Comprehensive Cancer Center
Tübingen-Stuttgart

Post EBMT 2026

Nachsorge und Diagnostik nach allo-SZT und CAR-T

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Disclosures

Friederike Schwartz: keine

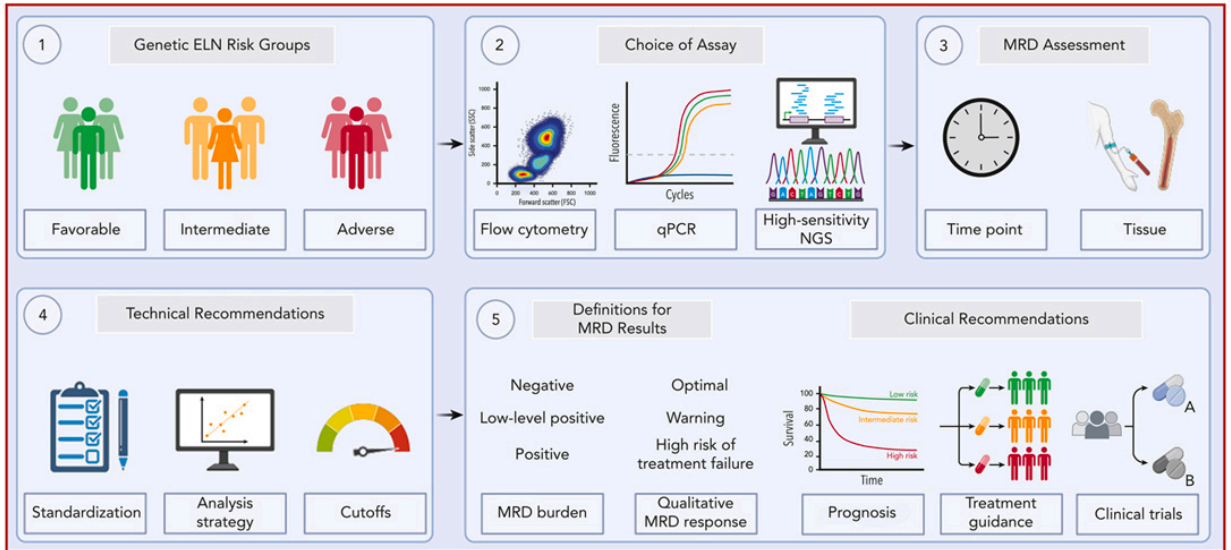
Kristina Reuß: keine

Übersicht

1. AML-MRD – wie ist der aktuelle Stand
2. Azacitidin-Venetoclax im Rezidiv nach allo-SZT
3. Spezifische und unspezifische Immunität bei GvHD vor und nach ECP
4. Messung der CAR-T-Präsenz im Verlauf nach CAR-T-Therapie
5. Nichtinfektiöse Komplikationen nach CAR-T-Therapie
6. Infektiöse Komplikationen nach CAR-T

MRD-Monitoring bei AML

2025 Update on MRD in Acute Myeloid Leukemia: A Consensus Document from the ELN-DAVID MRD Working Party



Created with BioRender.com Bachas C. (2026) https://BioRender.com/82o7yaw

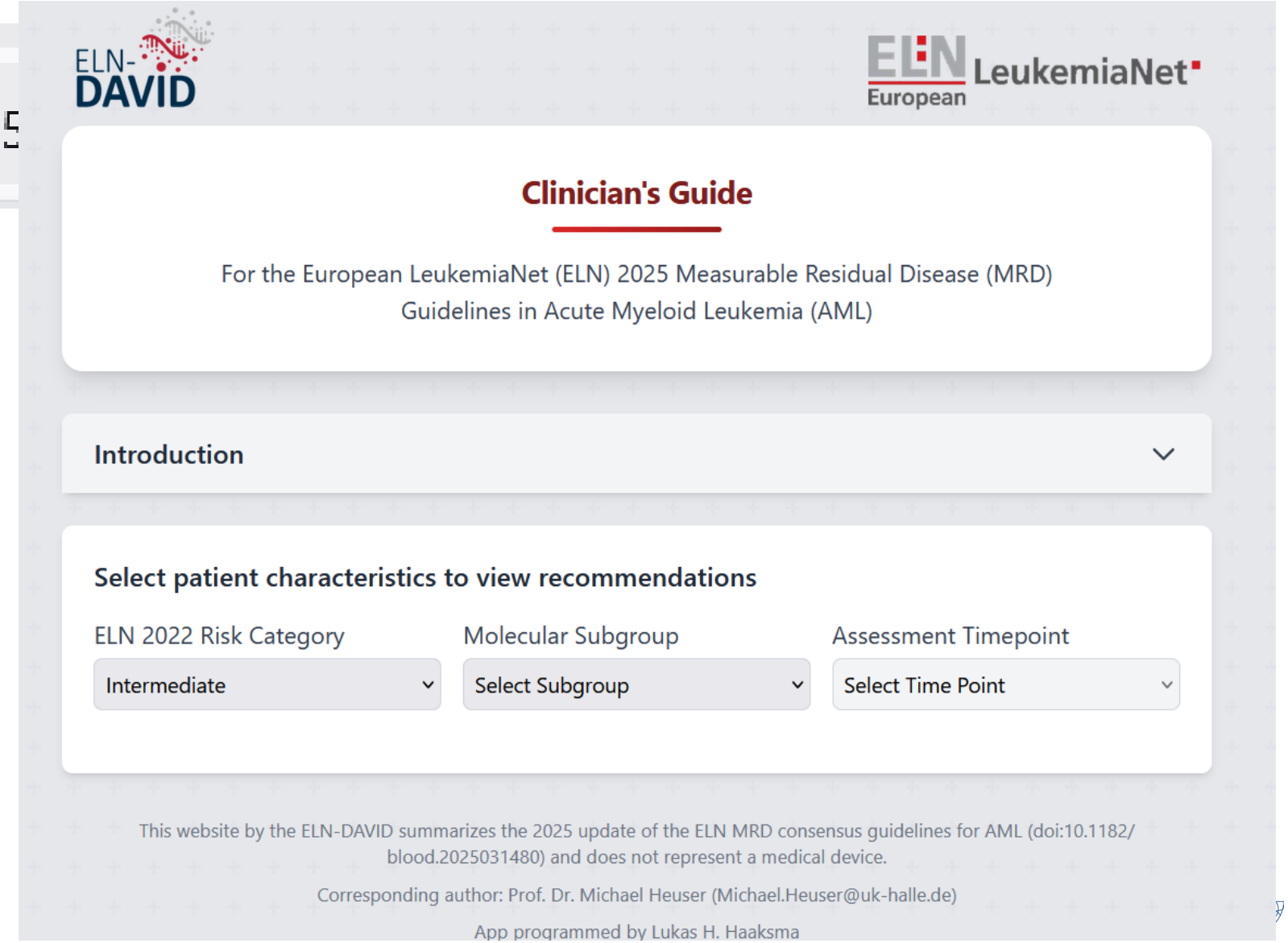
Conclusions: **The 2025 ELN MRD consensus recommendation for AML provides a unified framework for standardizing and clinically applying MRD assessment in AML. It outlines preferred assay selection, analysis strategies, and key parameters including timing, tissue type, and cutoffs across molecular subtypes, and defines MRD levels with corresponding clinical recommendations to enhance patient care.**

