Massimiliano Gambella

Ematologia e terapie cellulari
IRCCS Ospedale Policlinico San Martino, Genova

CAR-T cells: nuove indicazioni e nuove flow-chart nella terapia dei linfomi non Hodgkin: update

No disclosures

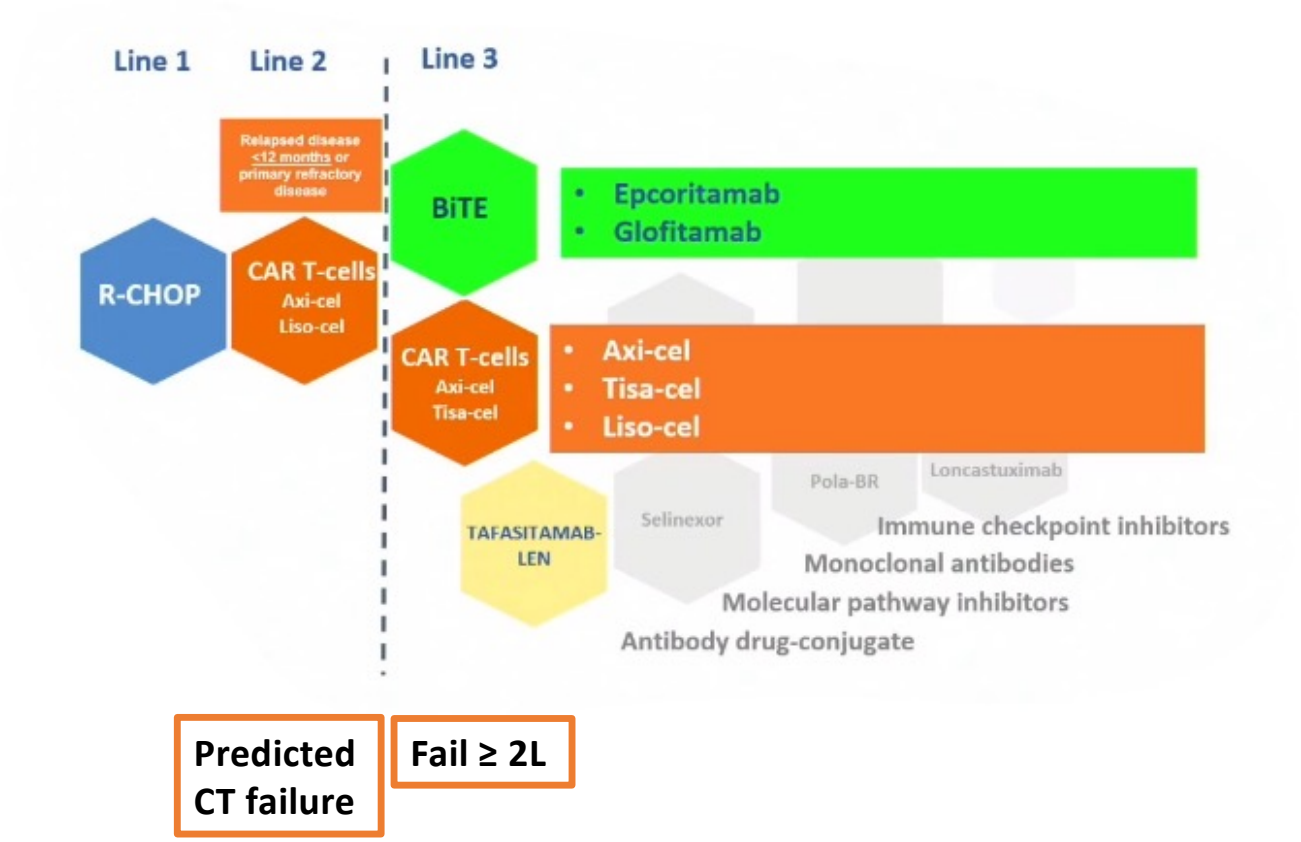
Aggressive B-cell Lymphoma

Updates from global trials

Real life

- **Efficacy**
- **Toxicity -> NRM**
- **Special populations**

Second-line



Thieblemont. EHA 2022, adapted

Aggressive B-cell Lymphoma

Updates from global trials

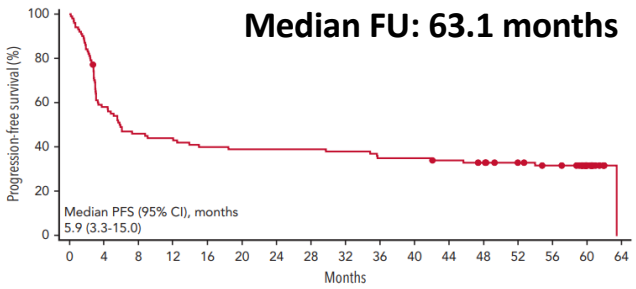
Real life
- Efficacy
- Toxicity -> NRM
- Special populations

Second-line

DLBCL in R/R aggressive B cell lymphoma

ZUMA-1 - 5 yrs follow-up

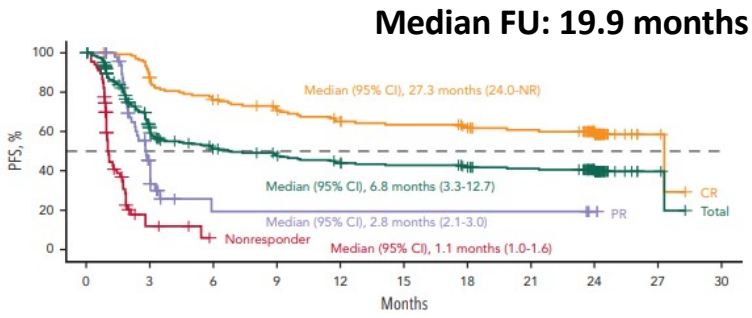
	N = 101
Best response, n (%, 95% CI)	
Objective response	84 (83, 74-90)
CR	59 (58, 48-68)
PR	25 (25, 17-34)



Neelapu et al. Blood 2024

TRANSCEND - 2 yrs follow-up

	Efficacy-evaluable set (N = 257)
ORR,* n (%, 95% CI†)	187 (73%, 66.9-78.1)
CR rate,* n (%, 95% CI†)	136 (53%, 46.6-59.2)

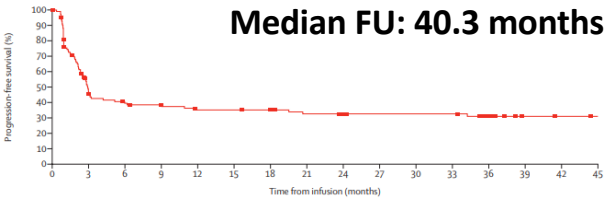


Abramson et al. Blood 2024

JULIET - 3 yrs follow-up

	Patients (n=115)
Best overall response	
Complete response	45 (39%)
Partial response	16 (14%)
Stable disease	15 (13%)
Progressive disease	30 (26%)
Unknown*	9 (8%)
Overall response rate	61 (53·0%, 43·5–62·4)
Median time to first response, days	29·0 (28·0–31·0)

Data are n (%), n (%, 95% CI), or median (IQR). *Data for the last assessment not available.



Schuster et al. Lancet Oncology 2021

Prospective trials – death by event

n (%)	N = 101						
	Total	Year 1	Year 2	Year 3	Year 4	Year 5	Year >5
Patients who died	59 (58)	40 (40)	10 (10)	4 (4)	3 (3)	1 (1)	1 (1)
Primary cause of death							
Progressive disease*	45 (45)	32 (32)	9 (9)	3 (3)	0	1 (1)	0
AE†	4 (4)	3 (3)	1 (1)	0	0	0	0
Secondary malignancy	1 (1)	0	0	0	0	0	1 (1)
Other‡	9 (9)	5 (5)	0	1 (1)	3 (3)	0	0

Neelapu et al. Blood 2024

Key Inclusion Criteria

1. Histologically confirmed:
    - Diffuse Large B Cell Lymphoma (DLBCL)
    - Primary Mediastinal Large B Cell Lymphoma (PMBCL)
    - Transformation Follicular Lymphoma (TFL)
    - High grade B-cell lymphoma (HGBCL)

Excluded

CNS-DLBCL

Richter's transformation

Eastern cooperative oncology group (ECOG) performance status of 0 or 1

Excluded

Frail (ECOG)

Key Exclusion Criteria

1. History of malignancy other than nonmelanoma skin cancer or carcinoma in situ (e.g. cervix, bladder, breast) or follicular lymphoma unless disease free for at least 3 years
2. History of allogeneic stem cell transplantation
3. Prior chimeric antigen receptor (CAR) therapy or other genetically modified T cell therapy
4. Presence of fungal, bacterial, viral, or other infection that is uncontrolled or requiring intravenous (IV) antimicrobials for management. Simple urinary tract infection (UTI) and uncomplicated bacterial pharyngitis are permitted if responding to active treatment
5. History of human immunodeficiency virus (HIV) infection or acute or chronic active hepatitis B or C infection. Individuals with history of hepatitis infection must have cleared their infection as determined by standard serological and genetic testing per current Infectious Diseases Society of America (IDSA) guidelines
6. Individuals with detectable cerebrospinal fluid malignant cells, or brain metastases, or with a history of central nervous system (CNS) lymphoma or primary CNS lymphoma, cerebrospinal fluid malignant cells or brain metastases
7. History or presence of CNS disorder such as seizure disorder, cerebrovascular ischemia/hemorrhage, dementia, cerebellar disease, or any autoimmune disease with CNS involvement

Aggressive B-cell Lymphoma

Updates from global trials

Real life

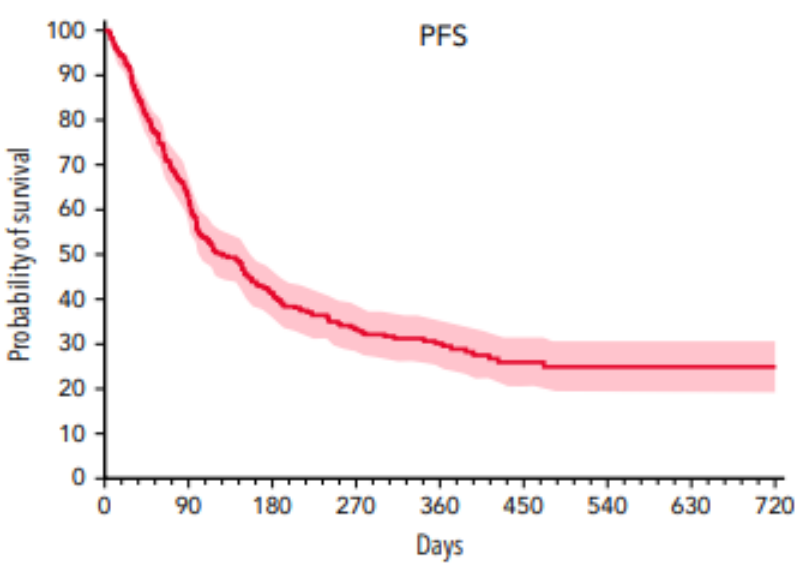
- **Efficacy**
- **Toxicity -> NRM**
- Special populations

