Comprehensive Cancer Center
Tübingen-Stuttgart

Post EBMT 2026

CAR-T Behandlungsstandards

Prof. Dr. W. Bethge

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Comprehensive
Cancer Center
Tübingen - Stuttgart

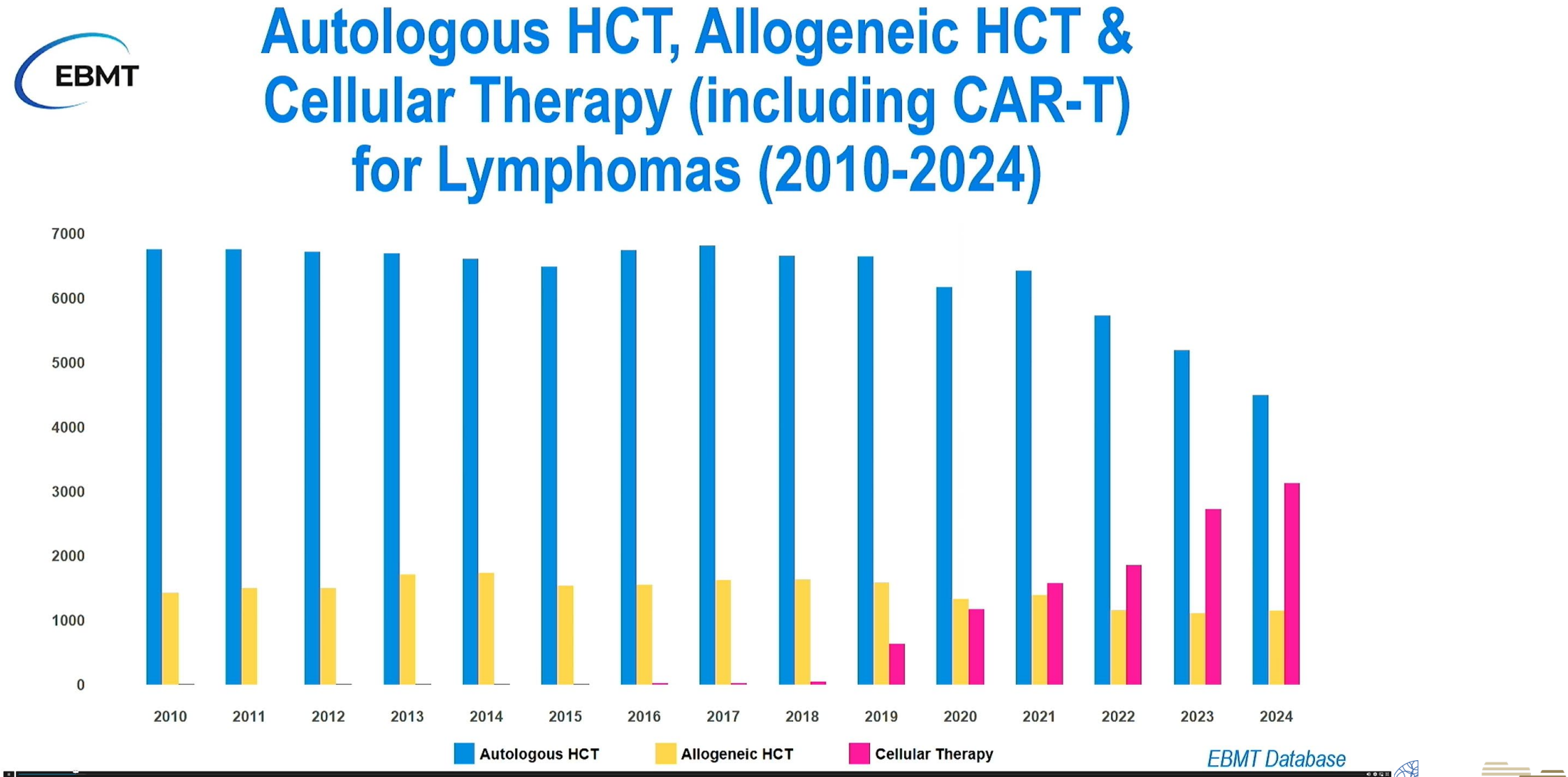
Universitätsklinikum
Tübingen

Themen

Zelluläre Therapie:

1. Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)
2. Day to Day Risk of CRS/ICANS with Lisocel (OS13-07)
3. Non Relapse Mortality after CAR-T: Data of EBMT Registry (GS2-6)
4. Standards of Infection Prevention Post CAR-T (W06)

Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)



Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)

EBMT

Comparative efficacy of Axi-cel vs Liso-cel in 2nd-line relapsed/refractory LBCL

- an analysis by the Lymphoma Working Party -

Anna Ossami Saidy, Mathilde Fekom, Philipp Berning, Francesca Sillito, Emma Nicholson, Gabriel Brisou, Ron Ram, Caroline Arber, Holger Auner, Rajesh Alajangi, Rachel Protheroe, Claude Eric Bulabois, Anne Huynh, Edouard Forcade, Malte von Bonin, Martin Bornhäuser, Christof Scheid, Catherine Thieblemont, Giorgia Battipaglia, Remy Dulery, Bertram Glaß, Ali Bazarbachi

EBMT Annual Meeting 2026 – Anna Ossami Saidy

Helios

#EBMT26

EBMT

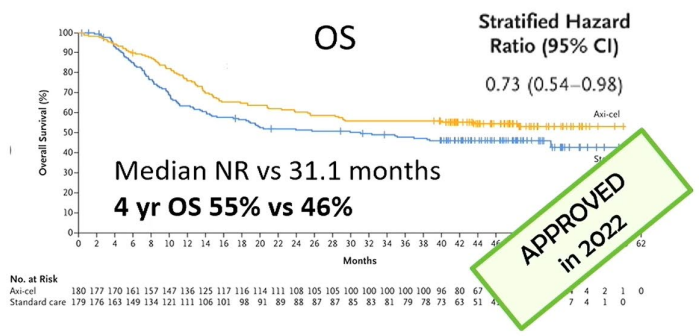
Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)

Helios

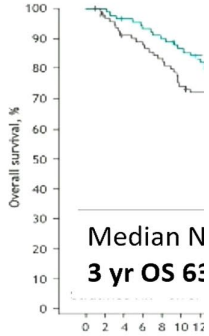
Background - Pivotal trials

- CAR-T established as standard of care in 2L r/r LBCL

ZUMA-7



TRANSFORM



EBMT Westin et al. N Engl J Med, 2023; Abramson et al. Oral presentation at EHA 2024; S272

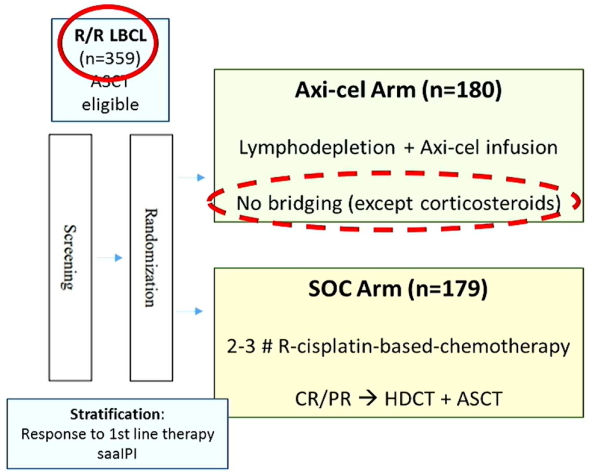
Anna Ossami Saidy

Helios

MSB

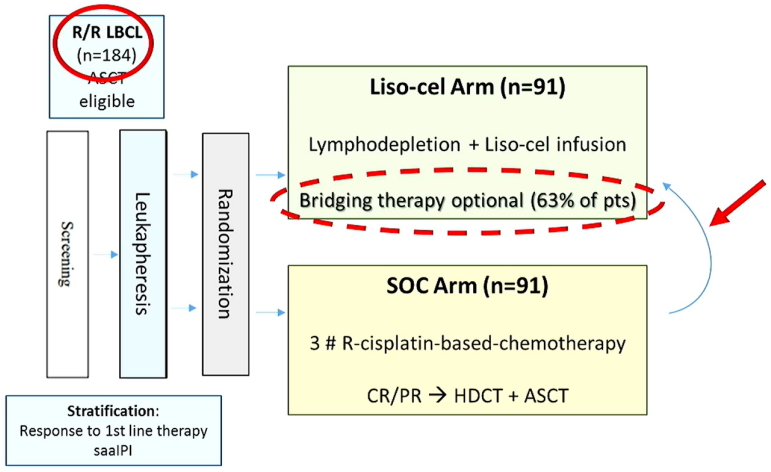
Background - Pivotal trials

ZUMA-7



Extracted from Locke FL et al, N Engl J Med 2022

TRANSFORM



Extracted from Kamdar, et al. Lancet 2022

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Anna Ossami Saidy

Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)

