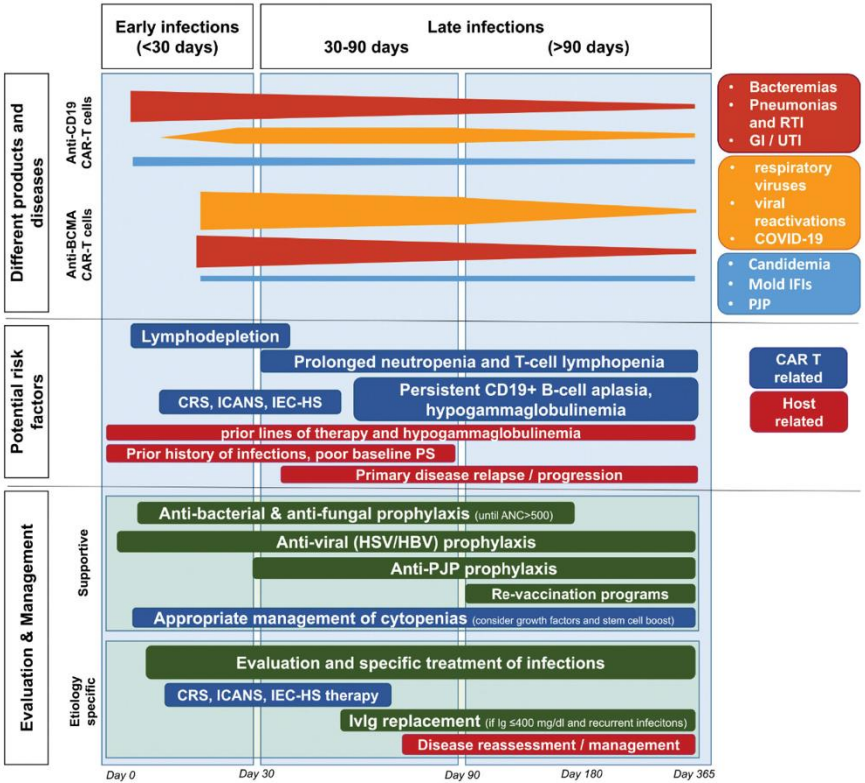


Infection= 50% de la NRM vs CRS+ICANS=9.9%

Poids de la pandémie Covid 19, update nécessaire

Lemoine J, Blood Adv 2023;Cordas Dos Santos D, Nat Med 2024

Facteurs de risque d'infection après CAR-T cells



Etudes rétrospectifs, souvent monocentriques, faibles effectifs

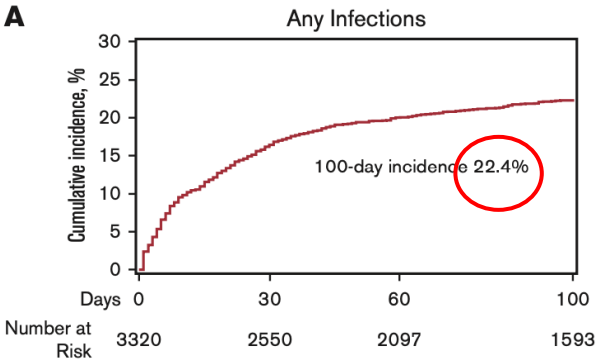
Facteurs de risque

- Liés au patient
- Liés au traitement et à ses complications
- Pre/post infusion
- Variables au cours du temps

→ reconstitution T et B cellulaire

Telli Dizman G, Exp Rev Anti Infect Ther 2022; Shaid Z, TCT 2024

CD19 CART: registre CIBMTR



	N	Hazard Ratio	95% CI
Infection Related Mortality, Day 0-100			
Age (decades)	3320	1.628	(1.186, 2.234)
KPS: 90-100	1350	1	-
KPS:80	982	6.179	(1.781, 21.433)
KPS:<80	635	14.306	(4.244, 48.266)
Baseline infection history in HCT-CI: No	3018	1	-
Baseline infection history in HCT-CI: Yes	132	3.92	(1.598, 9.615)
Grade 3-5 CRS Onset: No		1	-
Grade 3-5 CRS Onset: Yes		3.734	(1.996, 6.986)

Individualiser des patients a haut risque infectieux

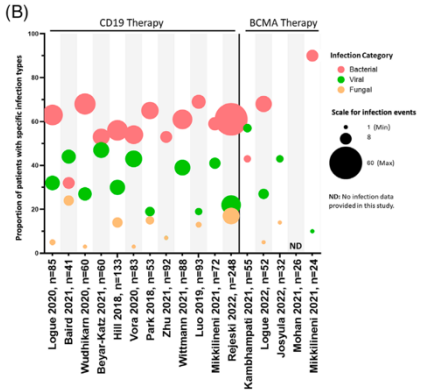
3350 pts 2017-2022
58%> 65 ans
12% des patients
décèdent d'une infection