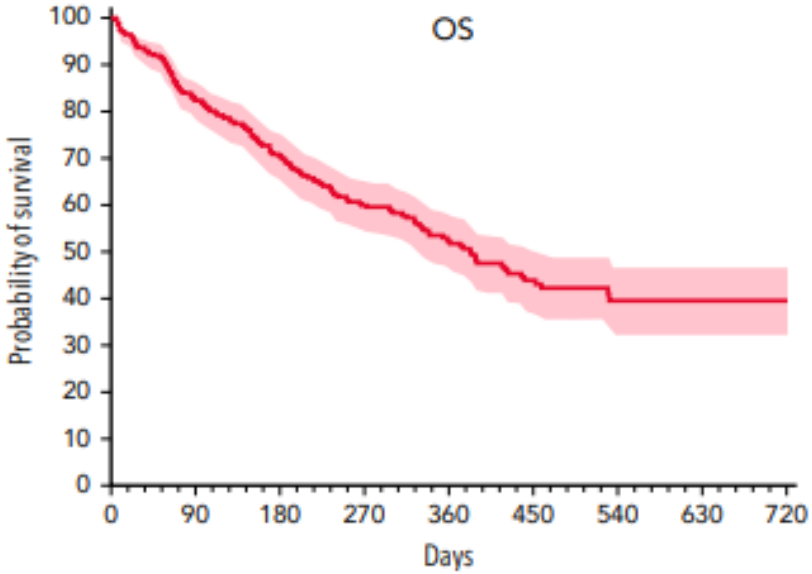
Second-line

LYMPHOID NEOPLASIA

GLA/DRST real-world outcome analysis of CAR T-cell therapies for large B-cell lymphoma in Germany

2018-2021
N = 354
Median FU = 11 months





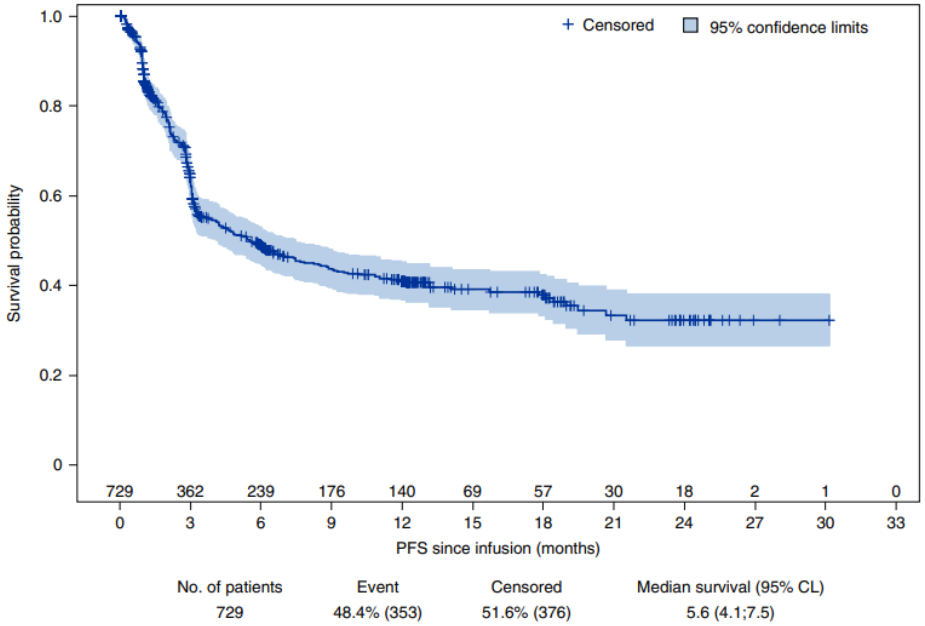
Betghe et al. Blood 2022

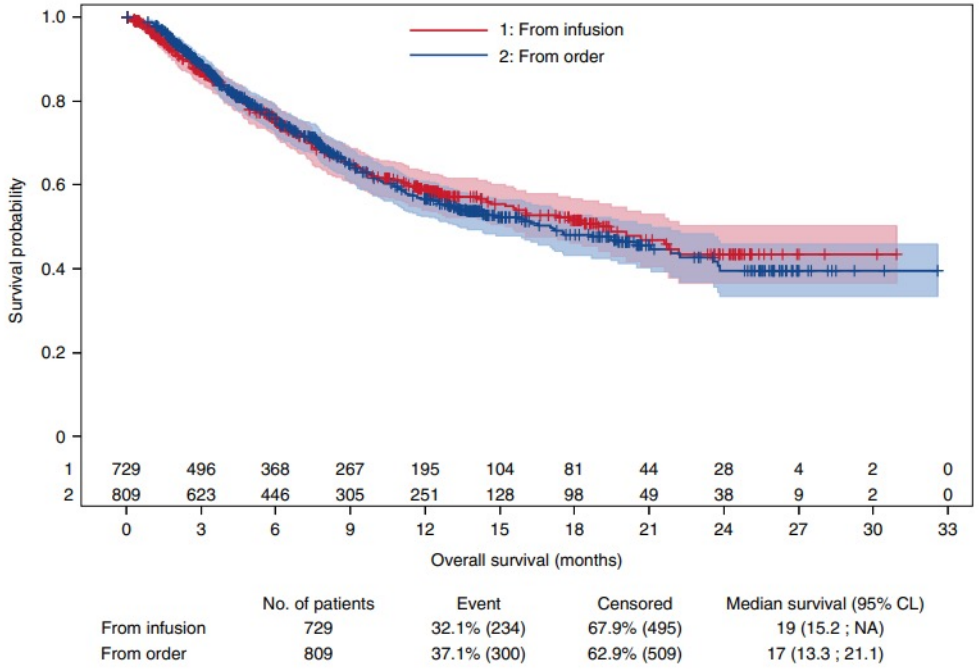
nature medicine
ARTICLES
https://doi.org/10.1038/s41591-022-01969-y
Check for updates

OPEN

A real-world comparison of tisagenlecleucel and axicabtagene ciloleucel CAR T cells in relapsed or refractory diffuse large B cell lymphoma

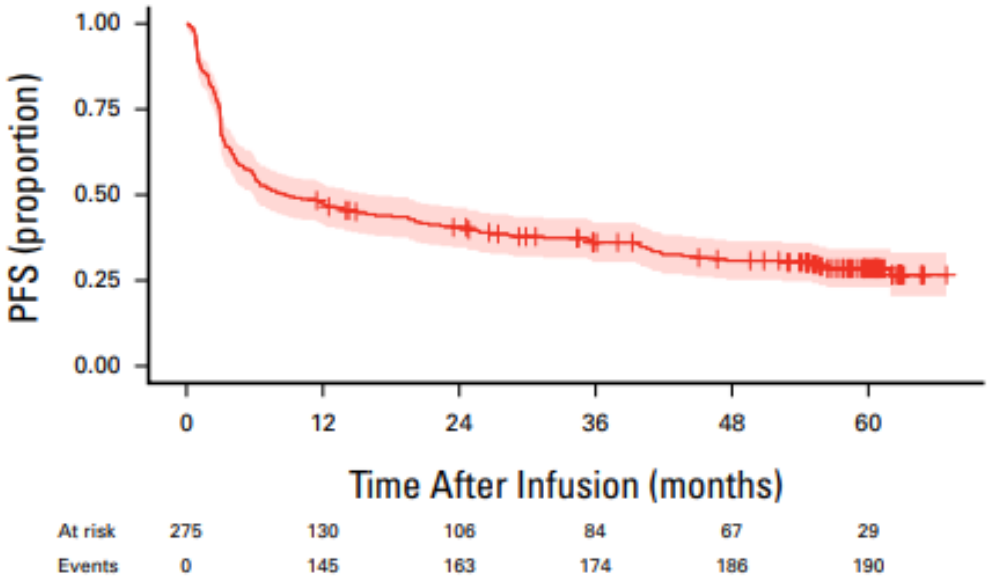
2019-2021
N = 729
Median FU = 11.7 months





Bachy et al. Nature Medicine 2022

Five-Year Follow-Up of Standard-of-Care Axicabtagene Ciloleucel for Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium



2017-2018
N = 275
Median FU = 58 months

Median PFS = 8.7months

Landmark PFS, %
- **1yr = 47.3**
- **3yr = 36.1**
- **5yr = 28.5**

Jain et al. JCO 2024

Aggressive B-cell Lymphoma

Updates from global trials

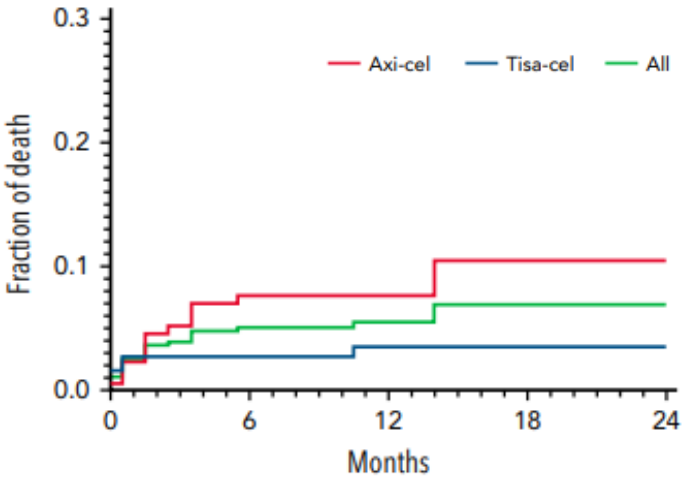
Real life

- Efficacy
- **Toxicity -> NRM and immune suppression**
- Special populations

Second-line

LYMPHOID NEOPLASIA

GLA/DRST real-world outcome analysis of CAR T-cell therapies for large B-cell lymphoma in Germany

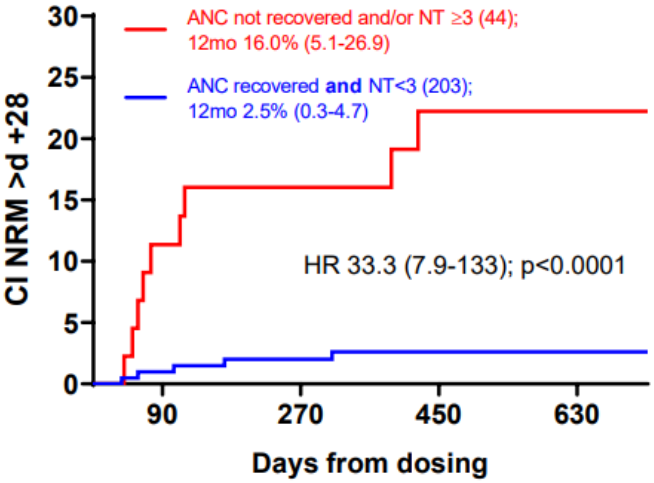


Non-relapse Mortality

12m CI NRM: 5.5%
- Axi-cel: 10.4%
- Tisa-cel: 3.5%

NR deaths
- 62% infections (13 pts, 8 bacterial)
- 10% ICANS (2 pts)