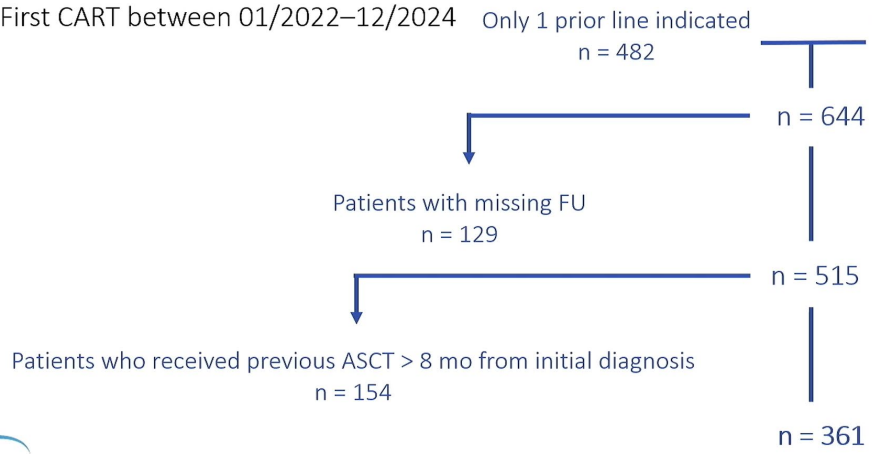
Helios

Inclusion criteria – prior lines of treatment

MSB

Inclusion criteria:

- Adult patients with r/r LBCL who received only one prior treatment line
- First CART between 01/2022–12/2024



EBMT

Helios

Patient characteristics

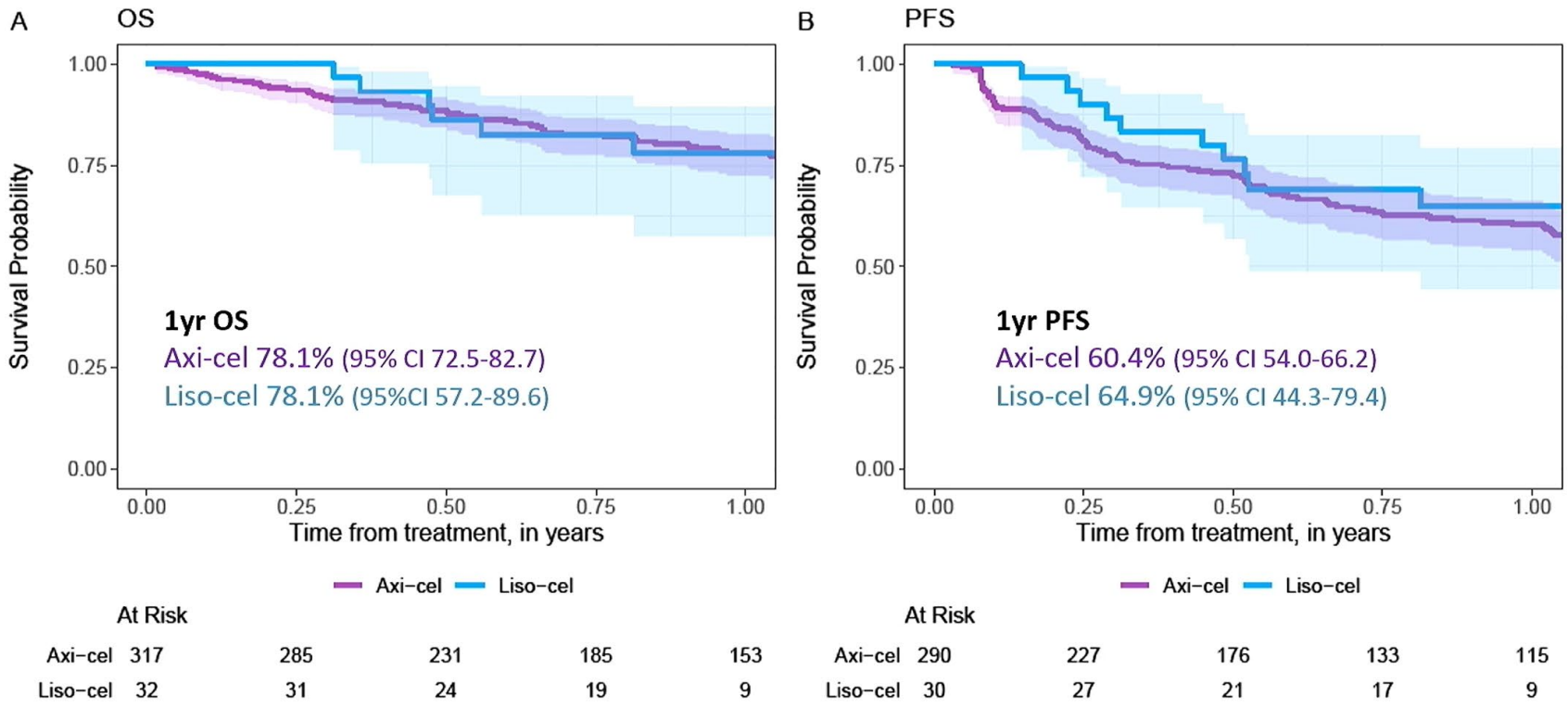
Characteristics (n=361)	Axi-cel (n = 329)	Liso-cel (n = 32)	p - value
Median age	63 (54, 70)	67 (54, 73)	0,2
male	211 (64%)	21 (66%)	0,9
DLBCL (all subtypes)	319 (97%)	30 (94%)	
Treatment year 2022 2023 2024	 41 (12%) 207 (63%) 81 (25%)	 1 (3.1%) 13 (41%) 18 (56%)	**0,001**
Time from diagnosis to infusion ≤ 12 months > 12 months	 206 (63%) 123 (37%)	 20 (63%) 12 (38%)	>0.9
Median time from apheresis to infusion (days)	39 (34, 49)	50 (48, 56)	**<0.001**
Remission status at infusion CR PR **Refractory disease**	48 missing 41 (15%) 74 (26%) **166 (59%)**	1 missing 7 (23%) 3 (9.7%) **21 (68%)**	0,081

Characteristics (n=361)	Axi-cel (n = 361)	Liso-cel (n = 32)	p - value
Elevated LDH at infusion	78 (44%) 152 missing	11 (41%) 5 missing	0,7
> 1 extranodal sites involved	57 (38%) 178 missing	5 (19%) 6 missing	0,6
HCT-CI at infusion 0 1-2 >=3	 155 (56%) 70 (25%) 54 (19%) 50 missing	 10 (34%) 8 (28%) 11 (38%) 3 missing	**0,038**

Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)

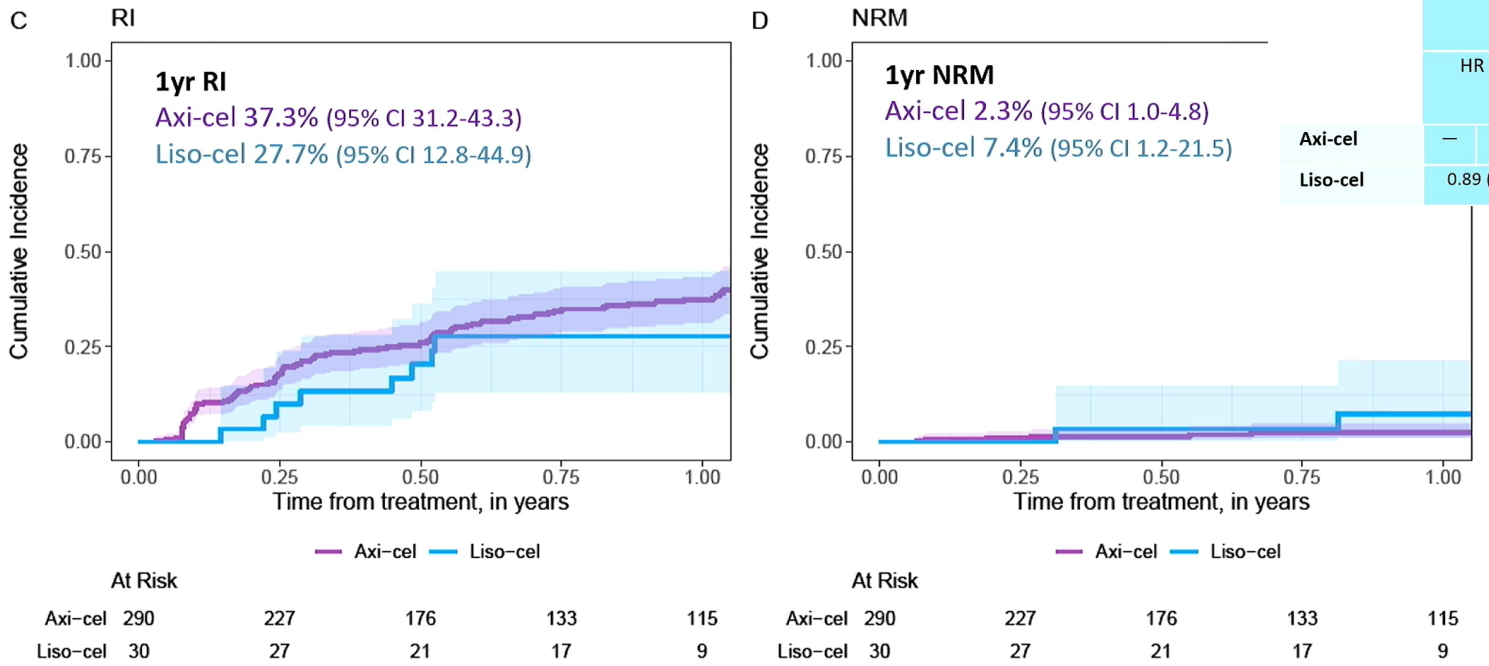
Results – Survival data

Median FU: 12 mo



Comparison Axicel and Lisocel in 2nd Line LBCL (LWP1-2)