*Cloos et al. DOI: 10.1182/**blood**.2025031480*

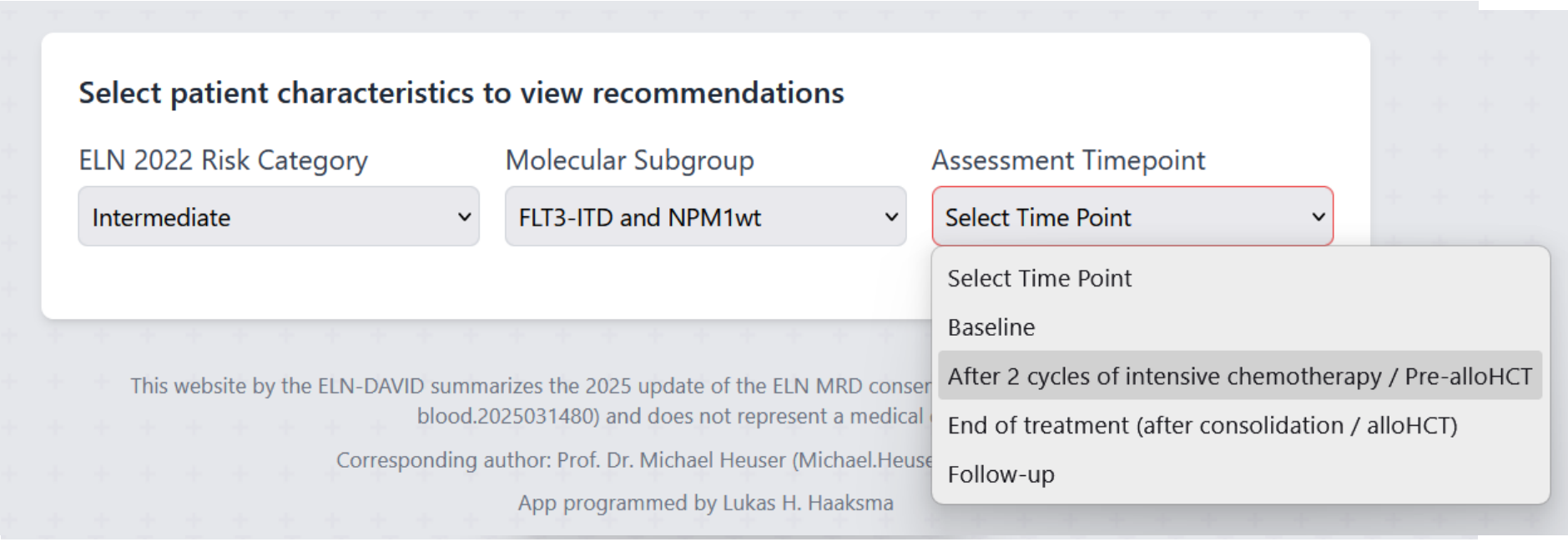
blood Visual Abstract

New ELN MRD consensus guidelines for AML 2025

eln-aml-mrd-2025



New ELN MRD consensus guidelines for AML 2025



For *FLT3*-ITD and *NPM1*wt:

FLT3-ITD UHS-NGS if available; otherwise MFC

Monitoring by targeted *FLT3*-ITD UHS-NGS

Timepoint: After 2 cycles of intensive chemotherapy / Pre-alloHCT
Recommended assay: FLT3-ITD UHS-NGS
Recommended tissue: Bone marrow (BM) preferred over peripheral blood (PB)

LOD MEASURED AS VAF (%)	QUANTITATIVE MRD BURDEN	QUALITATIVE MRD RESPONSE
<LOD[9]	Negative	Optimal
≥LOD[9]	Positive	High risk of treatment failure

[9]The assay should be validated to a limit of detection (LOD) of 10^{-4} to 10^{-5} (VAF).

Monitoring by MFC

Timepoint: After 2 cycles of intensive chemotherapy / Pre-alloHCT
Recommended assay: MFC
Recommended tissue: Bone marrow (BM)

MRD % (LAIP+ OR DfN+ BLASTS/CD45-EXPRESSING CELLS)	QUANTITATIVE MRD BURDEN	QUALITATIVE MRD RESPONSE
<0.01%[12] OR <LOD[12]	Negative	Optimal
≥0.01% to <0.1% AND >LOD	Low-level positive	Warning
≥0.1%	Positive	High risk of treatment failure

[12]Requirements for a sample that qualifies to determine MRD negativity: ≥500,000 CD45-expressing cells assessed for the best aberrancy(s) available (see recommendation B10). This results in LOQ at 50 LAIP cells (0.01%) and LOD at 20 LAIP cells (0.004%).