67% NRM events beyond day +28



Betghe et al. Blood 2022

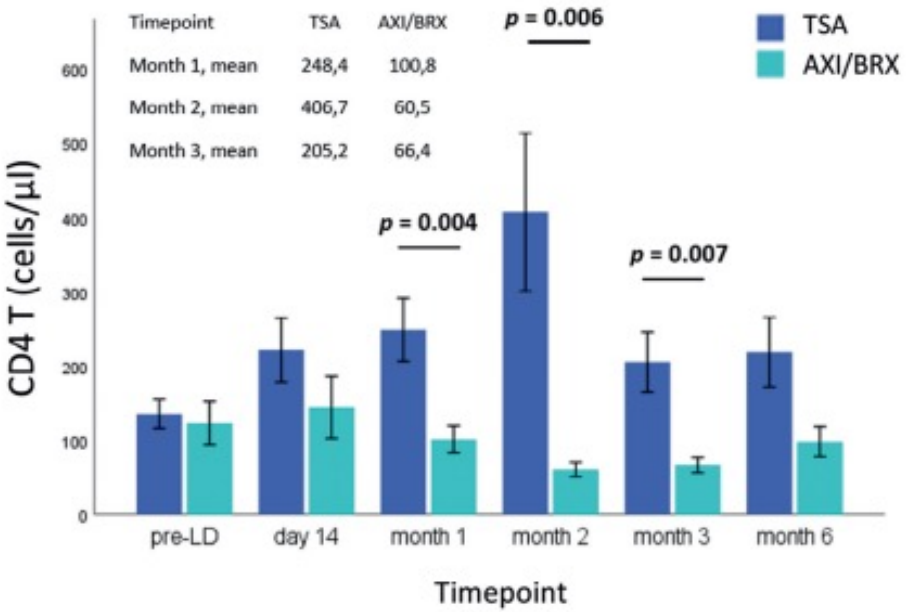
	Axicel	Tisacel	Lisocel
Fluda mg/m2 day 1-3	30	25	30
CY mg/m2 day 1-3	500	250	300

Table 3 | Toxicity after CAR T infusion according to CAR T product in the PSM cohorts

	axi-cel		tisa-cel		*P*
	n = 209		*n* = 209		
CRS of any grade	180	(86.1%)	158	(75.6%)	0.006
Grade 1–2	169	(80.9%)	139	(66.5%)	<0.001
Grade ≥3	11	(5.3%)	19	(9.1%)	0.130
ICANS of any grade	102	(48.8%)	46	(22.0%)	<0.001
Grade 1–2	73	(34.9%)	40	(19.1%)	<0.001
Grade ≥3	29	(13.9%)	6	(2.9%)	<0.001

Bachy et al. Nature Medicine 2022

	axi-cel		tisa-cel		*P*
	n = 209		*n* = 209		
Neutropenia of any grade at M1	124	(59.3%)	57	(27.3%)	<0.001
Grade 1–2	71	(34.0%)	37	(17.7%)	<0.001
Grade ≥3	53	(25.4%)	20	(9.6%)	<0.001



Gambella et al. eJHaem 2024

Aggressive B-cell Lymphoma

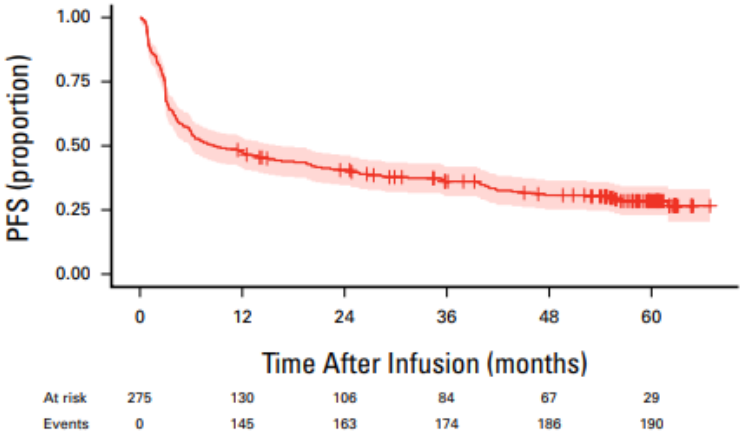
Updates from global trials

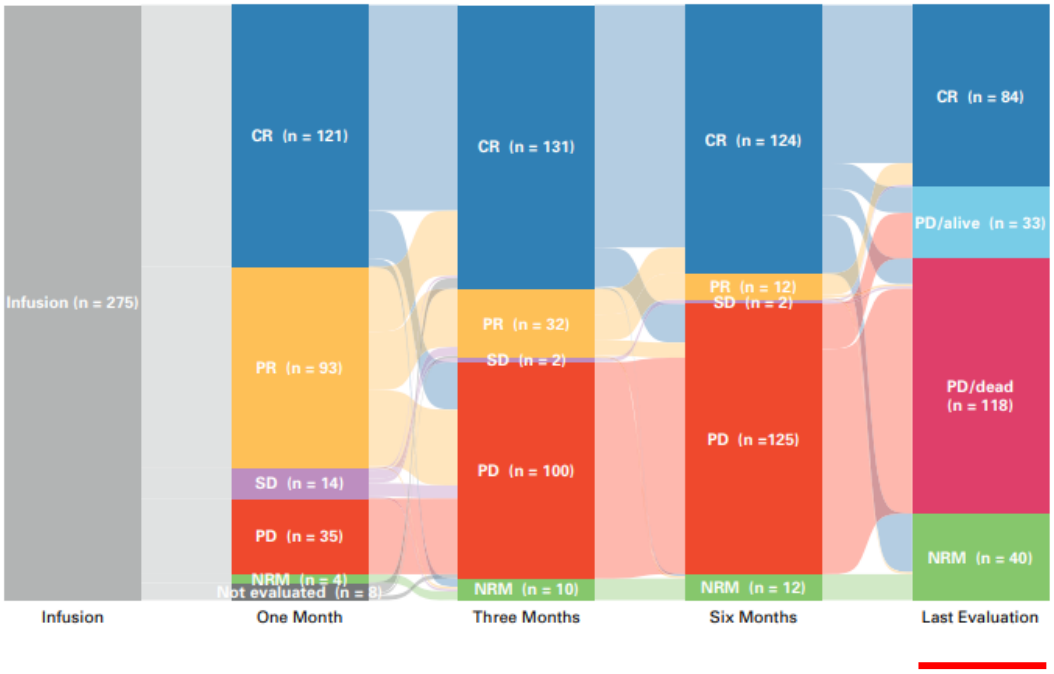
Real life

- Efficacy
- **Toxicity -> NRM and age / comorbidities**
- Special populations

Second-line

Five-Year Follow-Up of Standard-of-Care Axicabtagene Ciloleucel for Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium





N = 354

Median FU = 58 months

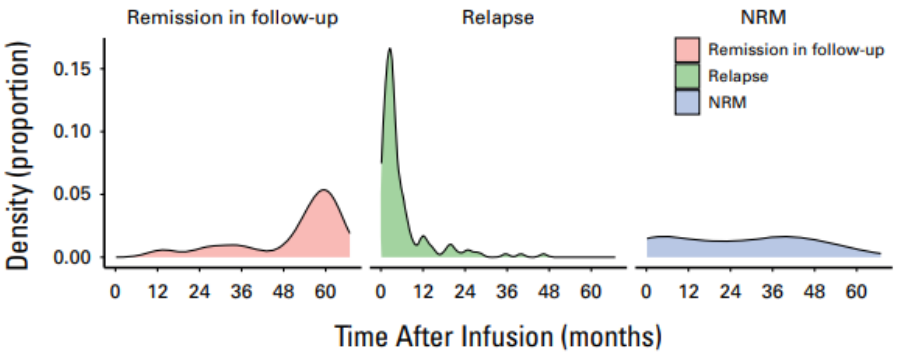
Jain et al. JCO 2024

Five-Year Follow-Up of Standard-of-Care Axicabtagene Ciloleucel for Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium

Cause of Death	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6 or Later	Total
Progressive disease	74	28	11	4	1	0	118
Infection	8	2	4	6	1	0	21
Secondary malignancy	0	3	1	3	1	1	9
CAR-T toxicity[a]	3	0	0	0	0	0	3
Unknown/Other[b]	2	1	1	1	2	0	7

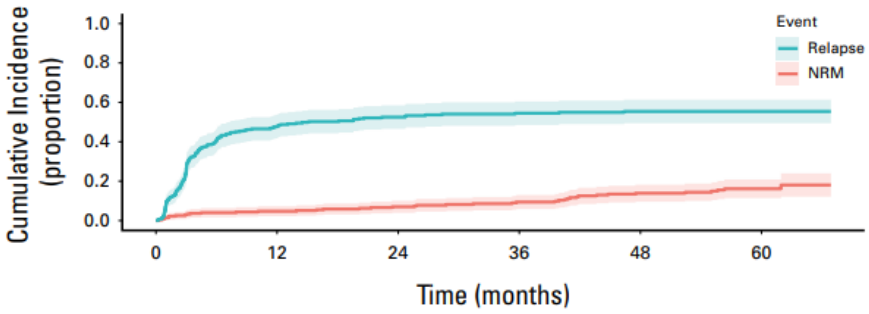
Infection (21/275 pts) -> main determinant of NRM

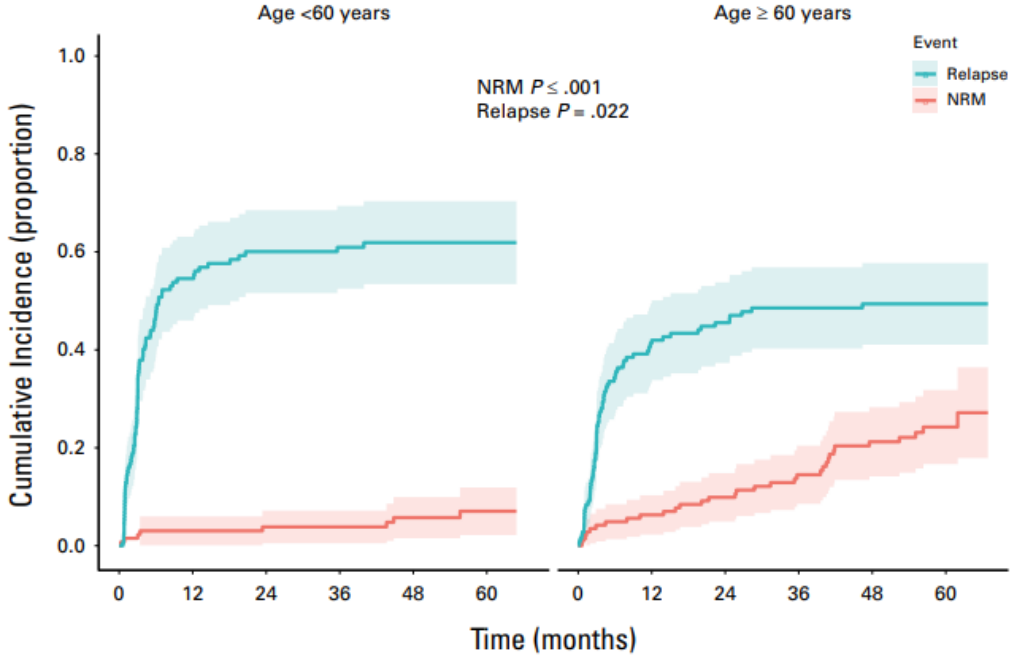
- Unclassified 6
- Pneumonia 5
- Bacterial Sepsis 4
- COVID-19 disease 2
- Candidemia 3 (1 + PJP)