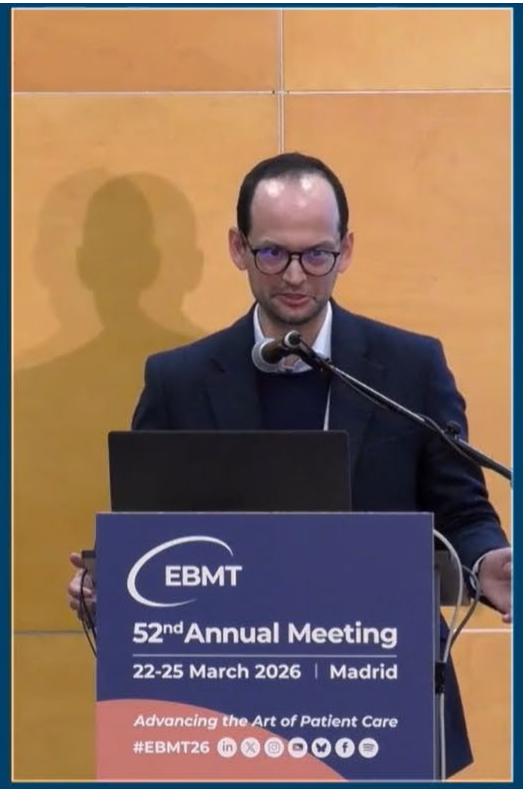
Results – Relapse incidence and NRM



Survival - Propensity Score Matching

	OS		PFS		RI		NRM	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Axi-cel	— —		— —		— —		— —	
Liso-cel	0.89 (0.34-2.33)	0.8	0.79 (0.40-1.57)	0.5	0.68 (0.32-1.47)	0.3	2.18 (0.38-12.6)	0.4

Day to Day Risk of CRS with Lisocel (OS13-07)



Quantifying day-to-day risk of cytokine release syndrome and neurological events after lisocabtagene maraleucel infusion: pooled analysis from 7 clinical trials

Valentin Ortiz-Maldonado,[1] Pere Barba,[2] Robert Lown,[3] Pim Mutsaers,[4] Kirit Ardeshna,[5] Peter Borchmann,[6] Paolo Corradini,[7] Michael Northend,[5] David Bernasconi,[8] Stefanie Buschor,[8] Peter J. Mueller,[8] Franck Morschhauser[9]

[1]Hospital Clinic of Barcelona, University of Barcelona, Barcelona, Spain; [2]Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain; [3]University Hospital Southampton NHS Foundation Trust, Southampton, UK; [4]Erasmus University Medical Center, Rotterdam, Netherlands; [5]University College London Hospitals NHS Foundation Trust, London, UK; [6]Universität zu Köln, Köln, Germany; [7]University of Milano, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; [8]Bristol Myers Squibb, Boudry, Switzerland; [9]Centre Hospitalier Universitaire de Lille, Groupe de Recherche sur les formes Injectables et les Technologies Associées, Lille, France

EBMT 2026, Presentation OS13-07

Day to Day Risk of CRS with Lisocel (OS13-07)

Methods

- Time to onset of CRS or NE data were pooled for lisa-cel–treated patients from 7 clinical trials in 2L/3L+ LBCL and 2L+ FL[a] (N = 691)
  - 2L LBCL: TRANSFORM, PILOT
  - 3L+ LBCL: TRANSCEND NHL 001, TRANSCEND WC
  - 2L+ FL: TRANSCEND FL
- Analyses estimated the risk of future onset of
  - at each day after infusion,
  - at each day after infusion, stratified into patier
  - at each day after infusion up to Day 15 in patie
- All analyses are descriptive; no formal hypoth

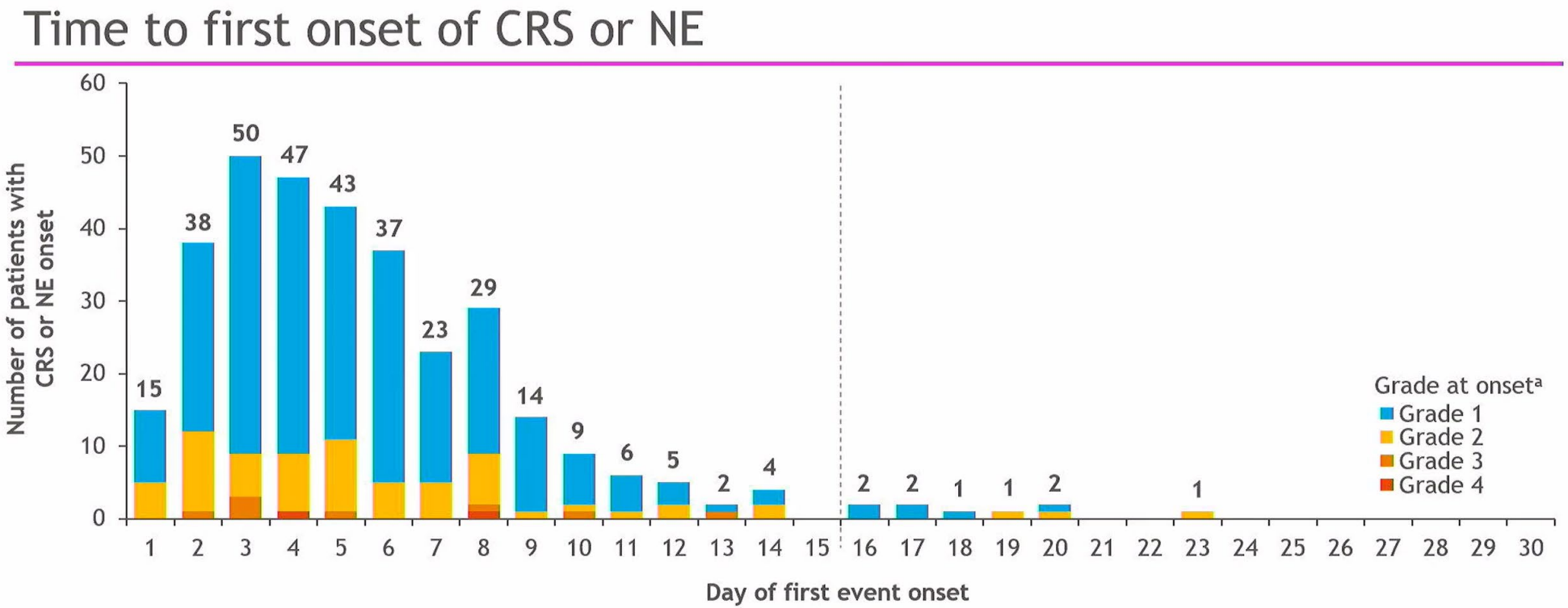
Demographics and baseline characteristics

	Patients without any CRS or NE (n = 355)	Patients with ≥ 1 CRS or NE (n = 336)	All patients (N = 691)
Median (range) age, y	65 (20–83)	62 (18–86)	64 (18–86)
Male, n (%)	226 (64)	210 (62.5)	436 (63)
Disease histology,[a] n (%)			
DLBCL NOS de novo	177 (50)	140 (42)	317 (46)
DLBCL transformed from indolent lymphoma	63 (18)	51 (15)	114 (16)
HGBCL	46 (13)	49 (15)	95 (14)
PMBCL	10 (3)	13 (4)	23 (3)
FL3B	8 (2)	3 (1)	11 (2)
THRBCL	0	1 (< 1)	1 (< 1)
FL grade 1, 2, or 3A	51 (14)	79 (24)	130 (19)
Disease relapsed or refractory to last therapy,[b] n (%)			
Relapsed[c]	101 (28)	125 (37)	226 (33)
Refractory[d]	253 (71)	211 (63)	464 (67)
LDH ≥ ULN before LDC, n (%)	165 (46)	195 (58)	360 (52)
Received bridging therapy, n (%)	187 (53)	208 (62)	395 (57)

All percentages are rounded to whole numbers except those with ".5%".
[a]As reported by the investigator; [b]Data were not provided for 1 patient without any CRS or NE; [c]Defined as CR with relapse on or after treatment lasting ≥ 3 months but no more than 12 months for LBCL and defined as relapse after an initial response of CR or PR to the prior therapy for FL; [d]Defined as SD, PD, PR, or CR with relapse before 3 months for LBCL and defined as best response of SD or PD after prior therapy for FL.
FL3B, follicular lymphoma grade 3B; HGBCL, high grade B-cell lymphoma; LDC, lymphodepleting chemotherapy; NOS, not otherwise specified; PMBCL, primary mediastinal large B-cell lymphoma; SD, stable disease; THRBCL, T-cell/histiocyte-rich large B-cell lymphoma.