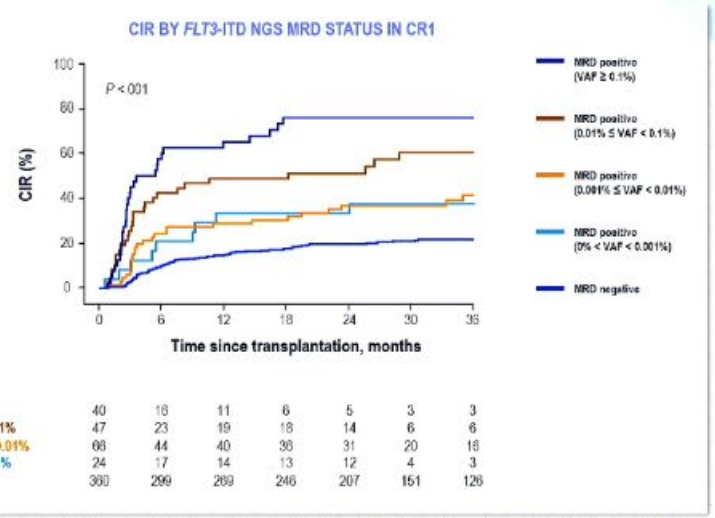
LIVE GOYA

IS14 Comprehensive Care of FLT3+ AML Patients: Pre-Transplant Assessment and Post-Transplant Management | Daiichi Sankyo

Sunday 14:30 - 16:00

FLT3-ITD MRD STRONGLY ASSOCIATED WITH OUTCOMES[a]

NO "SAFE" LEVEL OF *FLT3*-ITD PERSISTENCE IN CR1, BUT "MRD4" (0.01%) ASSOCIATED WITH HIGHEST RISK OF RELAPSE AND DEATH



Stratifying patients with AML in CR1 before allo-HCT by their level of residual *FLT3*-ITD revealed an **increased risk of relapse in those with higher disease burden** (n=537)

Allo-HCT, allogeneic haematopoietic cell transplant; AML, acute myeloid leukaemia; CIR, cumulative incidence rate; CR1, first complete remission; FLT3, FMS-like tyrosine kinase 3; ITD, internal tandem duplication; MRD, measurable residual disease; NPM1, nucleophosmin 1; VAF, variant allele frequency.

Dillon LW, et al. JAMA Oncol. 2024;10(8):1104–1110.

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Jurjen Versluis, EBMT 2026

Dillon LW, Gui G, Ravindra N, et al. Measurable Residual *FLT3* Internal Tandem Duplication Before Allogeneic Transplant for Acute Myeloid Leukemia. *JAMA Oncol.* 2024;10(8):1104–1110. doi:10.1001/jamaoncol.2024.0985

C.Ceballos …. M de la Cruz Viguria: Clinical outcomes of Azacitidine-Venetoclax in relapsed AML after allogeneic hematopoietic stem cell transplantation: A retrospective study of the ASOVASNA cellular therapy group

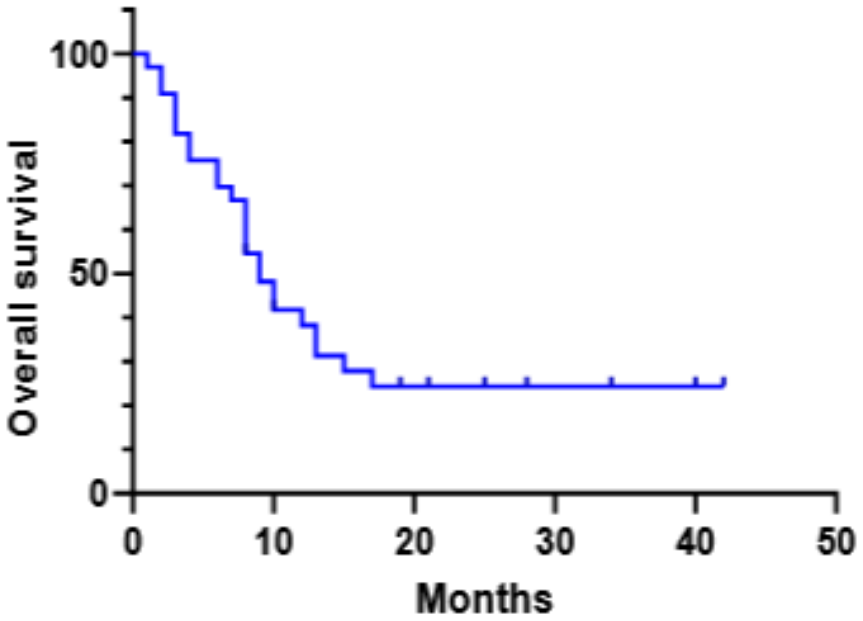


Figure 1.

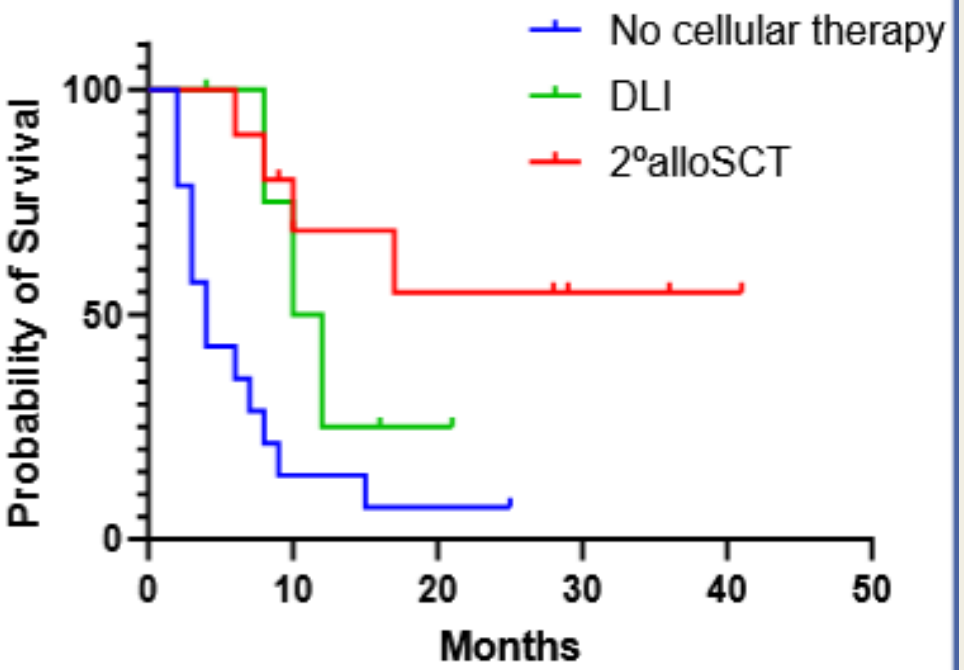


Figure 2.