Overall Survival, Day 100-365			
Infection post CAR-T cell: None	743	1	-
Infection post CAR-T cell: Days 1-30 and 31-100	50	1.976	(1.491, 2.618)

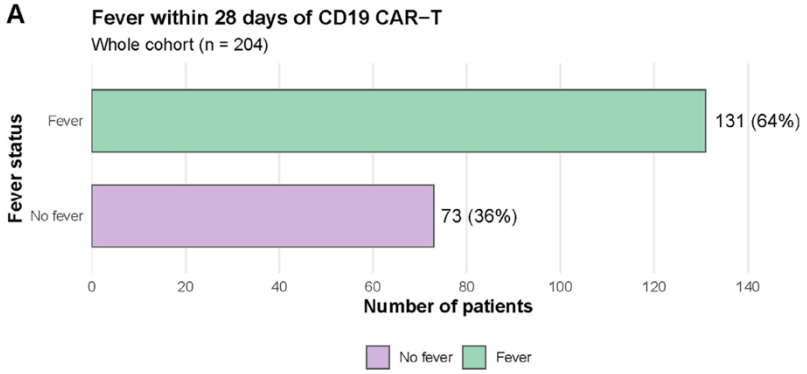
Infection: FdR indépendant de mortalité globale (expression du dérèglement immunitaire persistant?)

Wudikharn K, Blood Adv 2025

CD19 CART : infections bactériennes precoces Prophylaxie?



Infections bactériennes 1er étiologie précoce: 32-68%



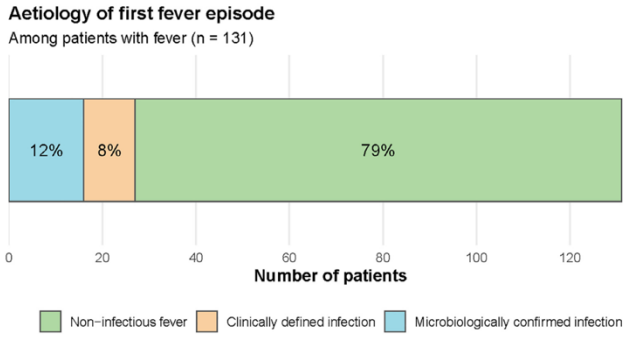
Fièvre dans les premiers 30 jours après l'infusion= 64%
20% documentée ou suspicion clinique d'infection
Bactériémie 7/204 (3.4%)

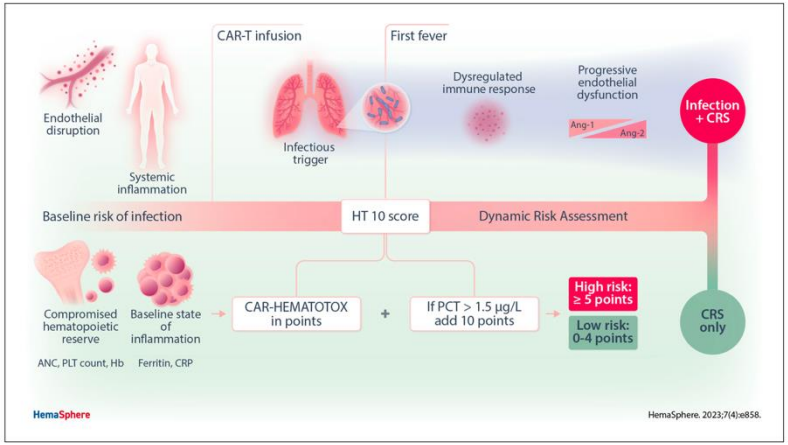
Pas de place pour la prophylaxie antibiotique

Shaid Z, TCT 2024; Kampouri E, Transplant Infect Dis 2023; Reynolds G, TCT 2024

CD19 CART : signature biologique CRS vs infection?