Ortiz-Maldonado V, et al. EBMT 2026 [Presentation #OS13-07]

Day to Day Risk of CRS/ICANS with Lisocel (OS13-07)



- A total of 336 (49%) patients experienced CRS or NE
- Among patients with any-grade CRS or NE, 12 (4%) had a grade ≥ 3 event at first onset and 96% of events occurred on or before Day 15 after infusion

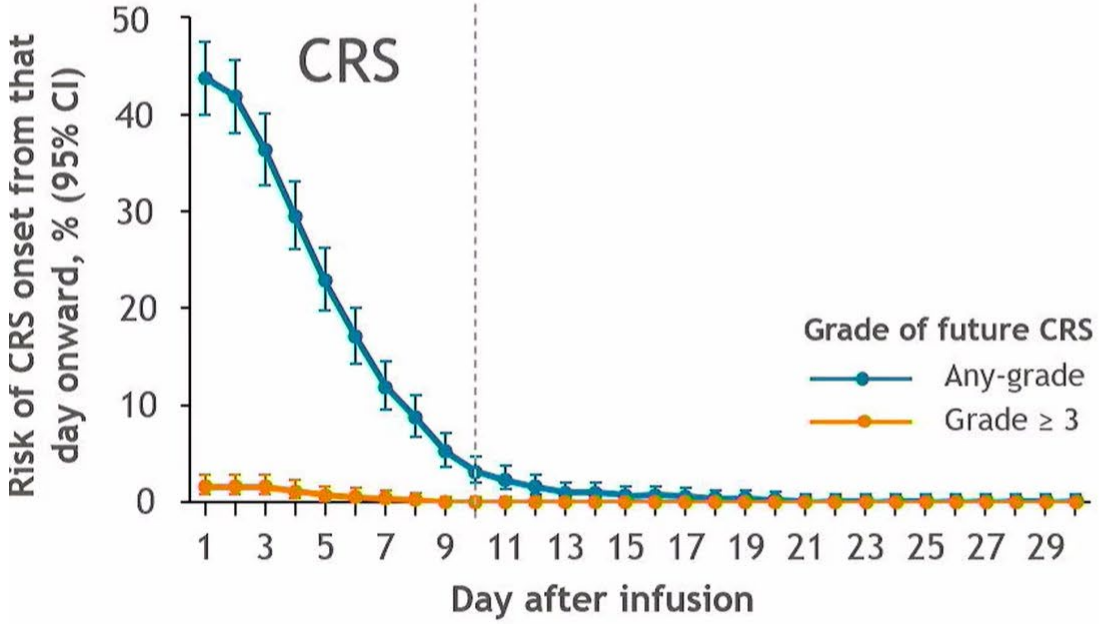
[a]There were no grade 5 events at onset.
After 30 days, an additional 5 patients had events (2 patients on Day 33, 1 patient on Day 34, and 2 patients on Day 63).

Ortiz-Maldonado V, et al. EBMT 2026 [Presentation #OS13-07]

Day to Day Risk of CRS/ICANS with Lisocel (OS13-07)

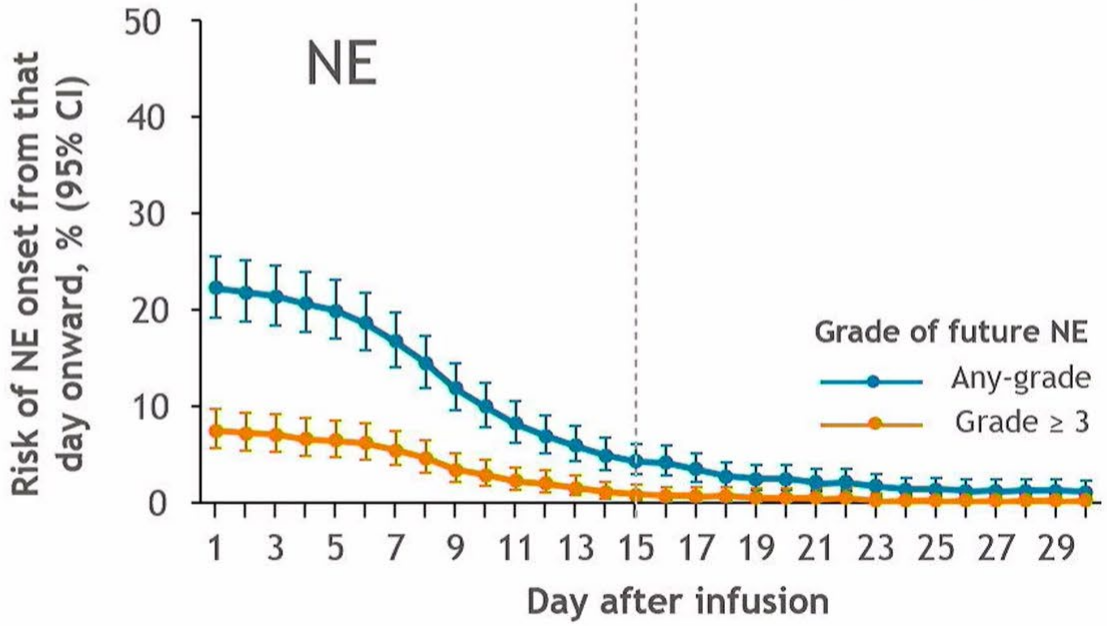
Risk of future CRS and risk of future NE (Days 1–30)

Future risk,[a] % (95% CI)	Day 1	Day 5	Day 7	Day 10	Day 15	Day 30
Any grade	44 (40–47)	23 (20–26)	12 (10–15)	3 (2–5)	1 (0.2–2)	0.1 (0–0.8)
Grade ≥ 3	2 (1–3)	1 (0.2–2)	0.4 (0.1–1)	0 (0–0.5)	0 (0–0.5)	0 (0–0.5)



No. at risk 691 691 691 691 689 689 689 689 687 686 686 685 684 680 679

Future risk,[a] % (95% CI)	Day 1	Day 5	Day 7	Day 10	Day 15	Day 30
Any grade	22 (19–26)	20 (17–23)	17 (14–20)	10 (8–13)	4 (3–6)	1 (1–2)
Grade ≥ 3	8 (6–10)	7 (5–9)	5 (4–7)	3 (2–4)	1 (0.3–2)	0.3 (0–1)



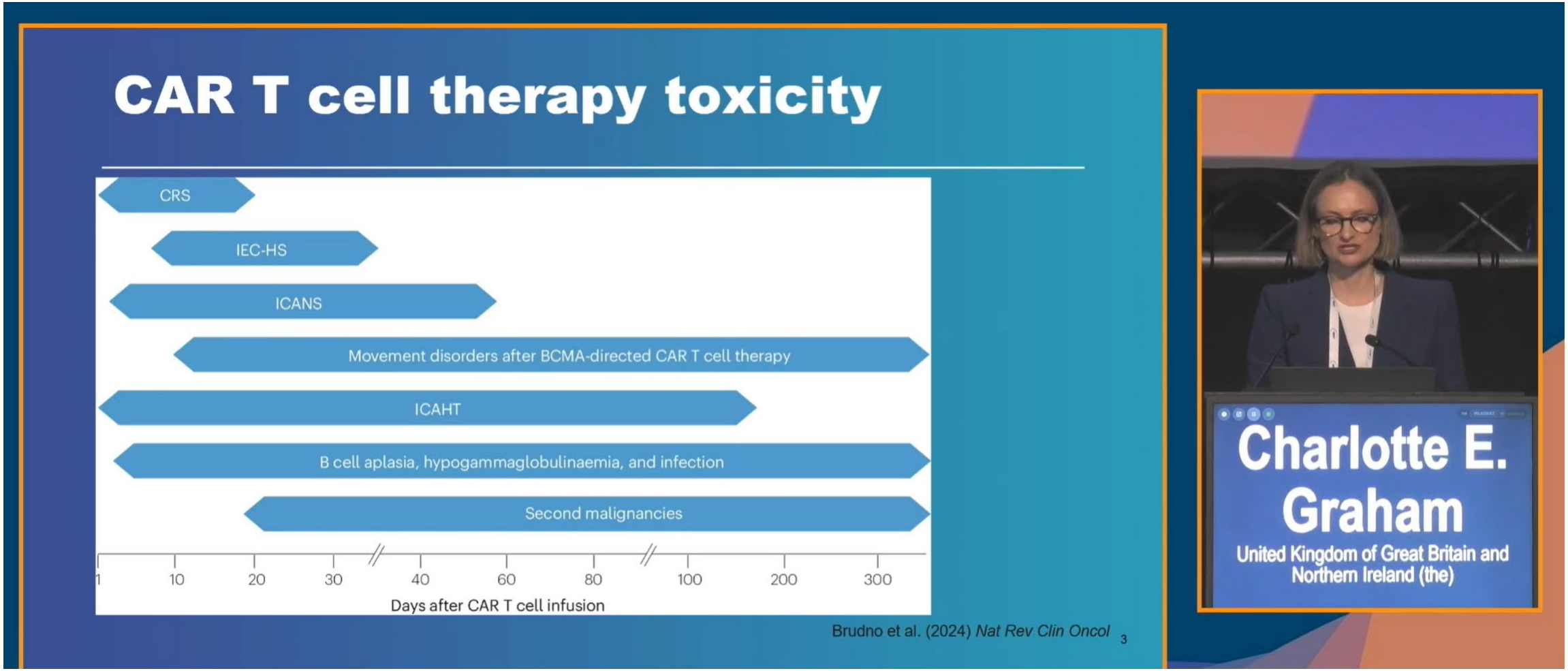
No. at risk 691 691 691 691 689 689 689 689 687 686 686 685 684 680 679