Jain et al. JCO 2024

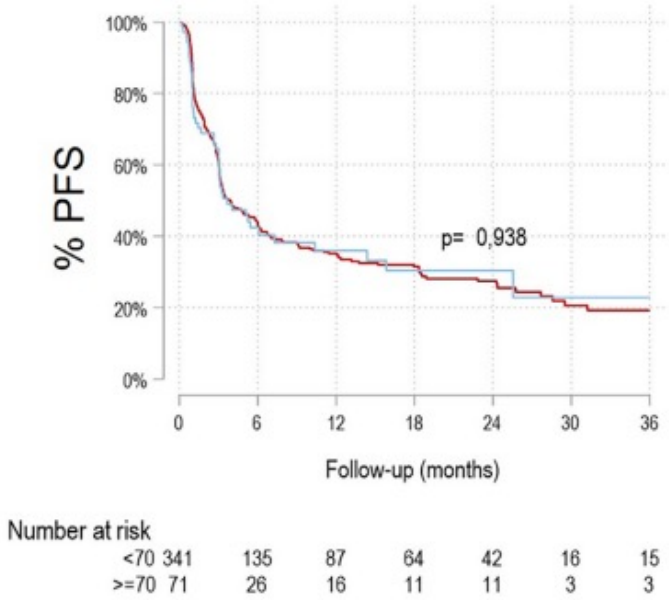
Five-Year Follow-Up of Standard-of-Care Axicabtagene Ciloleucel for Large B-Cell Lymphoma: Results From the US Lymphoma CAR T Consortium





Jain et al. JCO 2024

Anti-CD19 CAR-T Cell Therapy in Elderly Patients: Multicentric Real-World Experience from GETH-TC/GELTAMO



<70 vs ≥ 70
Median Age: 56 vs 73

NO DIFFERENCES

AXI/TSA

HCT-CI

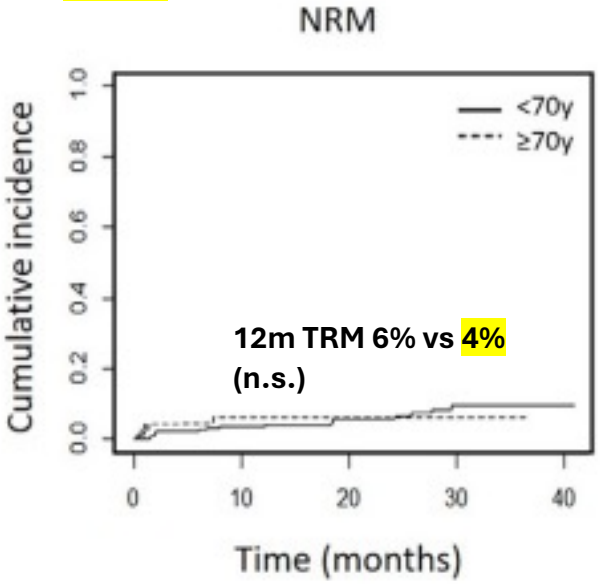
Disease status pre-LD

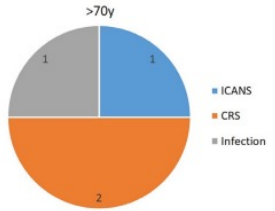
ECOG pre-LD

LDH pre-LD

Apparently, NO selection bias

2019-2023
N = 412
Median FU = 12 months (1-44)

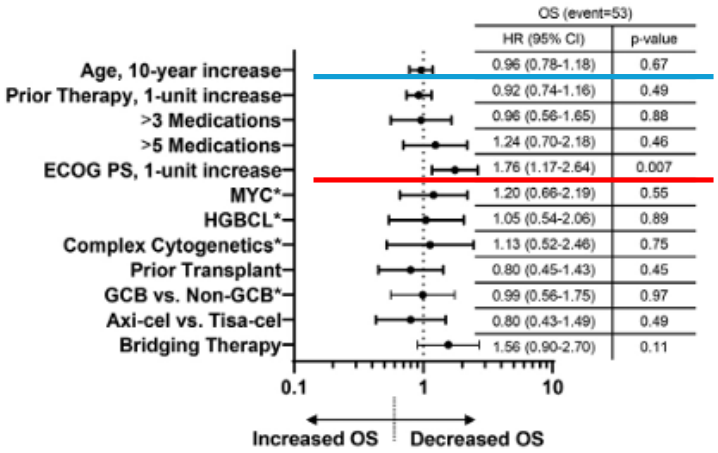


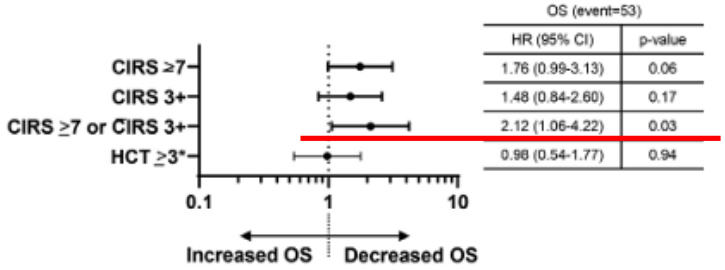


Bailén et al. TCT 2024

CAR-T: comorbidies and outcome

2018-2018
N = 130
Median FU = 13 months





Multivariable Analysis of CIRS ≥7 or CIRS-3+ Accounting for Patient Characteristics*

Characteristic	PFS		OS	
	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
CIRS ≥7 or CIRS-3+	1.70 (0.94-3.06)	.08	2.39 (1.10-5.20)	.03
Age, 10-yr increase	.86 (.96-1.06)	.15	.82 (.65-1.04)	.10
Previous therapy, 1-unit increase	.87 (.71-1.06)	.17	.90 (.71-1.13)	.35
ECOG PS, 1-unit increase	1.43 (.99-2.05)	.05	1.63 (1.06-2.51)	.03
HGBCL*	.87 (.46-1.63)	.66	.97 (.45-2.09)	.94
Complex cytogenetics*	1.15 (.58-2.26)	.69	1.10 (.45-2.67)	.84
GCB vs non-GCB*	.99 (.59-1.66)	.96	1.08 (.58-2.02)	.81
Axi-cel vs tisa-cel	.60 (.34-1.05)	.07	.61 (.31-1.20)	.15

CIRS = comorbidity index rating scale
Total CIRS, median =7
CIRS ≥7 56.9%
CIRS-3+ 56.2%

Age, median = 62.5 (23-82)