Overlap CRS- infection précoce

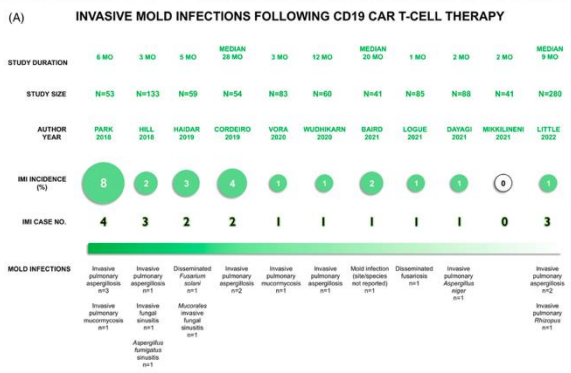


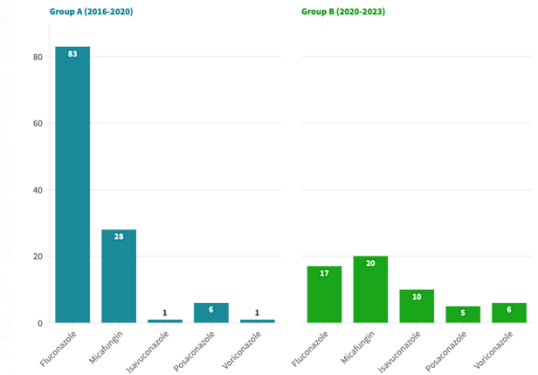


→ Infections précoces+ patient neutropénique: antibiothérapie large spectre/désescalade/arrêt si stabilité clinique et apyrexie

Reynolds G, TCT 2026; Rejeski K, Hemasphere 2023

CD19 CART: infections fongiques invasives





Infections rares
Mortalité élevée
Pas de place pour une prophylaxie systématique

- Toxicité, interactions
- Résistances

Variable	Univariate HR (95% CI)	Univariate p	Multivariate HR (95% CI)	Multivariate p
Age at treatment decision	1.05 (1.01–1.08)	0.02	1.05 (1.01–1.09)	0.02
Performance status at lymphodepletion (0-1 vs. ≥ 2)	0.36 (0.15–0.86)	0.02		
No. of prior treatment lines	1.37 (1.15–1.64)	<0.01	1.33 (1.09–1.64)	0.01
At least one prior allogenic transplant	5.32 (1.61–17.51)	0.01	8.38 (2.17–32.36)	<0.01
CRS	5.47 (0.75–40.06)	0.09		
ICANS	2.79 (1.34–5.78)	0.01	1.76 (0.81–3.85)	0.15
Macrophage activation syndrome	4.37 (1.04–18.42)	0.04		
Anti-IL-1 treatment received	6.02 (2.32–15.64)	<0.01	2.9 (1.07–7.86)	0.04
Anti-IL-6/anti-IL-6 receptor treatment received	3.81 (1.47–9.89)	0.01	2.44 (0.9–6.64)	0.08
Corticosteroids treatment received	2.92 (1.41–6.05)	<0.01		
Neutropenia	1.92 (0.83–4.44)	0.13		
G-CSF	2.41 (1.11–5.21)	0.03		
Gamma globulin administered	2.36 (1.04–5.39)	0.04		
Bacterial infection	6.06 (2.8–13.09)	<0.01	4.61 (2.11–10.06)	<0.01
Viral infection	2.86 (1.38–5.94)	<0.01		

Prophylaxie individualisée selon les facteurs de risque

Kampouri E, Transplant Infect Dis 2023; Melica G, TCT 2024; Bouvier A, CMI 2025

BCMA CART

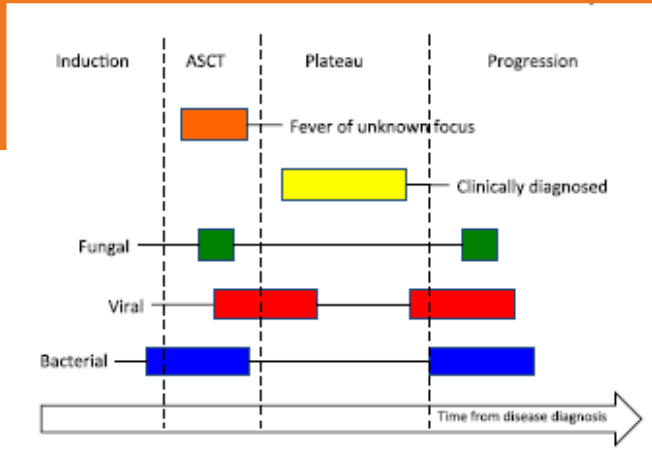
Risque infectieux ↑
Avant-après

Hypogamma (CART, bispe, dara)
Neutropenie (CART, bispe, dara)
Lymphopenie(CART, bispe, dara)
↑ **cytokines** (CART, bispe)