Day to Day Risk of CRS/ICANS with Lisocel (OS13-07)

Conclusions

- Data from liso-cel clinical trials in patients with 2L/3L+ LBCL and 2L+ FL indicate that 96% of first CRS or NE occurred within 15 days after infusion and were predominantly low grade
- The daily estimated risk of CRS or NE from that day onward decreased over time, with an estimated 4% risk of any-grade CRS or NE at Day 15 in patients without a prior event
- Across most days in the analysis period, patients without a prior CRS or NE had numerically lower risks of any-grade or grade ≥ 3 CRS or NE from that day onward compared with patients with a prior event
- In patients without a prior CRS or NE, risk of events from that day onward, particularly grade ≥ 3 events, was already low by Day 7, supporting more individualized discharge planning before Day 15 in selected patients
- These findings provide quantitative residual risk estimates that may help physicians decide when to discharge patients after liso-cel infusion, particularly from inpatient settings

NRM after CAR-T: Data of EBMT Registry (GS2-6)



NRM after CAR-T: Data of EBMT Registry (GS2-6)

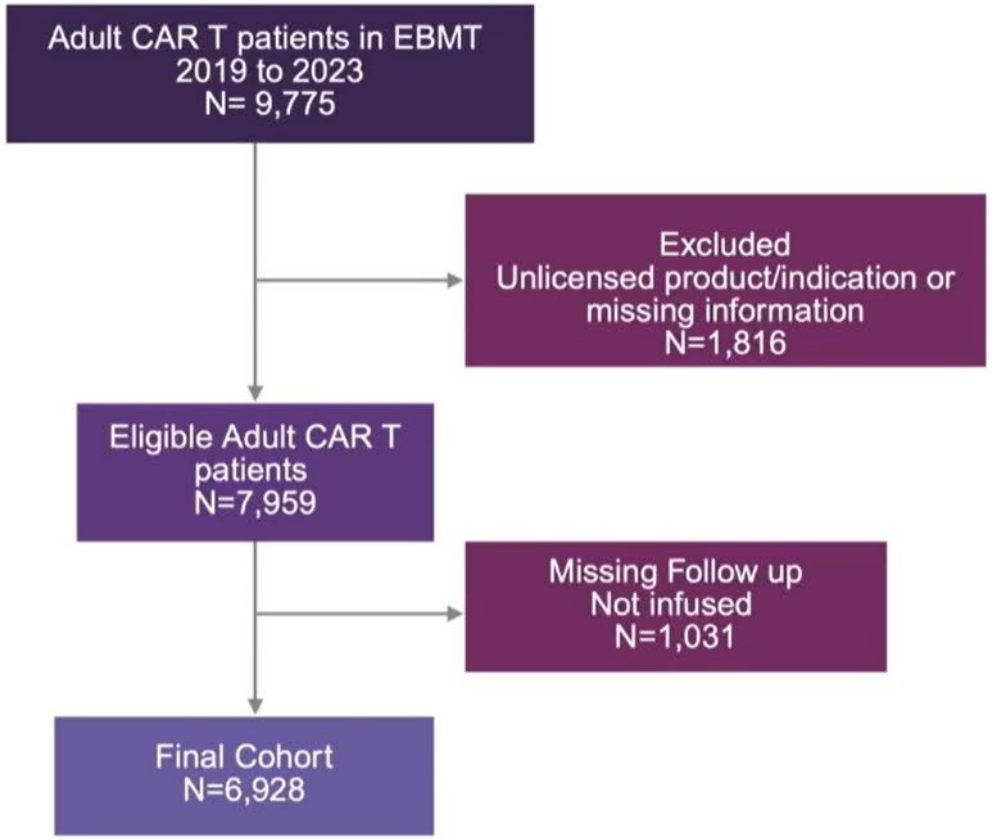
EBMT Registry Data

Inclusion Criteria:

- Adult patients ≥ 18 years at time of CAR T infusion
- First CAR T infusion between January 2019 to January 2024
- Indication for a haematological malignancy including B-Acute Lymphoblastic Leukaemia, Lymphoma and Multiple Myeloma

Exclusion criteria:

- Non commercial CAR T products
- Missing Follow Up



NRM after CAR-T: Data of EBMT Registry (GS2-6)

Non-Relapse Mortality post CAR T

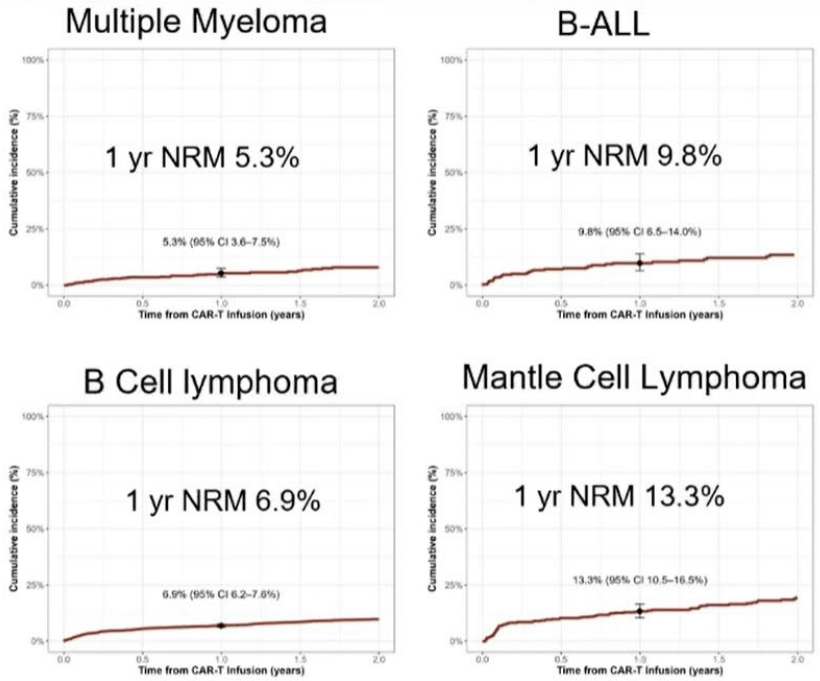
NRM is death from any cause without evidence of relapse

Final Cohort
N=6,928

2,887 Deaths

Relapse/Disease Progression
N=2,214 (80.4%)

Non-Relapse Mortality
N=673



Cumulative incidence of NRM by disease indication [8]