Kittai et al. TCT 2021

Aggressive B-cell Lymphoma

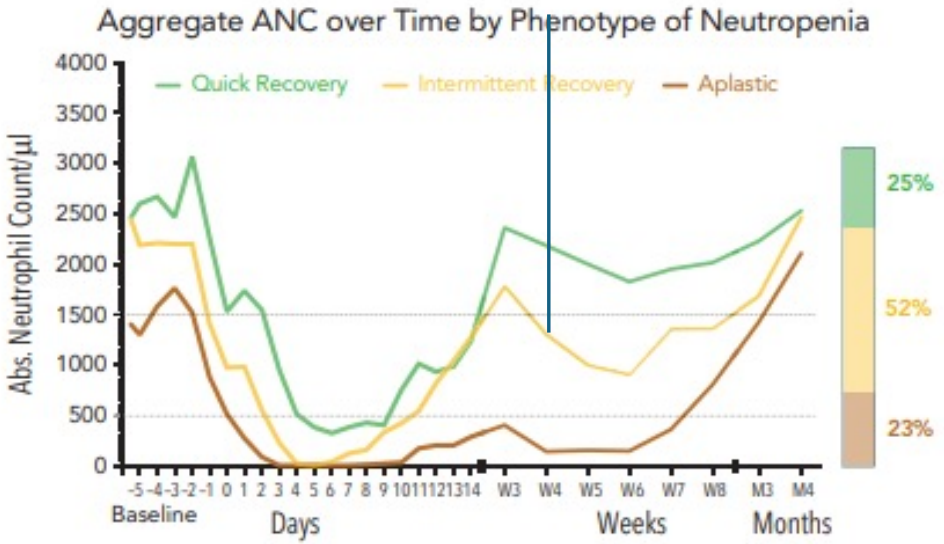
Updates from global trials

Real life

- Efficacy
- **Toxicity -> NRM, what we can do**
- Special populations

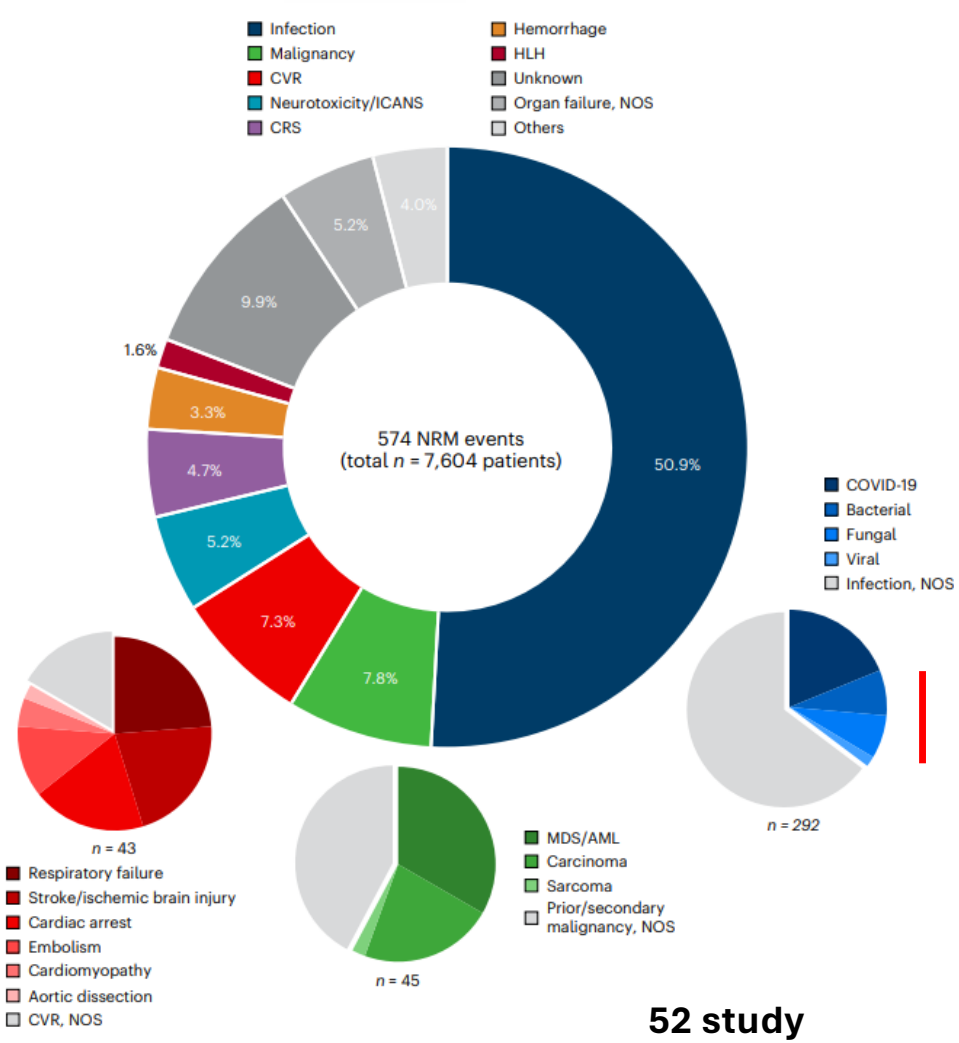
Second-line

(Age), Performance Status, cytopenia, NRM



Rejeski et al. Blood 2021

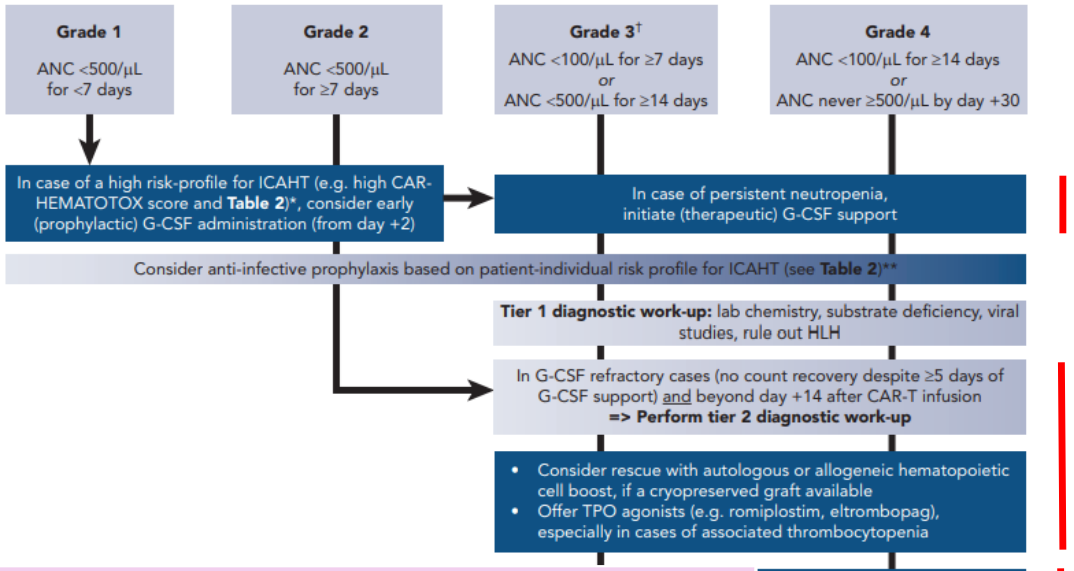
Karnofsky Performance Status (KPS)		Eastern Cooperative Oncology Group Performance Status (ECOG PS)	
Functional Impairment	KPS Grade	ECOG Grade	Functional Impairment
Normal, no evidence of disease	100	0	Fully active, no restriction in pre-disease performace
Minor signs or symptoms	90	1	Restricted in physically strenuous activity but ambulatory and able to carry out light work
Normal activity with effort; some signs or symptoms	80		
Cares for self; unable to carry on normal activity	70	2	Ambulatory; capable of all self-care but unable to work; up more than 50% of waking hours
Occasional assistance required; capable of most self-care	60		
Requires assistance, frequent medical care	50	3	Capable of only limited self-care; confined to bed/chair >50% waking hours
Disabled; requires special care/assistance	40		
Severely disabled; hospitalization indicated	30		
Hospitalization necessary; requires active supportive care	20	4	Not capable of self-care; totally confined to bed/chair
Moribund; progressing rapidly	10		
Dead	0	5	Dead



Cordas dos Santos et al. Nat Med 2024

52 study cohorts
N = 7604

Immune effector cell–associated hematotoxicity: EHA/EBMT consensus grading and best practice recommendations



Allo-SCT, aplastic phenotype -> last resort

ICHAT Grade 4 -> initiate donor search (early approach)

Refractory to G-CSF, TPO agonists, carefully weighed

Optimal timing for Allo-SCT -> 3-6 months after CAR-T

Rejeski et al. Blood 2023

Aggressive B-cell Lymphoma

Updates from global trials

Real life
- Efficacy
- Toxicity
- **Special populations**

Second-line

Special populations

Parameter	ZUMA-1 KTE-C19	JULIET CTL019	TRANSCEND JCAR017
active CNS, secondary	excluded	excluded	allowed
PCNSL	excluded	excluded	excluded (CNS-only)
Richter's	excluded	excluded	not included nor enrolled

Secondary CNS Lymphoma, TRANSCEND NHL 001

Secondary CNS Lymphoma
N = 9
CRS = 1/9 G2
ICANS = 1/9 G3

Efficacy of patients with secondary CNS involvement

	Initial liso-cel infusion[a] (n = 6)	Retreatment[a,b] (n = 2)	All patients with DLBCL (n = 8)	Patient with MCL[c] (n = 1)
Best ORR, n[d]	4	0	4	0
Best CRR, n	4	0	4	0
Median time to CR, months (range)	1.4 (0.9-8.7)	NA	1.4 (0.9-8.7)	NA
Median PFS, months (95% CI)	2.9 (0.2-NR)	NA	2.9 (0.2-NR)	NA
Median OS, months (95% CI)	10.7 (0.5-NR)	NA	10.7 (0.5-NR)	NA
Median follow-up, months (95% CI)	24.1 (12.3-24.1)	NA	24.1 (12.3-24.1)	NA
Patients still in response, n	2	0	2	0
Patients who died of disease progression, n	4	2	6	0

- All responses occurred after initial liso-cel treatment; no retreated patients responded
- Response or resistance to liso-cel was similar in sites of systemic and CNS lymphoma in all patients
- At relapse, one patient had both CNS and systemic disease, and one patient had only systemic disease

Primary CNS Lymphoma, tisagenlecleucel

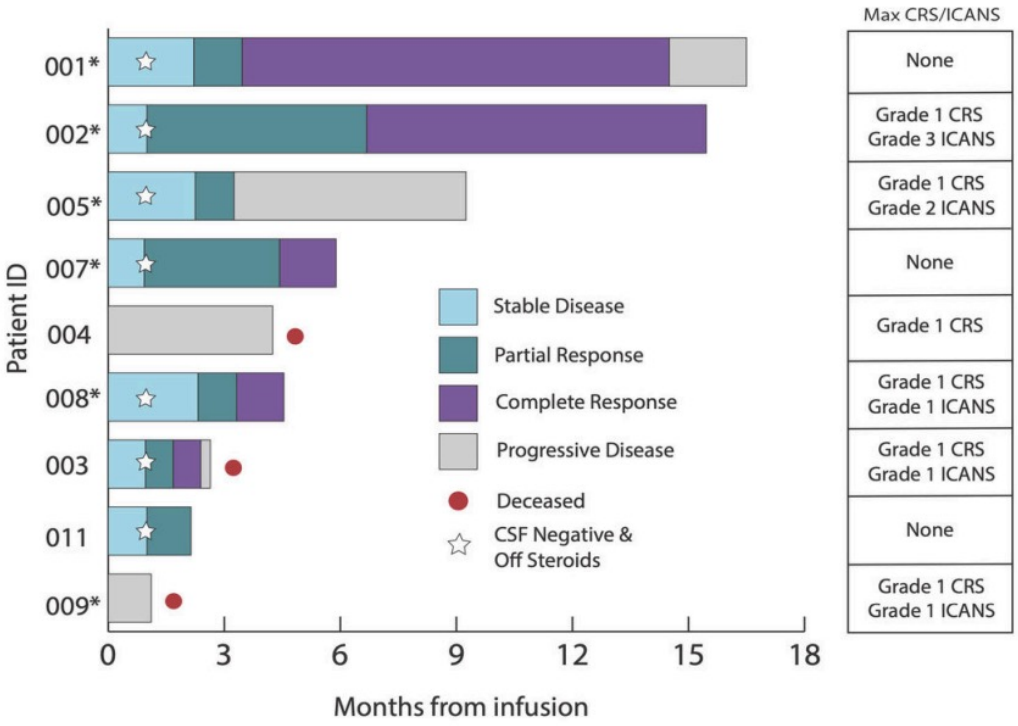
63rd ASH Annual Meeting Abstracts

ORAL ABSTRACTS

704.CELLULAR IMMUNOTHERAPIES: CLINICAL

Tisagenlecleucel Demonstrates Safety, Efficacy and CNS Trafficking in Primary CNS Lymphoma

Matthew J. Frigault[1], Jorg Dietrich[2], Kathleen M.E. Gallagher[3], Irene Scarfò[4], Mark Roschewski[5], Justin T Jordan[6], Deborah A. Forst[7], Scott R Plotkin[6], Daniella Cook[8], Keagan Casey[8], Katelin Katsis[6], Kevin Lindell[8], Michael Trailor[8], Nora Horick[6], Steven McAfee[2], Paul V O'Donnell[9], Thomas R Spitzer[10], Bimalangshu R Dey[11], Zachariah Defilipp[11], Areej El-Jawahri[12], Tracy Batchelor[13], Marcela V. Maus[8], Yi-Bin Chen[14]



N = 9

CR = 5/9

ICANS = 5/9

ICANS G3-4 = 1/9

Toxicity and efficacy of CAR T-cell therapy in primary and secondary CNS lymphoma: a meta-analysis of 128 patients

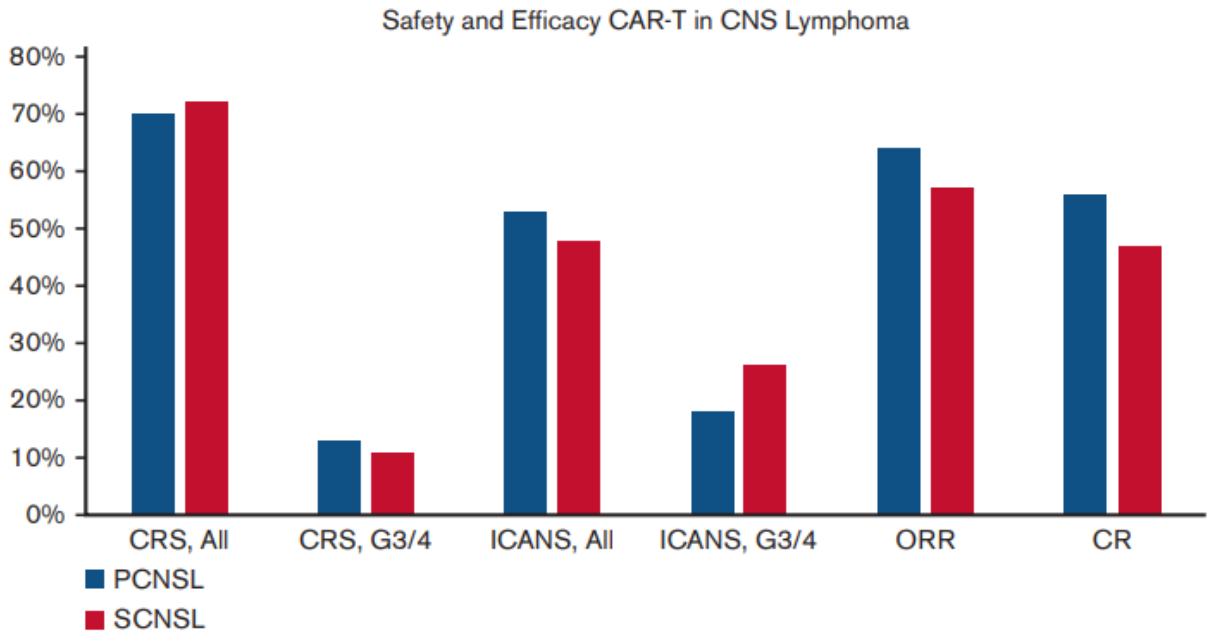
N = 128
Median FU =
- pCNS 12.2 months
- sCNS 10.1 months