K. Schreiner… H. Schmetzer: Adaptive and myeloid dynamics after allogeneic stem cell transplantation in acute or chronic GvHD undergoing ECP versus non GVHD and healthy donors

Messzeitpunkte: Start und Tag 90 der Therapie

Parameter: adaptiv (B-/T-Zellen: activated, memory, regulatory)

Parameter: myeloisch (DC-Zellen, Monozyten, myeloid derived suppressive cells)

NoGvHD vs. Healthy: Baseline (d0)

- Adaptive: Tregs ↓, T_{em} ↑, T_{cm} ↑, Bregs ↑
- Myeloid: DC_{tol} ↓, Mo ↓

cGvHD vs. NoGvHD: Baseline (d0)

- Adaptive: T_{mem} ↑, Tregs ↓, Bregs ↓
- Myeloid: DC_{tol} ↓, Myeloid derived suppressive cells (MDSCs) ↓

aGvHD vs. NoGvHD: Baseline (d0)

- Adaptive: strong late T cell proliferation ↑, Tregs ↓, B cells ↓
- Myeloid: Mo ↓, DC_{tol} ↓

cGvHD vs. NoGvHD: Post-treatment (d90)

- Adaptive: T_{mem} still ↑, but lower compared to d0, Tregs still ↓ despite partial recovery
- Myeloid: activated DCs stay ↑, MDSCs ↓

aGvHD vs. NoGvHD: Post-treatment (d90)

- Adaptive: T_{mem} ↑, activated T cells ↑, Tregs still ↓, B cells still ↓
- Myeloid: Mo still ↓, DC_{tol} ↑

K. Schreiner… H. Schmetzer: Adaptive and myeloid dynamics after allogeneic stem cell transplantation in acute or chronic GvHD undergoing ECP versus non GVHD and healthy donors

No response to ECP vs. response to ECP: Baseline (d0)

- Adaptive: activated T cells ↑, Tregs ↑↑, T_{cm} ↑, T_{cpm} ↑ ($2B4^+$ ↑↑, $TIM3^+$ ↑), Memory B cells (B_{mem}) ↑↑↑
- Myeloid: Mo ↓, MDSCs ↓

Refractory cGvHD after ECP vs. complete response after ECP: Baseline (d0)

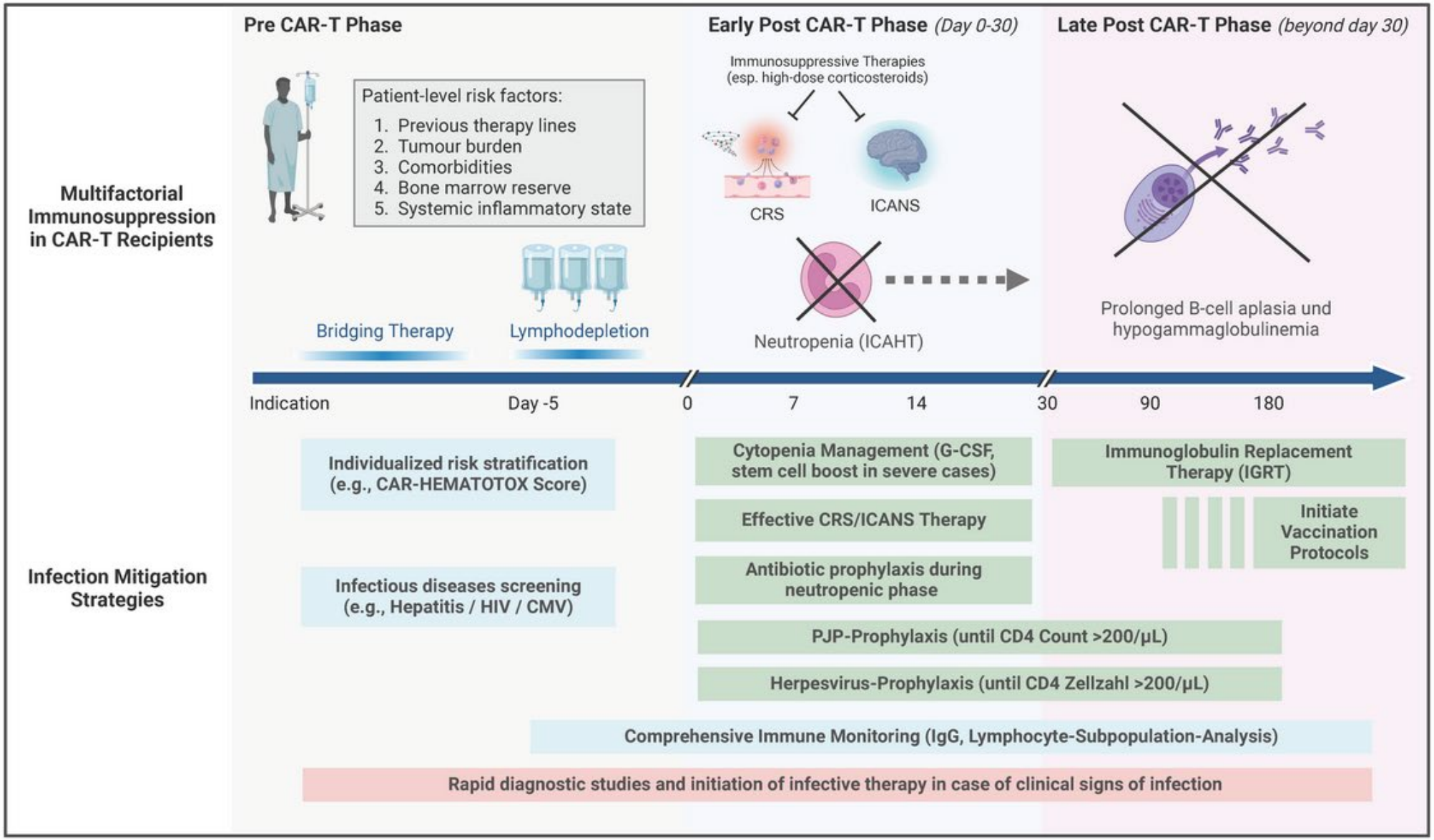
- Adaptive: activated T cells ↓ ($CD28^+$), Tregs ↑↑, T_{cm} ↑↑, T_{cpm} ↑ ($2B4^+$ ↑↑, $TIGIT^+$ ↑), B_{mem} ↑↑↑
- Myeloid: Mo↓, MDSCs ↓, Mo_{cpm} ↑ ($2B4^+$, $Tim3^+$)