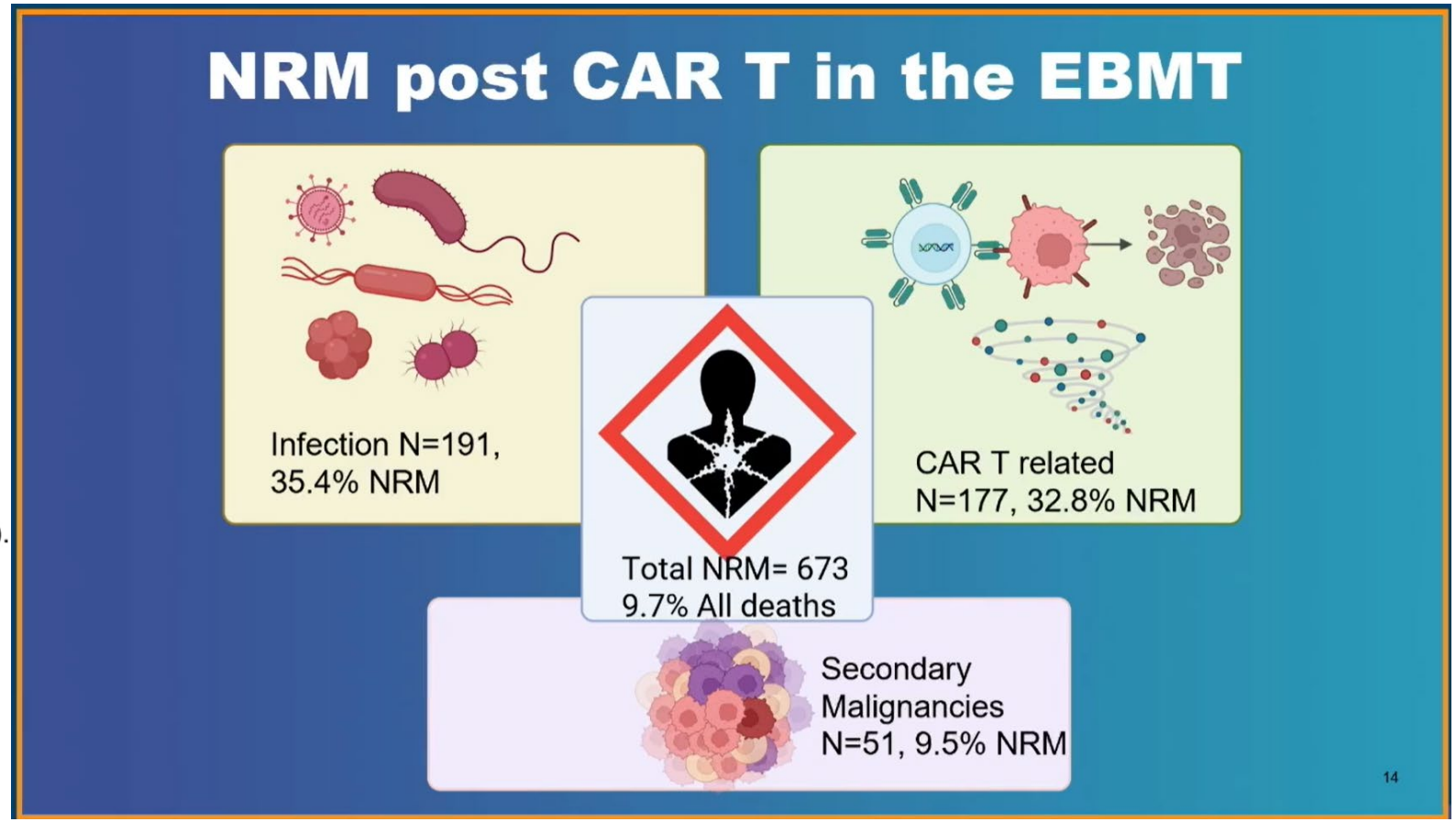
Diagnosis and CAR T product	NRM at 6 months (% (95% CI))	NRM at 1 year (% (95% CI))	NRM at 2 years (% (95% CI))
MCL Brexu-cel	10.3% (7.83%, 13.1%)	13.3% (10.5%, 16.5%)	19.4% (15.6%, 23.7%)

NRM after CAR-T: Data of EBMT Registry (GS2-6)

Multivariate Cox Analysis of NRM

Increased risk of NRM associated with:

- Older age at CAR-T infusion (HR 1.16, p<0.001)
- Male sex (HR 1.34, p=0.003)
- ECOG ≥1 (HR 2.00, p<0.001)
- Disease status (HR [PR vs. active disease] 0.75, p=0.01).



Standards of Infection Prevention Post CAR-T (W06)

CAR-T-cell Therapy: *A Paradigm Shift*

CAR-T-cell Therapy: *A Paradigm Shift*

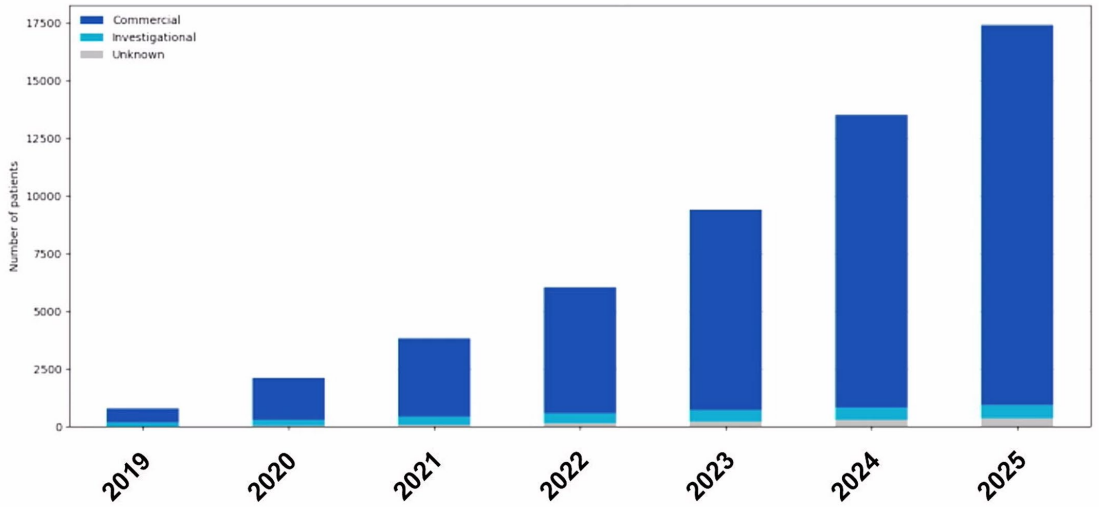
Oct 2017
Axi-cel (Yescarta) for
Large B-cell Lymphoma

Aug 2017
Tisa-cel (Kymriah) for
B-cell ALL (≤ 25 yo)

May 2018
Tisa-cel (Kymriah) for
Large B-cell Lymphoma

July 2020
Brex-cel (Tecartus) for
Mantle Cell Lymphoma

Number of CAR-T recipients in the EBMT registry



>17,000

https://www.cancer.gov/about-cancer/treatment/research/car-t-cells

Colored boxes: new FDA approvals; uncolored boxes: expansion of indications;
aqua: CD-19 targeted products; **lavender**: BCMA-targeted products

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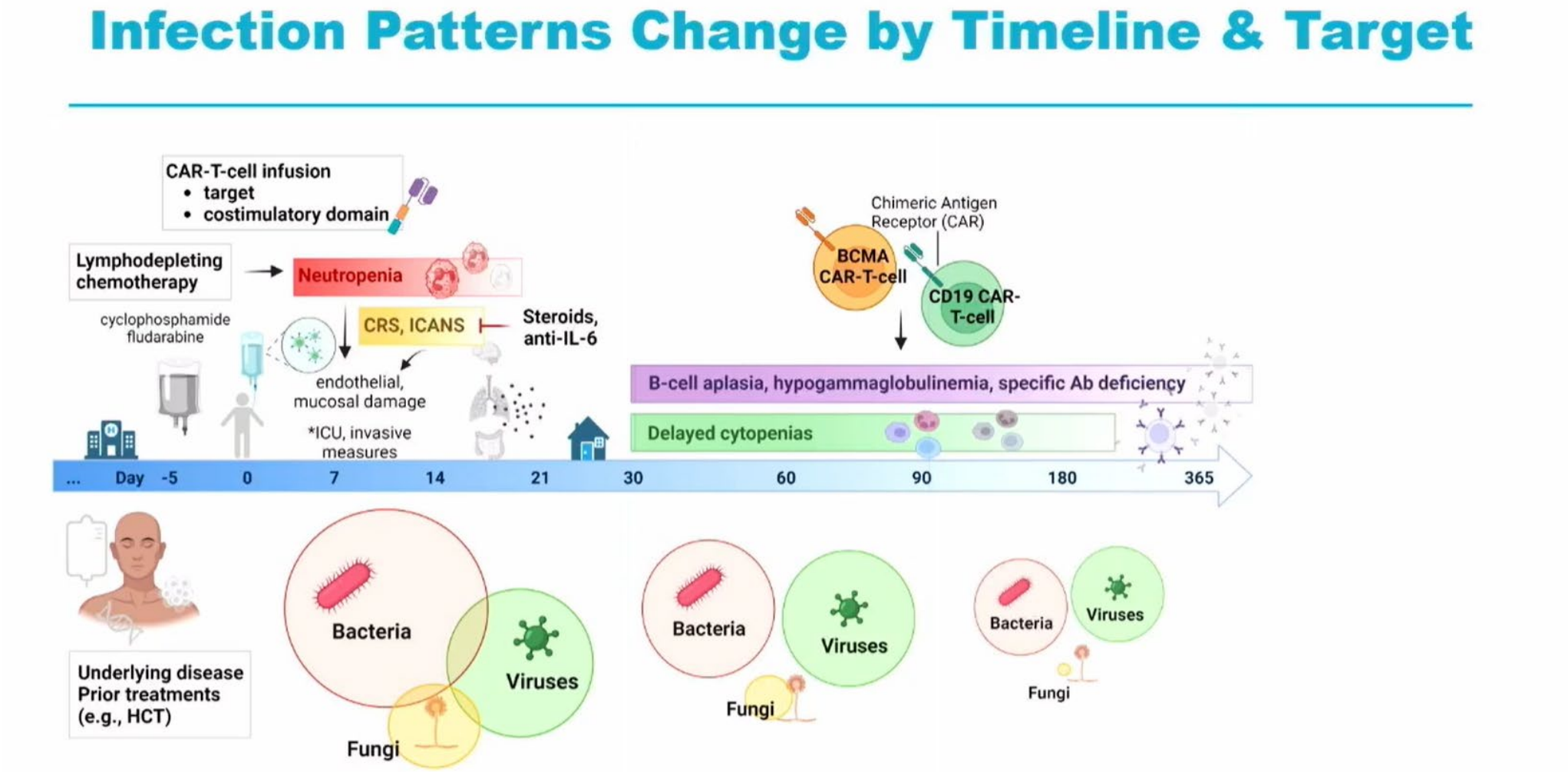
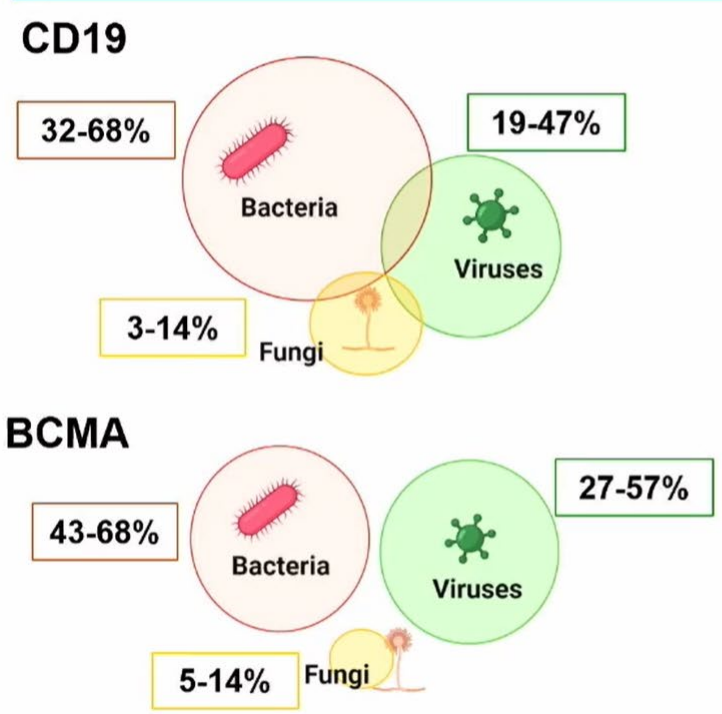
Standards of Infection Prevention Post CAR-T (W06)