Table 1. Primary and secondary CNS lymphoma demographics and pretreatment data

PCNSL		**SCNSL**	
Patients (n)	30	Patients (n)	98
Median age, y (range)	56 (44.5-67)	Median age, y (range)	50 (38-58)
Cell-of-origin, n (% of documented cases)		**Histology**	
non-GCB	15 (93.75)	DLBCL (GCB, non-GCB, NOS, HGBCL)	91
GCB n (%)	1 (6.25)	Transformed follicular lymphoma	3
NR	14	Primary mediastinal B-cell lymphoma	2
		Intravascular large B-cell lymphoma	1
		Post-transplant lymphoproliferative disorder	1
Prior lines of therapy, median (range)	3.75 (3-5)	Prior lines of therapy, median (range)	4 (3-7)
CAR Product, costimulatory domain n (%)		**CAR Product, costimulatory domain n, (%)**	
axi-cel, CD28	2 (6.67)	axi-cel, CD28	50 (51.02)
tisa-cel, 4-1BB	19 (63.33)	tisa-cel, 4-1BB	12 (12.24)
Trial anti-CD19, CD28	5 (16.67)	liso-cel, 4-1BB	7 (7.14)
Trial anti-CD19 + anti-CD22	4 (13.33)	Other	29 (29.59)

Cook et al. Blood Adv 2023

Toxicity and efficacy of CAR T-cell therapy in primary and secondary CNS lymphoma: a meta-analysis of 128 patients



	CD28 Based	4-1BB based
CRS G3-4	10.4%	-
ICANS G3-4	30%	11.1%
CRR	PCNSL: 56% SCNSL: 47%	
Ongoing Resp, data c/off	PCNSL: 37% SCNSL: 46%	

Cook et al. Blood Adv 2023

CNS Lymphoma, active selected trials

Active, not recruiting

Immunotherapy Using CAR T-cells to Target CD19 for Relapsed/Refractory CD19+ Primary CNS Lymphoma (CAROUSEL)

ClinicalTrials.gov ID NCT04443829

Sponsor University College, London

FluCY-Pembrolizumab LD

Recruiting

Intracerebroventricular Administration of CD19-CAR T Cells (CD19CAR-CD28-CD3zeta-EGFRt-expressing Tcm-enriched T-lymphocytes) for the Treatment of Primary Central Nervous System Lymphoma

ClinicalTrials.gov ID NCT05625594

Sponsor City of Hope Medical Center

Intraventricular infusion

Recruiting

A Study Evaluating the Safety and Efficacy of GLPG5101 (19CP02) in Participants With Non-Hodgkin Lymphoma (Atalanta-1)

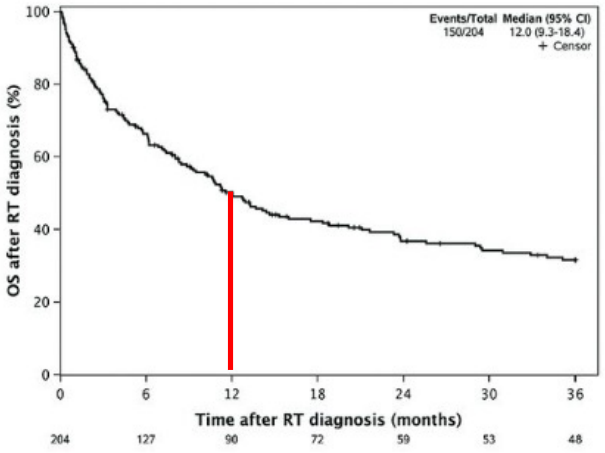
ClinicalTrials.gov ID NCT06561425

Sponsor Galapagos NV

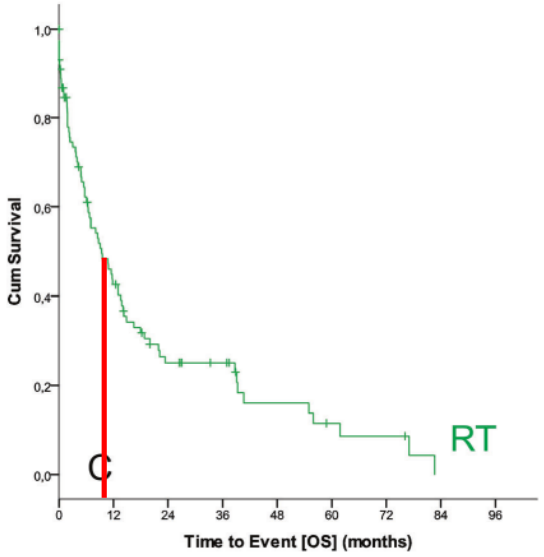
Vein-to-Vein TA: 7 days

Richter's transformation of CLL

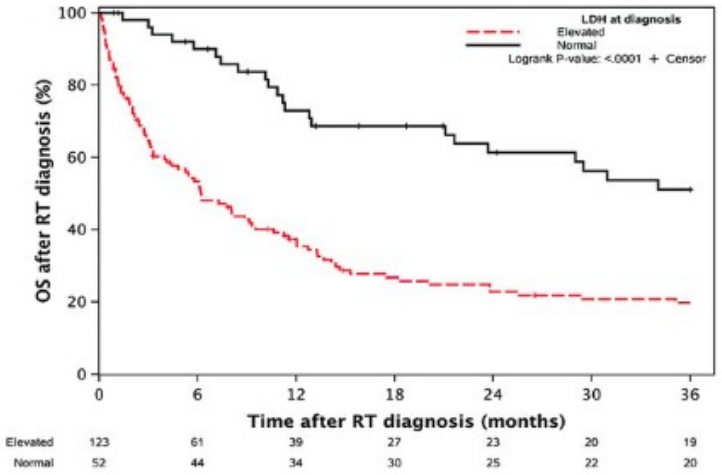
- Incidence 0-5-1% newly diagnosed CLL
- Prevalence 2-10% CLL -> rare entity
- 90% -> DLBCL, 80% clonally related to CLL
- Frequent mutations or disruptions of *TP53*, *NOTCH1*, *MYC*, and *CDKN2A* -> aggressive