	Daratumumab[a]	Isatuximab[a]	Anti-BCMA CAR T	All BsAbs	Anti-BCMA BsAb	Anti-GPRC5D BsAb	Belantamab mafadotin^
				All infections			
All grade infections	13%–85% [54,55]	23% [28]	26%–58% [46,50]	38%–90% [56,57]	72% [58]	47% [58]	2%–14% [59,60]
Grade ≥3 infections	10%–35% [26,61]	19% [28]	8%–79% [36,62]	41%–55% [56,63]	ND	ND	1%–7% [59,60]
				Infections by pathogen[b]			
Viral	29%–57% [26,64]	ND	18%–68% [46,48]	38%–58% [56,65]	41%–43% [66,67]	43% [58]	ND
Bacterial	18%–41% [26,64]	ND	22%–74% [35,62]	39%–56% [56,65]	46%–56% [58,67]	46% [58]	ND
Fungal	3%–8% [26,64]	ND	2%–9% [35,51]	0%–11% [56,67]	5%–11% [66,67]	11% [58]	ND
Parasitic	1% [57,64]	ND	ND	1% [65]	ND	ND	ND
				Infection by site[c]			
Respiratory	23%–54% [26,27]	ND	63%–71% [46,48]	33%–58% [63,67]	51%–58% [66,67]	ND	ND
Bloodstream infection	8% [26]	ND	2%–9% [36,46]	22%–27% [63,65]	ND	ND	ND
Gastrointestinal tract	ND	ND	9%–11% [46,48]	7%–10% [56,65]	8% [67]	ND	ND
Other (including urinary tract, skin and soft tissue)	3%–17% [26,54]	ND	5%–30% [36,48]	11%–30% [63,67]	30% [67]	ND	ND
				Other risk factors for infection			
Neutropenia	26%–75% [26,27]	65% [29]	41%–98% [36,62]	17% [65]	17% [65]	20% [65]	8%–12% [68,69]
Lymphopenia	40%–59% [26,54]	ND	98%–100% [36,51]	ND	ND	ND	ND
CRS	NA	NA	81%–89% [36,62]	51%–72% [56,63]	53% [66]	ND	NA
Hypogamma-globulinaemia	ND	ND	88% [51]	28%–87% [56,66]	ND	ND	ND

Liu A, Leuk Lymphoma 2025

Myelome Multiple et risque infectieux



- Immunosénescence et comorbidités
- Hypogammaglobulinemie et déficit fonctionnel B
- Lymphopénie T (corticoïdes)
- Déficit immunité innée (IMIDs)
- Déficit Th1, MHC II-présentation antigénique (inhibiteurs du protéasome)
- Activité CTL réduite avec inhibiteurs protéasome

	Total			Suivi à 1 an		
	Myélome (n9253)	Contrôle (n=34931)	Hazard ratio (IC 95%)	Myélome	Contrôle	Hazard ratio (IC 95%)
Tout type Infection	3781	6519	7,1 (6,8-7,4)	1626	672	11,6 (10,6-12,7)
Infections bactériennes	3361	5792	7,1 (6,8-7,4)	1388	574	11,5 (10,4-12,7)
Pneumopathie	2150	3504	7,7 (7,2-8,1)	770	279	12,7 (11(1-14,6
Ostéomyélite	37	100	3,5 (2,4-5,2)	19	12	6,9 (3,4-14,3)
Septicémie	1336	960	15,6 (14,3-17,1)	464	69	29,9 (23,2-38,6)
Pyélonéphrite	152	570	2,9 (2,4-3,5)	50	51	4,3 (2,9-6,4)
Cellulite	164	564	3 (2,5-3,6)	47	58	3,7 (2,5-5,4)
Méningite	51	28	16,6 (10,2-27,1)	12	3	17,3 (4,9-61,3)
Endocardite	35	73	5,3 (3,4-8,1)	12	6	8,7 (3,3-23,1)
Infections virales	607	556	10 (8,9-11,4)	215	54	17,6 (13,1-23,8)
Grippe	150	245	6,1 (4,9-7,6)	52	22	10,5 (6,4-17,3)
Zona	282	171	14,8 (12,1-18,2)	92	16	25,8 (15,2-43,8)