Clinical response to ECP: d90 vs. d0

- Adaptive: activated T cells ↑↑↑ ($CD28^+$), Tregs ↓, T_{mem} ↑↑↑, B_{mem} ↓, T_{cpm} ↓↓ ($LAG3^+$, $KLRG1^+$, $TIGIT^+$)
- Myeloid: Mo ↑, DC_{tol} ↑, Mo_{cpm} ↑ ($2B4^+$, $TIM3^+$, $PD\text{-}L1^+$)

Patients with complete response after ECP: d90 vs. d0

- Adaptive: B cells ↓, B_{mem} ↓, T_{cpm} ↓ ($PD\text{-}L1^+$ ↓↓↓, $KLRG1^+$ ↓↓, $TIGIT^+$ ↓↓↓)
- Myeloid: DC_{cpm} ↓ ($2B4^+$ ↓↓, $LAG3^+$ ↓↓↓), DC_{tol} ↑↑



Secondary Malignancies

Created in BioRender. Rejeski, K. (2025) https://BioRender.com/e45s994

CAR-T Cell Pharmakokinetics – EBMT Handbook and Passport - EBMT GoCART Coalition

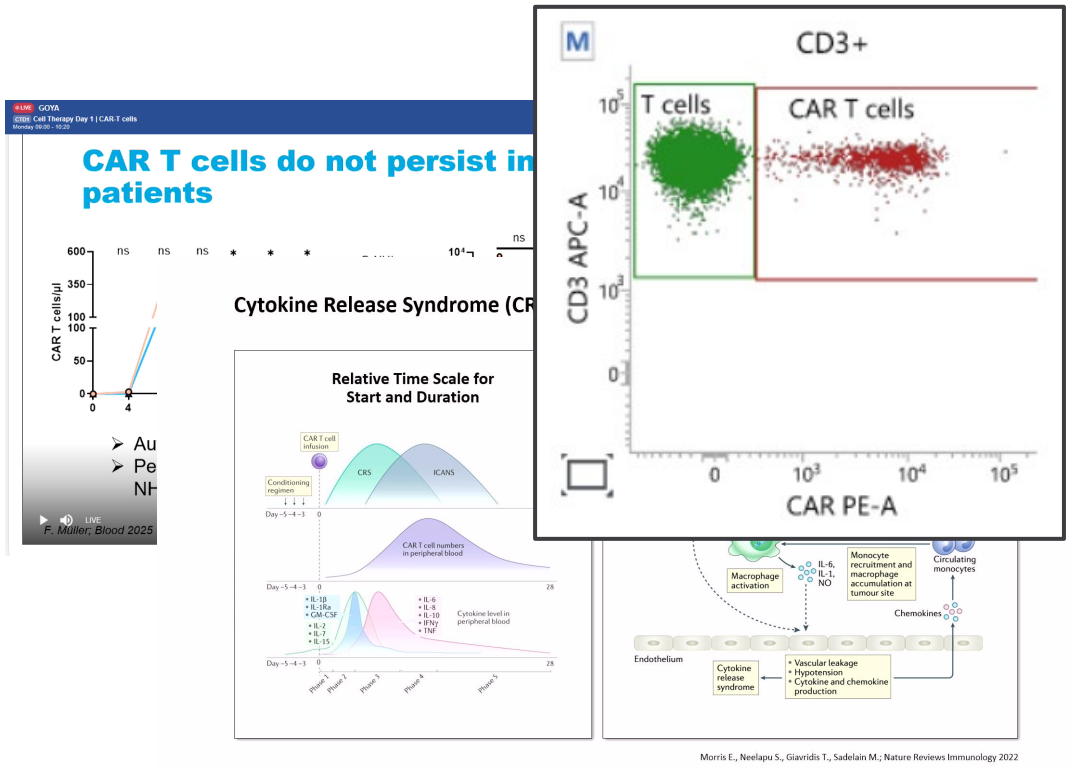
1. Expansion and persistence correlates with toxicity, efficacy and long term outcome
2. It is the core immunity biomarker
   - Modulators are:
   - T-cell subset composition of initial product (particularly balance of memory vs effector t cells or presence of Tregs
   - Distinct genomic integration sites of the CAR-T Construct
   - CAR-Structure (particularly the choice of and number of costimulatory domains (CD28 vs 41BB)
   - Interaction with tumour, surrounding immune milieu and host
   - Development of anti-CAR Immune response (attributed to immune recognition of murine-derived sequences within certain anti CD19 and anti-BCMA cells)