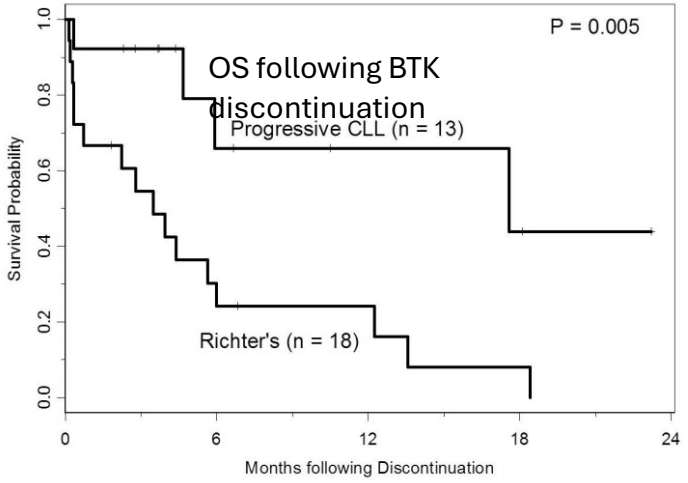


Wang et al. Haematologica 2020



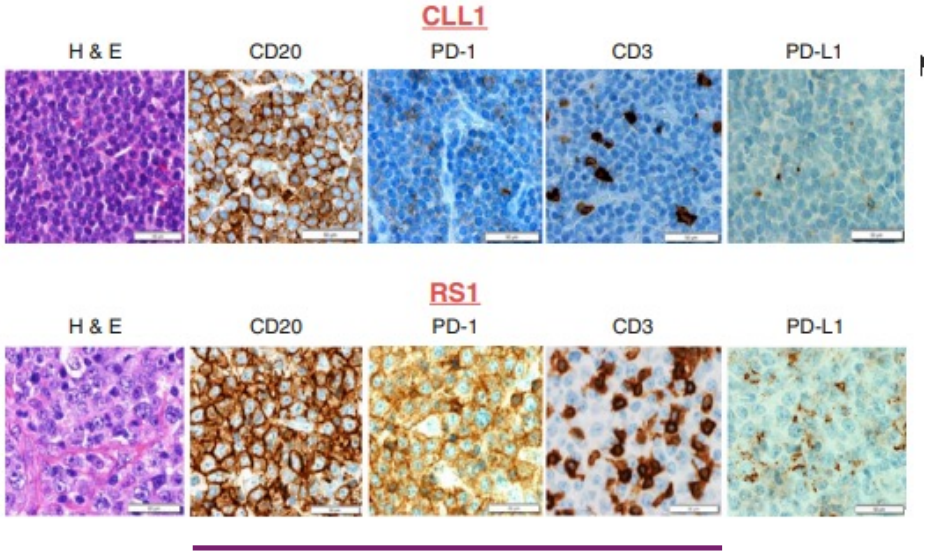
Al-Sawaf et al. Leukemia 2021





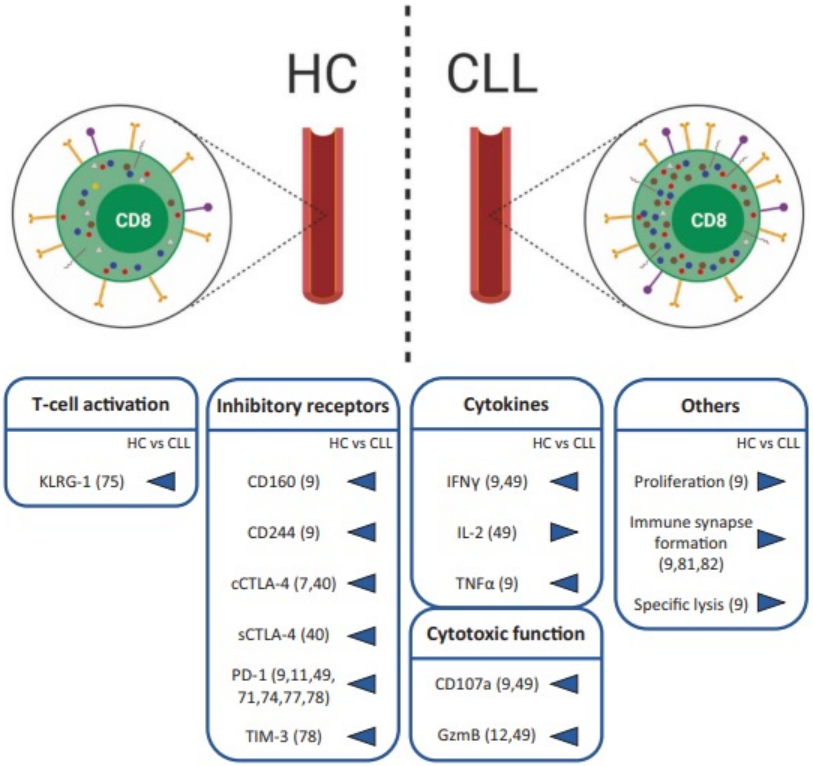
Maddocks. JAMA 2015

Unfavourable immune-contexture for CAR-T cell therapy in RT



Majority of PD-1 staining positive on tumor B cells

Ding et al. Blood 2017

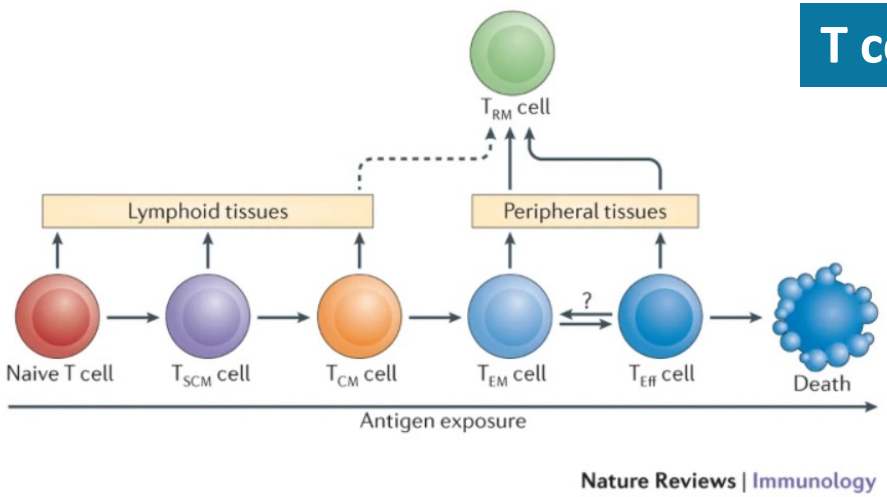


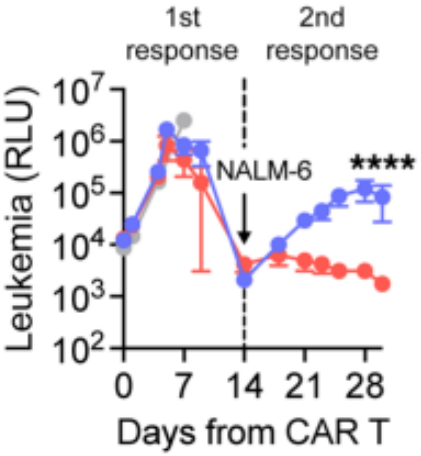
Chronic antigen stimulation induces T cell exhaustion

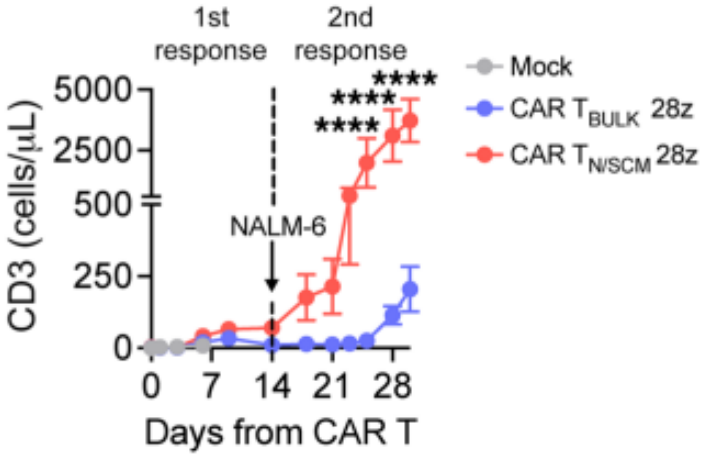
CLL T cell compartment enriched in TEM and T effectors

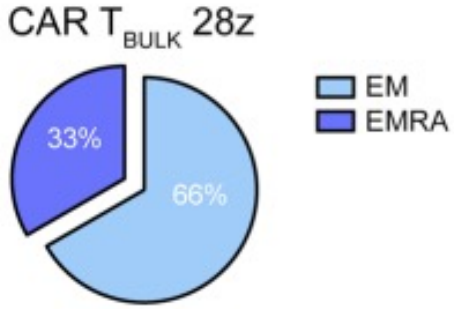
Roessner et al. Leukemia 2020

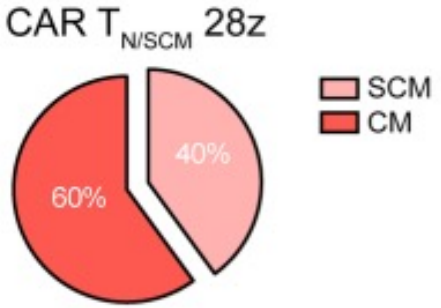
T cell subsets influence CAR-T dynamics and outcome







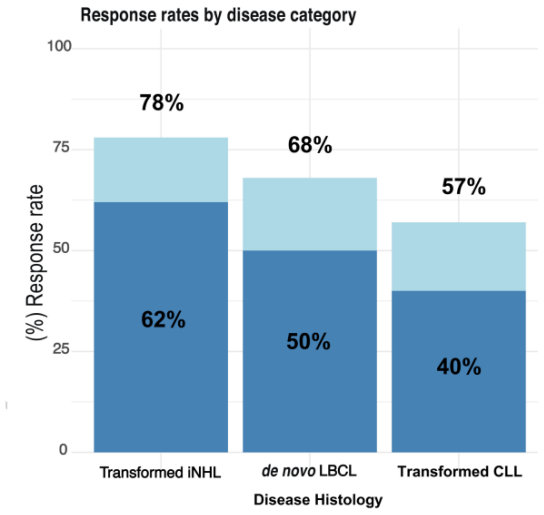


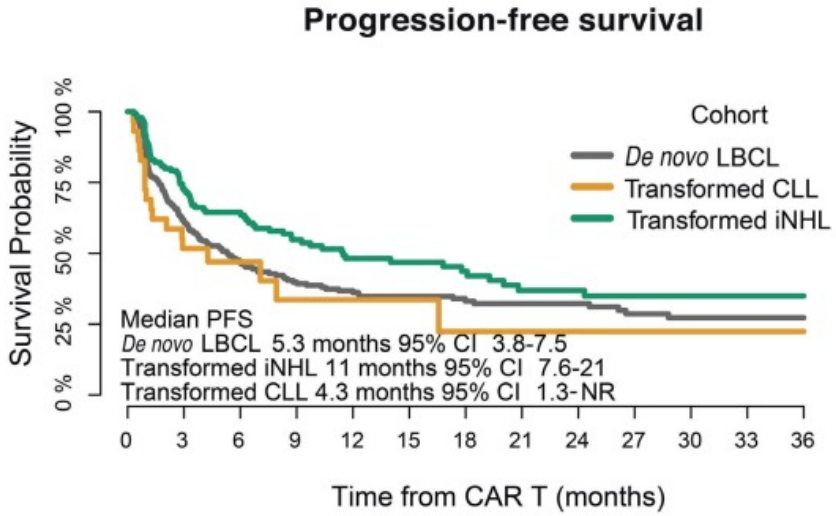


Arcangeli et al. JCI 2022

Table 2. Characteristics of patients with chronic lymphocytic leukemia pretransformation.

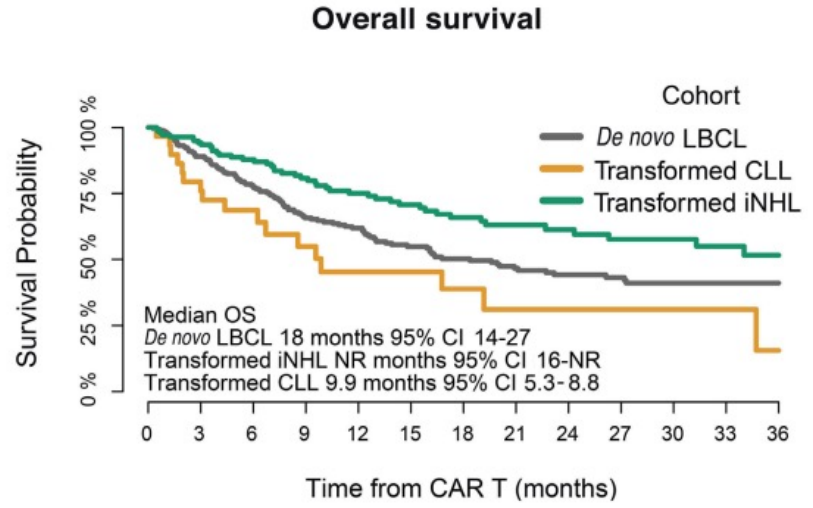
Characteristics pretransformation, N (%)	Overall N=30
CLL lines of therapy	
0	9/28(32)
1	6/28(21)
2	5/28(18)
≥3	8/28(29)
Targeted therapy	17/19 (89)
BTKi	14/19 (74)
PI3Ki	3/19 (16)
BCL2i	9/19 (47)
FCR/BR	11/19 (58)
Other chemotherapy	4/19 (21)





2016-2023
N = 30 (RT)
FU = 19 months

24m PFS, RT = 22%



24m OS
LBCL = 44%
T iNHL = 61%
RT = 31%

Benjamini et al. Haematologica 2024

Table 4. Univariate and multivariate analysis to identify prognostic factors for overall survival.