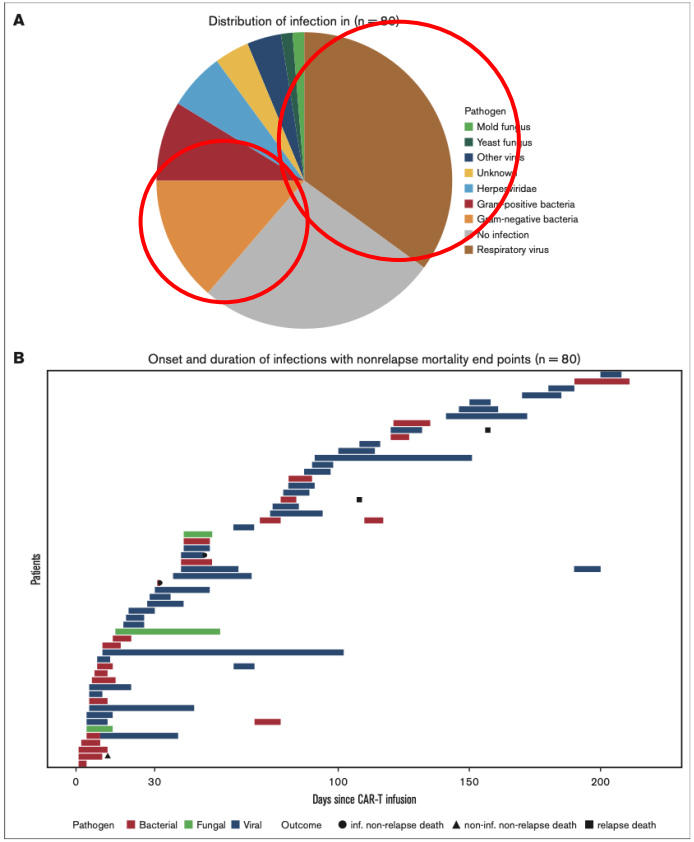
Cohorte observationnelle suédoise des infections chez 9259 MM patients diagnostiqués 1988-2004 et suivis jusqu'à 2007

Blimark C. et al. Haematologica 2015; Teh BW, Br J Haematol 2015

Risque infectieux BCMA CART

Summary of microbiologically confirmed infections (bacterial, viral, fungal).

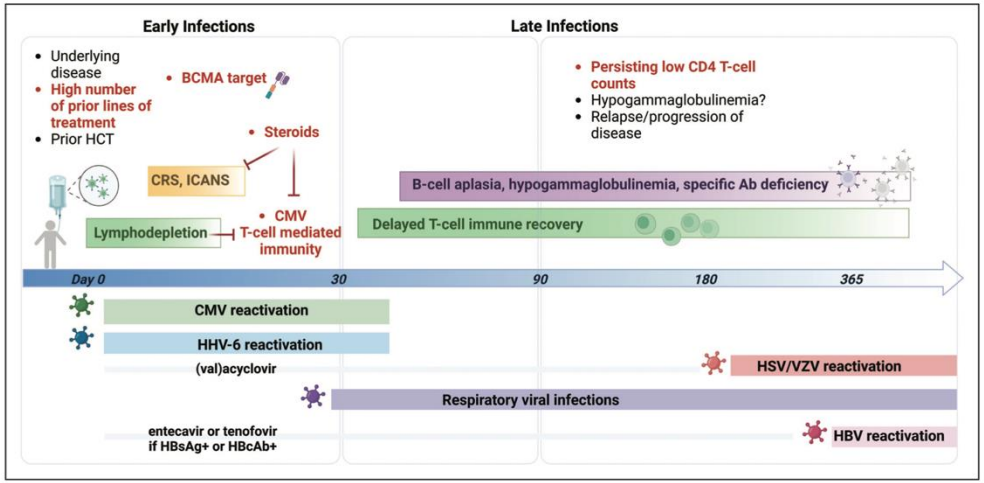
	Non Hodgkin's Lymphoma N (%)	Acute Lymphoblastic Leukaemia N (%)	Multiple Myeloma N (%)	Chronic Lymphocytic Leukaemia N (%)
Incidence of microbiologically confirmed infections amongst CAR-T treated patients, as defined by the studies				
Included Patients	1487	256	265	41
Total Infection Events	834	141	187	24
Incidence	0.56 events / treated patient	0.55 events / treated patients	0.7 events / treated patients	0.58 events / treated patients
	N (% of events)	N (% of events)	N (% of events)	N (% of events)
Bacterial Events	414 (50)	89 (63)	89 (48)	14 (58)
Viral Events	318 (38)	37 (26)	80 (43)	8 (33)
Fungal Events	78 (9)	15 (11)	18 (9)	2 (8)



Virus (respiratoires++)
Bacteries (bacilles G-) tôt après infusion (neutropénie)
Site clinique: poumon