CAR-T Cell Pharmakokinetics – EBMT Handbook and Passport - EBMT GoCART Coalition

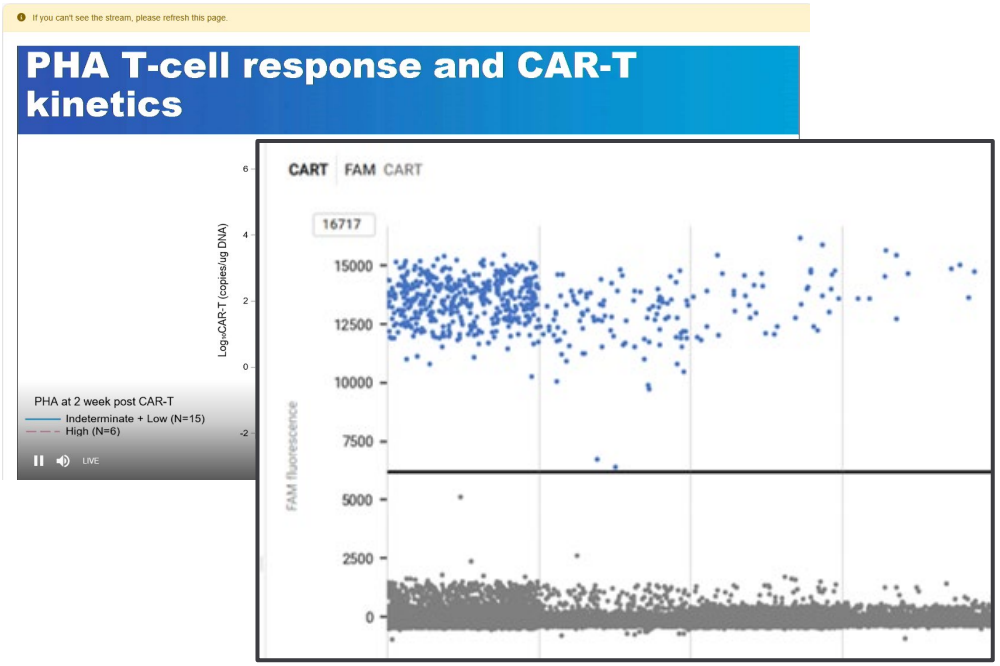
1. Expansion: C_{max} and AUC $_{0\text{-}28}$ (CAR-T cell levels detected in 0-28 days postinfusion) (PB/BMMC/CSF/Tumor tissue)
2. What methods can be used to detect CAR-T cells?
   - **FACS** based methods detect CAR-proteins or co-expressed markers (esp. Useful for early postinfusion for monitoring toxicity and response
   - **qPCR or dPCR** (superior sensitivity and precision) gold standard for low-level CAR-T detection and assessing long-term persistence
3. Why:
   - r/r B-ALL CAR-T persistence is associated long-term disease free survival (28)
   - r/r DLBCL CAR-T persistence at 6 months is associated with lower relapse rates 29% vs 60% (29)
   - Patients with CR had greater expansion at peak than PR/NR and a longer median CAR-T lifespan (8.3 vs. 1.0 months)

Wie werden CAR-T Zellen bestimmt? EBMT 2026

Mittels Immunphänotypisierung (cells/µl)

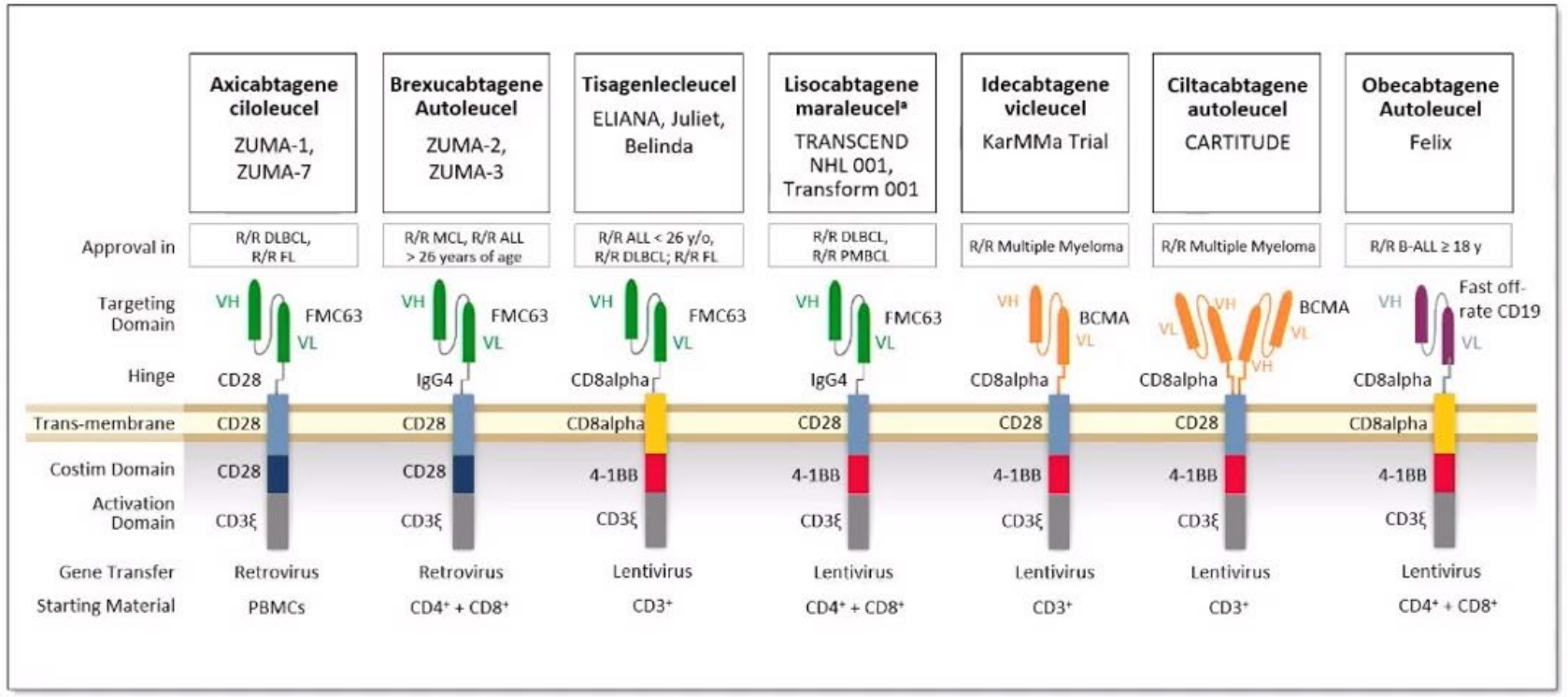


Mittels dPCR und qPCR (copies/µl)