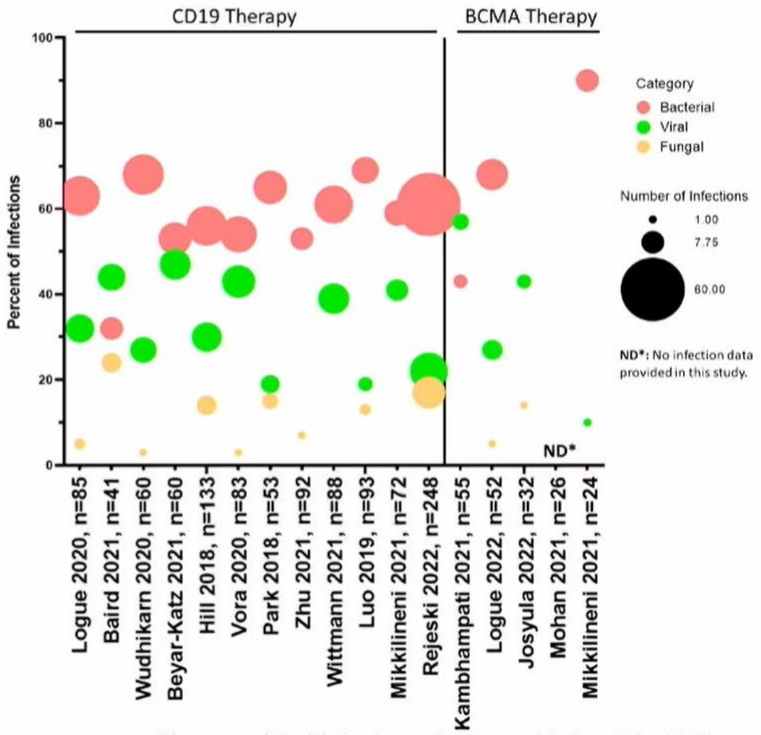


Kampouri E, Little J, et al. Transpl Infect Dis 2023

Standards of Infection Prevention Post CAR-T (W06)

Infection Types Differ Between CAR-T Targets





Kampouri E, Little J, et al. Transpl Infect Dis 2023

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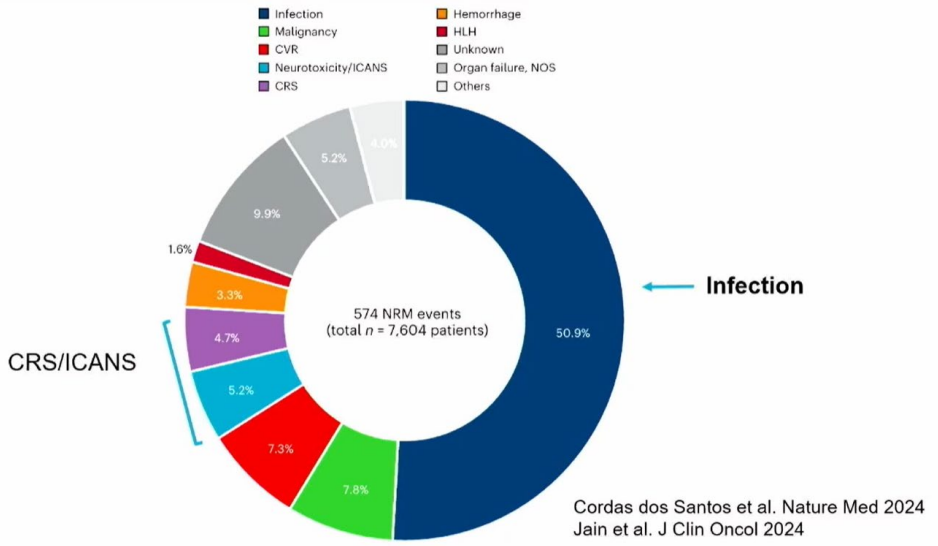

Cordas dos Santos et al. Nature Med 2024
Jain et al. J Clin Oncol 2024

Standards of Infection Prevention Post CAR-T (W06)

Prevention: Consensus (*or lack there of*)

	FQ ppx	Antiviral ppx	CMV Monitoring	CMV PET	Antifungal (fluconazol)	Antimold ppx	Anti-PjP ppx
Fred Hutch Cancer Center	✓	≥1 y	>3d of steroids ✓	≥150 IU/mL (plasma) ✓	✓	Neutropenia >20d/ steroids >3 days ✓	≥6 m
Dana-Farber Cancer Institute	✓	≥6 m*	>5 doses dexa ✓	✗	✗	✗	≥6 m*
CHUV	✗	6-12 m	High-risk ✓	✗	✓	Prior allo-HCT/ steroids/prior IF ✓	≥6 m*
LMU Ludwig-Maximilians-Universität München	✓	≥6 m*	✗	✗	✓	Risk-adapted (CAR-HT, BMT infiltration etc.) ✓	≥6 m*

*or CD4>200 cells/µL

✓ Recommended

✓ Recommended under conditions

✗ Not recommended

Kampouri E, Little J, et al. Transpl Infect Dis 2023

Standards of Infection Prevention Post CAR-T (W06)

Received: 3 May 2022 | Revised: 6 July 2023 | Accepted: 14 July 2023
DOI: 10.1111/tid.14109

REVIEW ARTICLE

Vaccine schedule recommendations and updates for patients with hematologic malignancy post-hematopoietic cell transplant or CAR T-cell therapy

Gemma Reynolds[1,2,3] | Victoria G. Hall[1,2] | Benjamin W. Teh[1,2]

Recommendations frequently extrapolated from HSCT guidelines

Hayden PJ, et al. 2021 best practice recommendations of EBMT/ JACIE/EHA *Ann Oncol*. 2022;33(3):259-275; 2023 ASH-ASTCT

Universal approach

TABLE 3 Recommendations on revaccination timing post cellular therapy from expert international guidelines, expert center protocols, and expert opinion.