Richardson T, Blood Adv 2025; Reynolds G, Crit Rev Oncol Hematol 2023

CMV



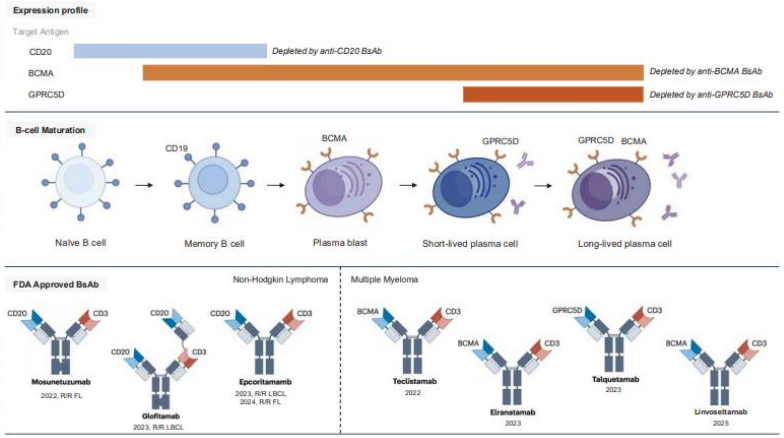
Réactivation CMV après CART

- 46% BCMA
- 23% CD19

Réactivations fréquentes et précoces
Fdr: corticoïdes
Maladie CMV rare
Stratégie préemptive: 6 semaines
Effets indirects: mortalité et impact sur la rechute

Kampouri E, Curr Op Infect Dis 2024

Anticorps bispécifiques



MajesTEC-1: Study of Teclistamab (BMCA x CD3) in RRMM (key efficacy and safety data)

MajesTEC-1 phase I/II

Patients	N=165
Median Age	64 (33-84)
High-risk cytogenetics*, %	25.7
EMD, %	17%
Median prior LOT, n	5 (2-14)
Triple-class exposed/refractory, %	100/77.6

Patients (N=165)

Efficacy	N=165
ORR, %	63
≥VGPR	58.8
mDOR (n=71), months	18.4 (14.0-NE)
mPFS, months	11.3 (8.8-17.1)
mOS (n97), months	18.3 (15.1-NE)

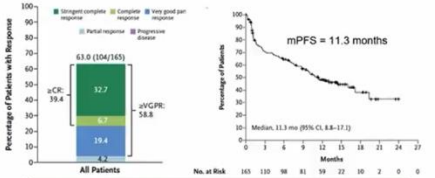
Efficacy

Adverse events, %	All grades	G3/4
Infection	76.4	44.8
CRS	72.1	0.6
Neurotoxicity	14.5	0.6
Neutropenia	70.9	64.2
Anemia	52	37

Safety

*t(4;14), t(14;16), del17p

- 165 patients treated at the RP2D 1.5 mg/kg sc QW
- Treatment until disease progression
- Median follow-up 14.1 months



- 19 patients died from AEs, including 12 deaths due to COVID-19
- 123 patients (74.5%) had evidence of hypogamma-globulinemia

AEs: adverse events; CR: complete response; CRS: cytokine release syndrome; EMD: extramedullary disease; LOT: lines of therapy; mDOR: median duration of response; mOS: median overall survival; mPFS: median progression free survival; ORR: overall response rate; RP2D: recommended phase 2 dose; RRMM: relapsed/refractory MM; VGPR: very good partial response

Moreau P et al. NEJM 2022; 367:495-50

Procédé plus simple que pour CAR
Durée de traitement ↑

+ Infections sévères vs CART (clinical trials, vie reelle)

Courtesy of Dr K Belhadj

Risque Infectieux et Ac Bispécifiques

1185 patients MM
542(50%) épisodes infectieux
272(24,5%) infection grade > 3
Hypogammaglobulinémie (4 etudes) 75%
Infections sévères> anti BCMA

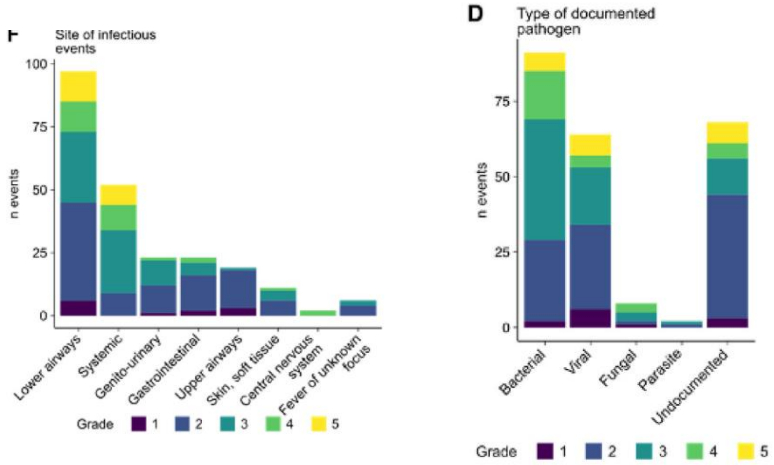
Mazahreh F et al.Blood Adv. 2023

229 patients
234 infections
123(53%) infections > grade 3
Infections respiratoires 50%
Corticoïdes HR 2,13 (1,38-3,28)