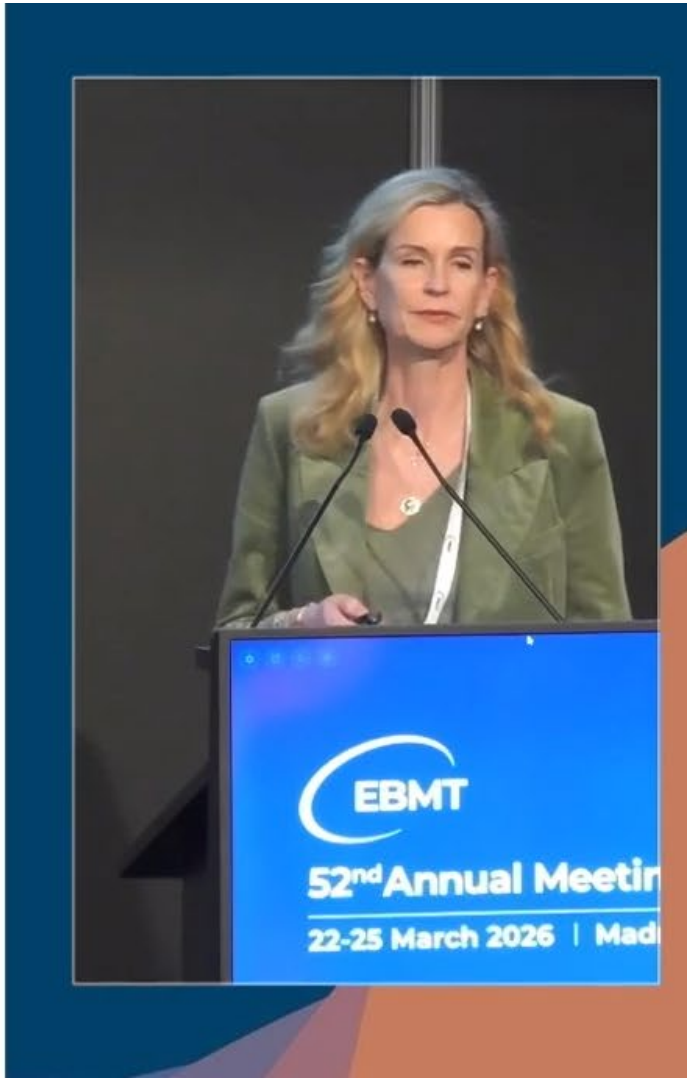


7 CART Products approved: 5/7 targeting CD19 and 2/7 targeting BCMA

Differences in CART Design: Spacer-, Transmembrane and co-stimulatory Domains, Type of Gene Transfer, Starting Material



Adapted from v. d. Steegen SJ, et al. Nat Rev Drug Discov 2015; 14:499–509; Larson et al, Nature Reviews Cancer 2021, Roddie et al, NEJM 2024