	Consensus guidelines (EBMT/JACIE/EHA, ASH-ASTCT)	Expert center protocols	Expert opinions
Killed and inactivated vaccines: PCV13 (3 doses) PPSV23 (1 doses) DTaP (3 doses) HBV (3 doses) HAV (2 doses) SARS-CoV-2 (3+ doses) IIV (2 doses) VZV (aRZV) (2 doses) ACYW-135 (2 doses)[a] Hib (3 doses)[a]	≥3 months after CAR-T therapy AND Demonstrated immune reconstitution* AND No ongoing immunosuppression (see text).	No IVIg in prior 2 months No anti-CD19 or anti-CD20 antibody therapy in prior 6 months Demonstrate vaccine response on one killed vaccine prior to revaccination with remaining schedule	Demonstrate detectable serum IgA (evidence of class switching) If no vaccine response demonstrated, re-check immune reconstitution in 6 months and continue IVIg
Live vaccines MMR (2 doses) VZV (LAVV) (2 doses) Many travel vaccines (e.g., typhoid, yellow fever, and polio oral vaccine)	≥12 months after CAR-T therapy AND Demonstrated immune reconstitution*AND No ongoing immunosuppression AND No IVIg in prior 8 months	No IVIg in prior 5 months No anti-CD19 or anti-CD20 antibody therapy in prior 6 months No HCT ≤2 years prior No systemic immunosuppression in prior 12 months Demonstrated response to killed/inactive vaccine	Demonstrate detectable serum IgA (evidence of class switching)

Abbreviations: ACYW-135, meningococcal quadrivalent conjugate vaccine; aRZV, adjuvanted recombinant zoster virus vaccine; CAR-T, chimeric antigen receptor T cell; CD19, cluster of differentiation 19; CD20, cluster of differentiation 20; DTaP, higher dose diphtheria, tetanus, and acellular pertussis vaccine; HAV vaccine, hepatitis A virus; HBV vaccine, hepatitis B virus; HCT, hematopoietic cell transplant; Hib, *Haemophilus influenzae* type B conjugate vaccine; IgA, immunoglobulin A; IIV, inactivated influenza vaccine; IVIg, intravenous immunoglobulin; LAVV, live-attenuated varicella vaccine; MMR, measles, mumps, and rubella live virus vaccine; PCV, pneumococcal conjugate vaccine; PPSV23, pneumococcal 23-valent polysaccharide vaccine; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VZV, varicella zoster virus.

[a]Revaccination against meningococcal and hemophilus to be considered in patients with CAR-T patients and additional risk factors, such as splenectomy.

* CD4+ >0.2 × 10_9/L, CD19 or CD20+ B cells >0.2 × 10_9/L.

Standards of Infection Prevention Post CAR-T (W06)

Transplantation and Cellular Therapy 30 (2024) 955–969

Transplantation and Cellular Therapy

journal homepage: www.astctjournal.org

Guideline

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

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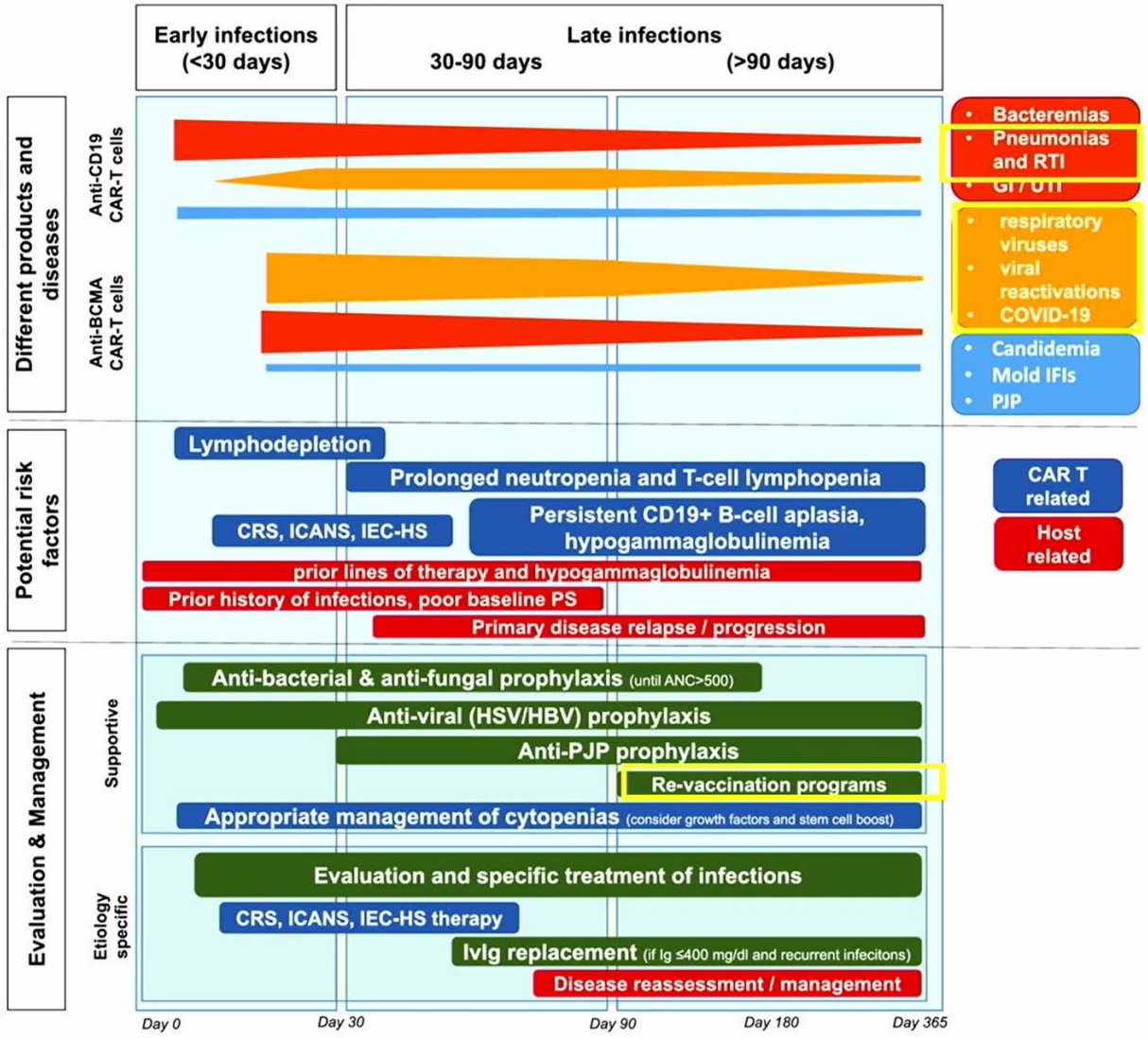
Tailored approach

Assess serological responses both pre and postvaccination to tailor immunization strategies

For patients without a history of HCT or who completed the entire series of post-HCT vaccines, **no additional vaccinations are needed** **if the patient developed seroprotective titers to the first post-CAR T-cell therapy vaccine series with PCV, DTaP, HAV, HBV vaccines.**

Patients who did not respond to the first post-CAR T-cell vaccines should defer additional vaccination until improved immune reconstitution is documented



SARS-CoV-2

Flu

PCV

HiB

(RSV)

HZ

meningococci

DTaP

HBV/HAV

Klinische Studien CAR-T Zelltherapie Tübingen

Entity	Description	Status
Myelom	**A Phase 3 Randomized Study Comparing Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (DVRd) followed by Ciltacabtagene Autoleucel versus Daratumumab, Bortezomib, Lenalidomide and Dexamethasone (DVRd) followed by Autologous Stem Cell Transplant (ASCT) in Participants with Newly Diagnosed Multiple Myeloma who are Transplant Eligible** **CARTITUDE-6**	**open** Infos Dr. Besemer
Lymphomas/ALL	**A phase I/II dose finding and efficacy study of MB-CART-CD19/CD22 in patients with relapsed/refractory B-cell malignancies**	**open** Infos: Prof. Dr. Bethge
Autoimmune Diseases	**An open-label phase I/IIa, multicentre, interventional single-arm trial of MBCART19.1 in patients with refractory SLE**	**open** Info: Prof. Dr. Henes
	Use of MB-CART19 also for autoimmune diseases: Basket (SLE, MS, myositis)	**planned** Info: Prof. Dr. Henes
	A phase I/II safety, tolerability and preliminary efficacy study of UKT-CART-19.1 in patients with primary progressive multiple sclerosis	**planned** Info: Dr. Malte Rörden
Lymphomas	**Phase-II-Studie zur Bewertung der Wirksamkeit und Sicherheit von MB-CART2019.1 im Vergleich zur Standardtherapie bei Teilnehmern mit rezidiviertem/refraktärem diffus-großzelligem B-Zell-Lymphom (R-R DLBCL) | DALY 2-EU**	**open** Infos: Prof. Dr. Bethge
Lymphomas/ Car-T cells	**Phase II study to evaluate the efficacy and safety of MB-CART2019.1 compared with standard therapy in participants with relapsed/refractory diffuse large B-cell lymphoma (RR DLBCL) |** DALY 2-EU	**reopened** Info: Prof. Dr. Bethge

und am Ende....

Vielen Dank für Ihre Aufmerksamkeit

Universitätsklinikum Tübingen