Jourdes A, CMI 2024

Infections 40-80%
Incidence poolée 44% LNH, 54% MM
Grade > 3=25%
Infections bactériennes=virales
Fongiques: PJP
Risque infectieux stable vs temps

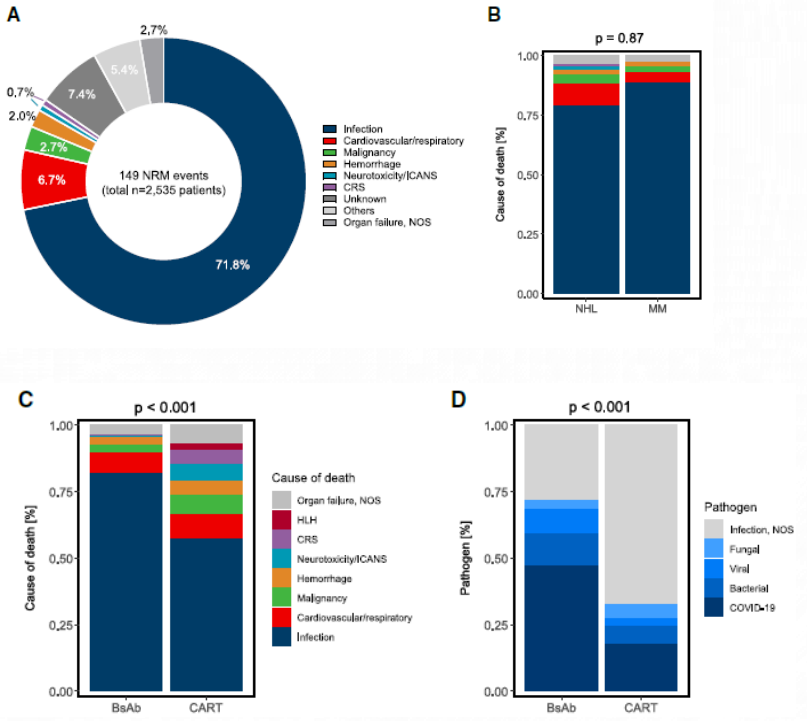
Rejeski K, Blood 2026



Impact sur la mortalité non liée à la rechute

BsAbs:
↓Toxicité type CRS et ICANS
↑ **infections** (effet on target off tumor) 71,8%

Dose dépendent
Effet durée prolongée?
Besoin de données actualisées hors pandémie Covid



2022-2024

Tix T, Molecular Ther 2025

CART vs bsAbs et hémopathies B

REGULAR ARTICLE

blood advances

Comparative infection risk in CAR T vs bispecific antibodies in B-cell lymphoma: a systematic review and meta-analysis

Herman van Besien,[1,*] Neela Easwar,[1,*] Michelle Demetres,[2] Michelle Pasciolla,[3] Tsiporah Shore,[1] John Leonard,[1] Juliet Barker,[1] Peter Martin,[1] and Samuel Yamshon[1]

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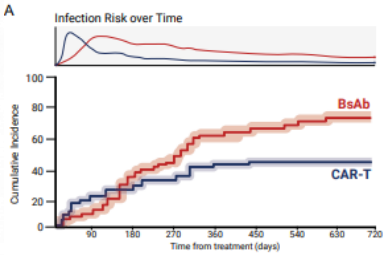


CART vs bsAbs pour hémopathies B
25 études, 3200 patients
Incidence 44% vs 54% toute infection
Incidence/patient/mois > bsAbs
Risque sur le long cours, traitements prolongés?