JM Cerezo Martin: Non-infectious complications after CAR-T-Cell-Therapy

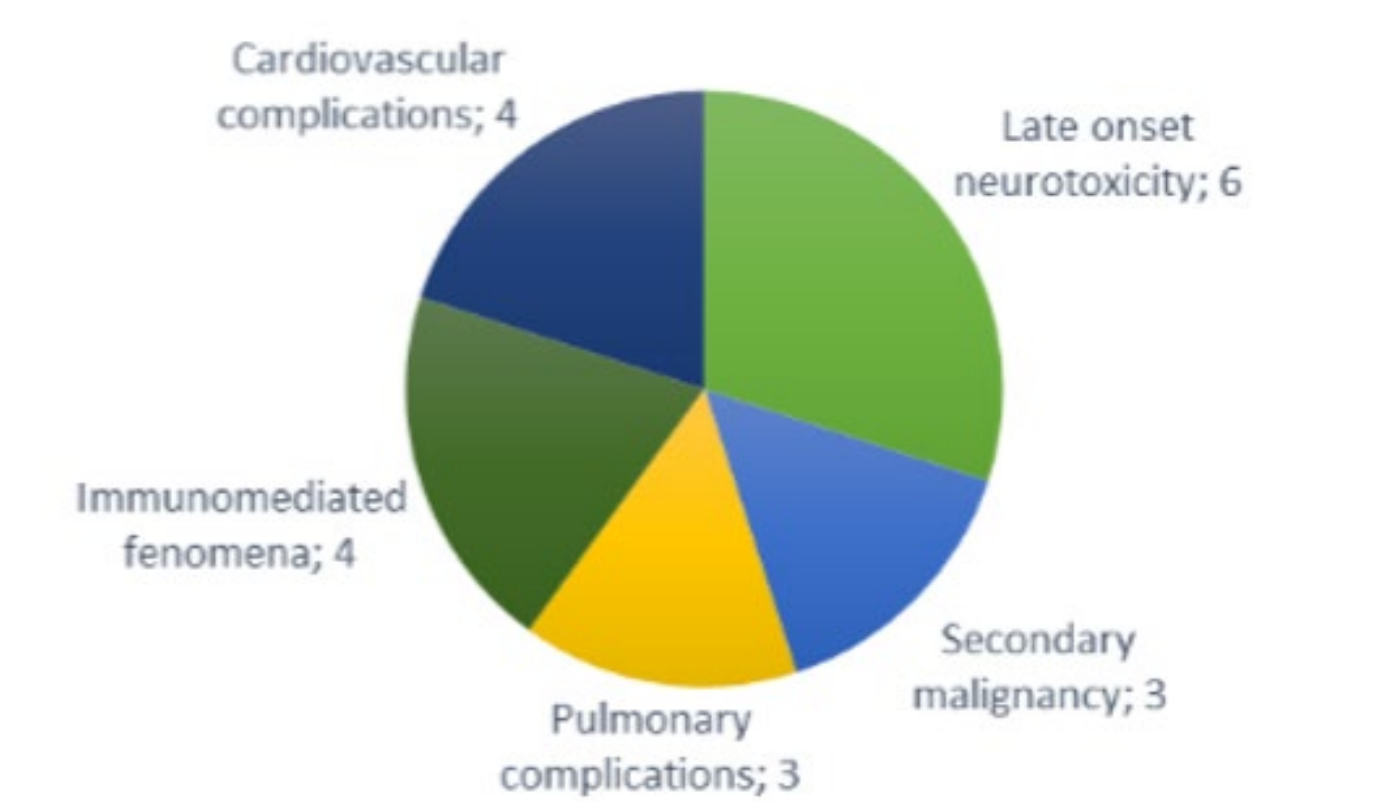
60 Patienten (m,f), 32 wg. Myelom

37-79 Jahre

44% vorher HD + autologe SZT

1-5 Vortherapien

10% in CR, 38% rr

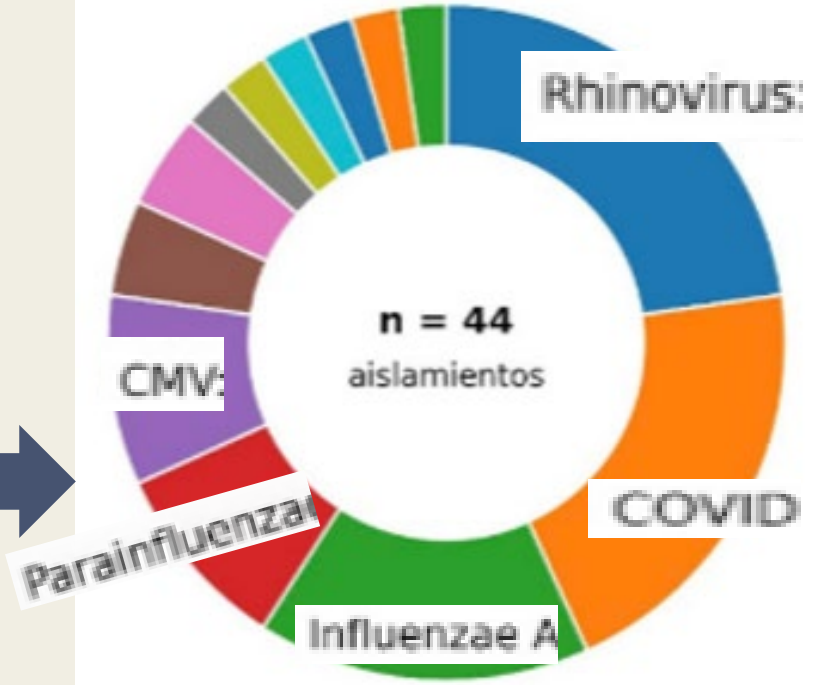


H. Cruz Barquin: Risk of infection after CAR-T-Cells is high and difficult to predict

94 Patienten, 36-81 Jahre, 60% DLBCL, 1/3 nach auto-SZT, 85% kommerzielles CAR-Produkt

	TOTAL		
	D30 % (95% CI)	D30-90 % (95% CI)	D>90 % (95% CI)
CI bacterial infections	22 (14-31)	28 (20-38)	32 (23-43)
CI fungal infections	1 (0.2-6)	4 (1-12)	9 (4-19)
CI viral infections	7 (4-15)	21 (14-32)	33 (24-45)
CI global infections	27 (18-36)	44 (34-55)	61 (50-72)

Values are % (95% CI). D indicates days after infusion (D30: 0-30; D30-90: 31-90; D>90: >90).
Abbreviations: CI, cumulative incidence.



Zusammenfassung

1. Die Menge an FLT3-ITD-Resterkrankung in CR1 vor allo-SZT
   bestimmt die Rezidivwahrscheinlichkeit nach allo-SZT.
2. Aza-Ven als Rezidivtherapie nach allo-SZT: 57,6% ORR, medianes OS 4 Monate,
   bei Kombination mit DLI 10 Monate, bei Zweittransplantation 17,3 Monate
3. Der Immun-Setpoint zu Beginn einer ECP-Therapie entscheidet über das Ansprechen,
   die ECP führt zum Erreichen eines neuen Gleichgewichts, ist kein Neustart
4. Expansion und Persistenz der CAR-T-Zellen sind wesentlich für den Langzeiterfolg,
   Messung im FACS oder als qPCR (Goldstandard für low-level/Langzeit-Follow up)
5. Nicht-infektiöse Komplikationen nach CAR-T-Therapien: late-onset-Neurologie, Autoimmunphänomene,
   IEC-Hämophagozytose, Neoplasien (hämatologisch + solide)
6. Infektiöse Komplikationen nach CAR-T-Therapie:
   Cave insbesondere respiratorische Virusinfektionen in der mittel- und langfristigen Nachsorge!

Programm

16.00 **Come together & Industrieausstellung**

16.25 Uhr **Begrüßung** Claudia Lengerke, Tübingen

Panel I Stammzelltransplantation und Gentherapie

16.30-16.45 Uhr

Konditionierung für allogene SZT

Christoph Faul, Tübingen

16.45-17.00 Uhr

SZT und Gentherapie für nicht maligne Erkrankungen

Peter Lang, Julia Skokova, Tübingen

17.00-17.15 Uhr

Transplantatquelle und Spenderauswahl

Tim Flaadt, Tübingen

17.15-17.30 Uhr

Post allo-SZT Immunrekonstitution/Infektionen

Adrian Fehn/Benedikt Obermaier, Tübingen

17.30-17.45

Nachsorge und Diagnostik nach allogener SZT und CAR-T

Kristina Reuß, Friedericke Schwartz Tübingen

17.45-18.00 Uhr Panel Diskussion I

Moderation & Diskussion: Schaich, Kaufmann, Greiner

18.00-18.30 Pause mit Industrieaustellung

Panel II CAR-T Zelltherapie und adoptive Zelltherapie

18.30-18.45 Uhr

CAR-T Zelltherapie Behandlungsstandards

Wolfgang Bethge, Tübingen

18.45-19.00 Uhr

CAR-T neue Targets und Indikationen

Malte Rörden, Tübingen

19.00-19.15 Uhr

CAR-T bei Autoimmunerkrankungen

Jörg Henes, Tübingen

19.15-19.30 Uhr

GMP-Manufactoring, Point of Care CAR-T

Luca Hensen, Tübingen

19.30-19.45 Uhr

NK Zellen und CAR NK Zelltherapie

Claudia Lengerke, Tübingen

19.45-20.00 Uhr

Moderation & Diskussion: Jawhar, Medinger, Bethge

und am Ende....

Vielen Dank für Ihre Aufmerksamkeit

Universitätsklinikum Tübingen