Risk factors for infections	BsAb	CAR-T
Therapy target		
BCMA	++	++
CD19	+	+
CD20	+	+
GPRC5D	+	+
Initial risk factors (within first month)		
Lymphodepletion		+++
T-cell dysfunction/exhaustion	+	
Early ICAHT	+	++
CRS	+	++
Tocilizumab and/or anakinra	+	++
Corticosteroids	+	++
Delayed risk factors (after first month)		
Repeated dosing	+++	
T-cell dysfunction	++	+
Delayed cytopenias	+	++
Infection prevention strategies (see textfor details)		
Viral		
HSV and VZV prophylaxis	+++	+++
CMV monitoring	+	+
Bacterial and fungal		
Fluoroquinolones		+
PJP prophylaxis	+++	+++
Mold prophylaxis		+
IGRT based on target		
BCMA	+++	+
CD19	+	+
CD20	+	+
GPRC5D	++	+

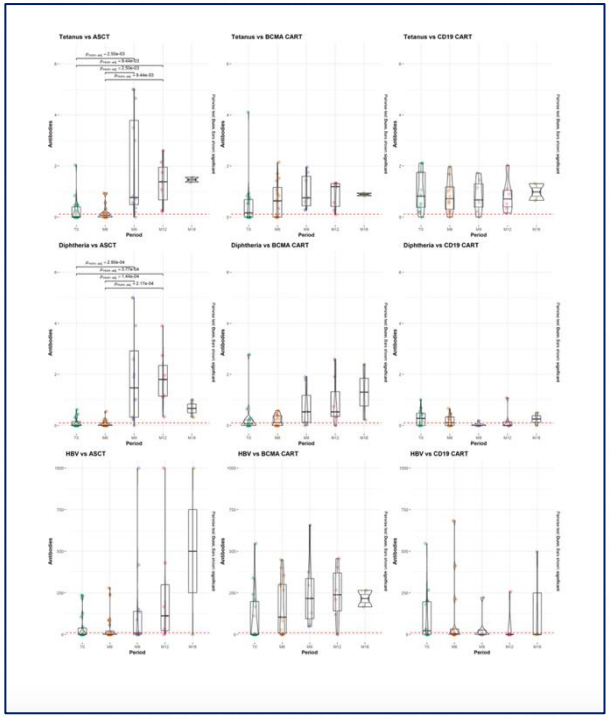
Rejeski K, Blood 2026; Van Besien H, Blood Adv 2025

Quelles prophylaxies, quel monitorage?

Entecavir++

Pre thérapeutique:

- sérologies HIV et hépatites
- Sérologie toxoplasmose
- Sérologie CMV
- Screening TB, HTLV selon pays d'endemie
- Attention aux faux positifs des patients sous IGIV
- sérologie anguillulose si pas ivermectine systématique



Place de la vaccination pre bsAb? (timing/traitement avant bsAbs)

Rejeski K, Blood 2026; Badoual P, submitted CMI

Quelles prophylaxies, quel monitorage?

- Prophylaxie antibactérienne: non
- Prophylaxie anti filamenteux: non sauf si corticoïdes ou neutropénie prolongée ou atcd IFI
- G-CSF si neutropénie grade 3
- Valaciclovir 500 mg x 2/j up to 6 mois après dernier bsAbs/si CD4 > 200
- Bactrim idem (attention: PJP +++)
- Pre emptif CMV, surtout si corticoïdes > 3 jours

Rejeski K, Blood 2026

Strategy	Target			Notes
	CD20	BCMA	GPRC5D	
IGRT	IgG < 200-400 mg/dL	Regardless of IgG level	IgG < 400 mg/dL	Start preemptively at defined thresholds regardless of infection history (see text for details)
CMV monitoring	If on corticosteroids	If on corticosteroids; consider routinely given higher risk	If on corticosteroids	Duration of monitoring: weekly for at least 4 weeks after corticosteroids and/or the first two dosing cycles. CMV treatment: consider based on institutional thresholds for preemptive therapy
Anti-HSV/VZV	Prophylaxis universally indicated			Continue until 6 mo after bsAb completion and CD4 > 200 cells/μL, whichever is longer
Anti-PJP				
Antibacterial	Prophylaxis during intermediate or high-risk neutropenia			Consider G-CSF if ANC ≤ 500 cells/μL (with infection) or ≤100 cells/μL (regardless of infections)
Antifungal	Prophylaxis during high-risk neutropenia or corticosteroid use			
Seasonal vaccines*	3-mo bsAb washout period ideal but not required			If on IGRT, also consider 2-mo washout from last IGRT dose
Other nonlive vaccines	6-mo washout period ideal but not required			
Live vaccines	12-mo washout strongly preferred			If on IGRT, also consider 8-mo washout from last IGRT dose

Chaque mois supplémentaire sous BCMA bsAbs, 3% des patients développent une infection sévère

Prophylaxie primaire si BCMA: ↓ 90% > 3 grade infections

PHRC PREV-CART

Banerjee R, Blood advances 2025: Lancman G, Blood Cancer Discov 2023

Merci