Variable	Univariate analysis			Multivariate analysis		
	N, event	HR (95% CI)	*P*	N, event	HR (95% CI)	*P*
Cohort	453, 180		<0.001	418, 167		<0.001
De novo LBCL		-	-		-	-
Transformed iNHL		0.63 (0.57-0.69)			0.59 (0.53-0.65)	
Transformed CLL		1.64 (1.20-2.24)			1.96 (1.75-2.19)	
Age at CAR T infusion	453, 180	1.00 (0.98-1.01)	0.40	418, 167	1.00 (0.99-1.02)	0.38
LDH range prelymphodepletion	426, 180		<0.001	418, 167		<0.00.1
normal		-	-		-	-
elevated		2.54 (1.74-3.70)			2.65 (1.86-3.75)	
CAR T co-stimulatory domain	453, 180		0.34	418, 167		0.52
4-1BB		-	-		-	-
CD28		0.93 (0.8-1.08)			0.93 (0.75-1.16)	
Pre-apheresis treatment lines	445, 177		0.043	418, 167		<0.00.1
≤3		-	-		-	-
4-5		1.18 (0.91-1.52)			1.00 (0.69-1.45)	
≥6		1.62 (1.11-02.38)			1.61 (1.9-2.17)	

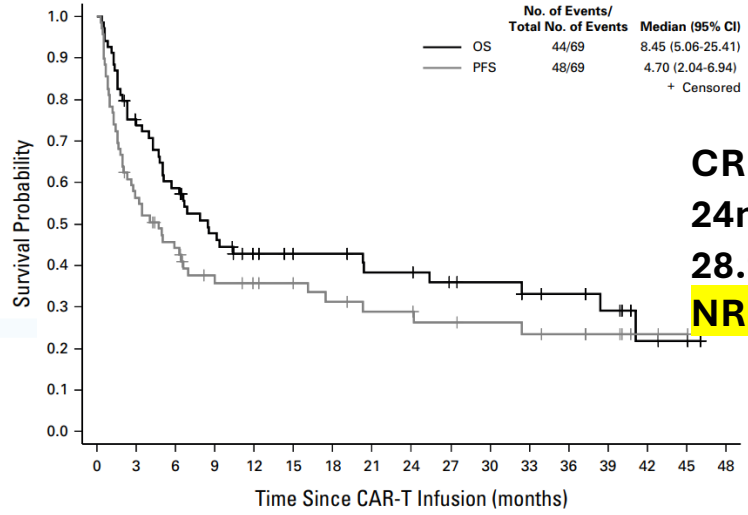
HR: hazard ratio; CI: confidence interval; LBCL: large B-cell lymphoma; CAR: chimeric antigen receptor; iNHL: low grade non-Hodgkin lymphoma; CLL: chronic lymphocytic leukemia; LDH: lactate dehydrogenase.

Benjamini et al. Haematologica 2024

Anti-CD19 Chimeric Antigen Receptor T-Cell Therapy for Richter Transformation: An International, Multicenter, Retrospective Study

2016-2023
N = 69 (RT)
FU = 24 months

Characteristic	N = 69
Unknown	2
Received therapy for RT before CAR-T, No. (%)	
No	2 (2.9)
Yes	67 (97.1)
Lines of therapy for RT, median (range)	2 (0-7)
Receipt of previous BTKi or BCL2i, No. (%)	
No previous BTKi or BCL2i	11 (15.9)
Received BTKi or BCL2i for both CLL and RT	43 (62.3)
Received BTKi or BCL2i for CLL but not RT	4 (5.8)
Received BTKi or BCL2i for RT but not CLL	11 (15.9)
Total No. of previous therapies for RT and CLL, median (range)	4 (1-15)



CR = 32/69 (46%)
24m PFS, RT = 28.9%
NRM = 17%

TABLE 2. Multivariable Model for PFS and OS

	PFS		OS	
Variable	HR (95% CI)	*P*	HR (95% CI)	*P*
LDH, 2-fold increase	1.63 (1.19 to 2.23)	.0023	1.68 (1.16 to 2.43)	.0062
CRP, 10-unit increase	1.08 (1.04 to 1.13)	.0003	1.06 (1.01 to 1.12)	.02
Ki67 index, 10% increase	—	—	1.52 (1.20 to 1.91)	.0004
No. of previous lines of therapies for RT	—	—	1.55 (1.21 to 2.00)	.0006

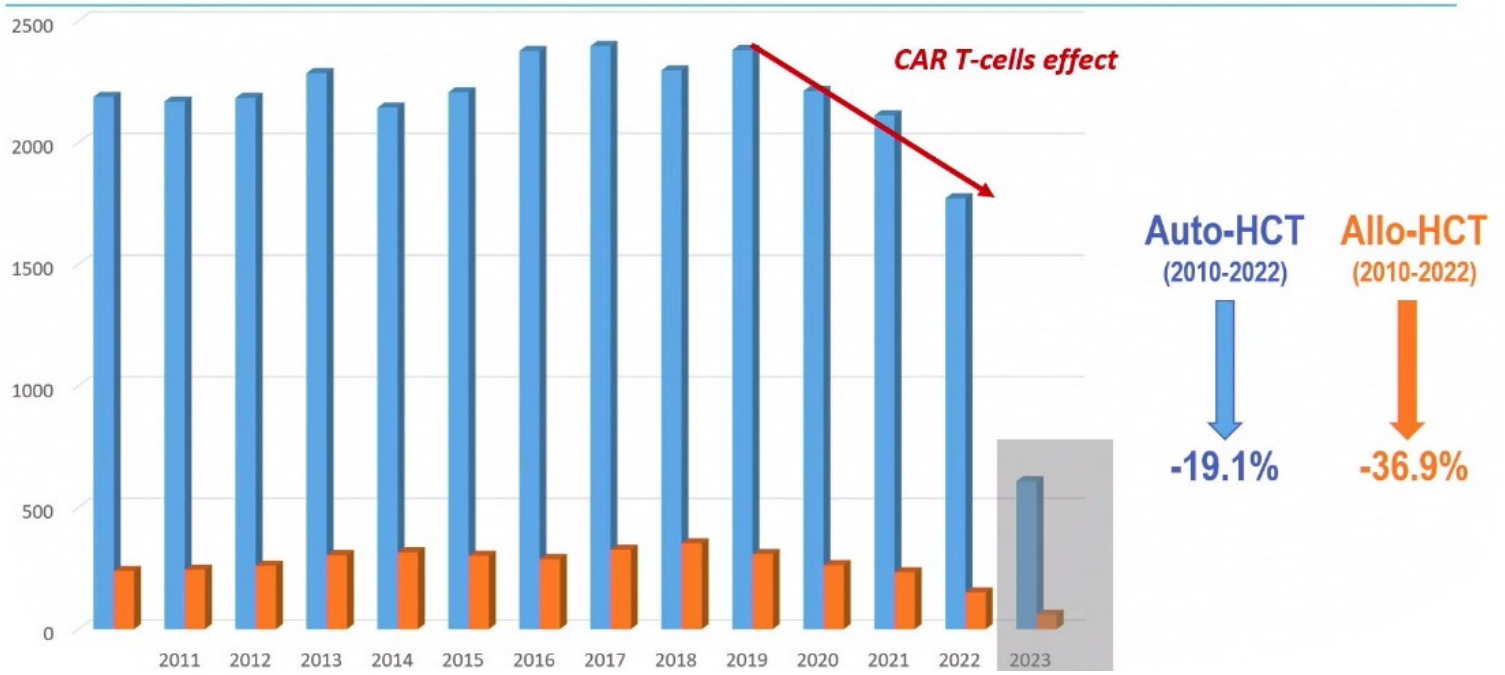
Aggressive B-cell Lymphoma

Updates from global trials

Real life
- Efficacy
- Toxicity
- Special populations

Second-line

HCT in RR DLBCL. Evolution Over Time

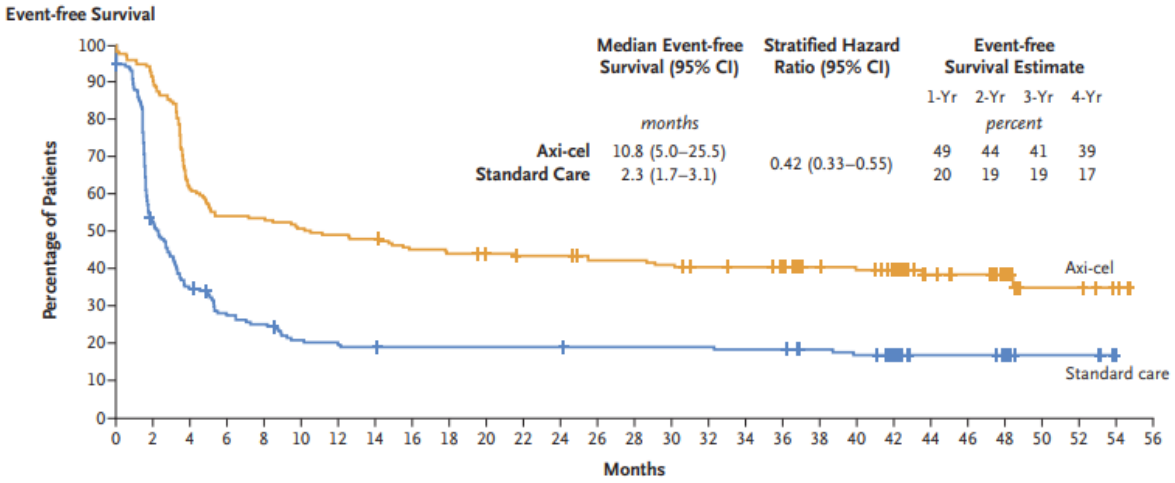


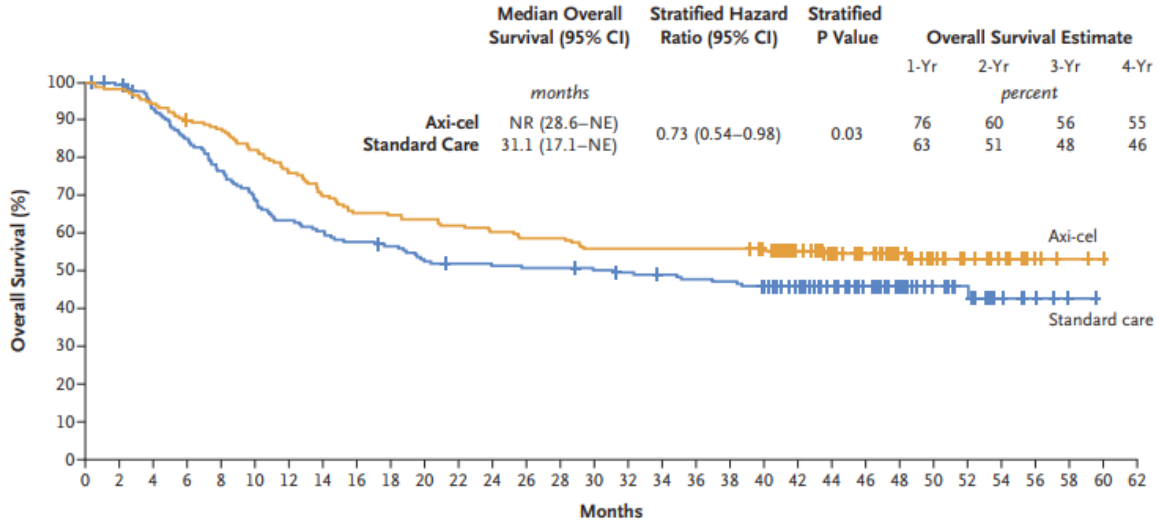
EBMT registry

Second-line CAR-T, results

	ZUMA-7		BELINDA		TRANSFORM	
	CAR-T	SOC	CAR-T	SOC	CAR-T	SOC
Patients, n	180	179	162	160	92	92
Primary REF, %	74	73	66	67	73	73
Bridging,%	36	-	83	-	63	-
ORR,%	83	50	46	43	86	48
CR,%	65	32	28	28	66	39
Median EFS, months	8.2	2	3	3	10.1	2.3
Crossover, %	-	56	-	51	-	55

EFS from randomisation: impacted by the response rate to salvage CT (SOC arm)





ZUMA-3
5 years update

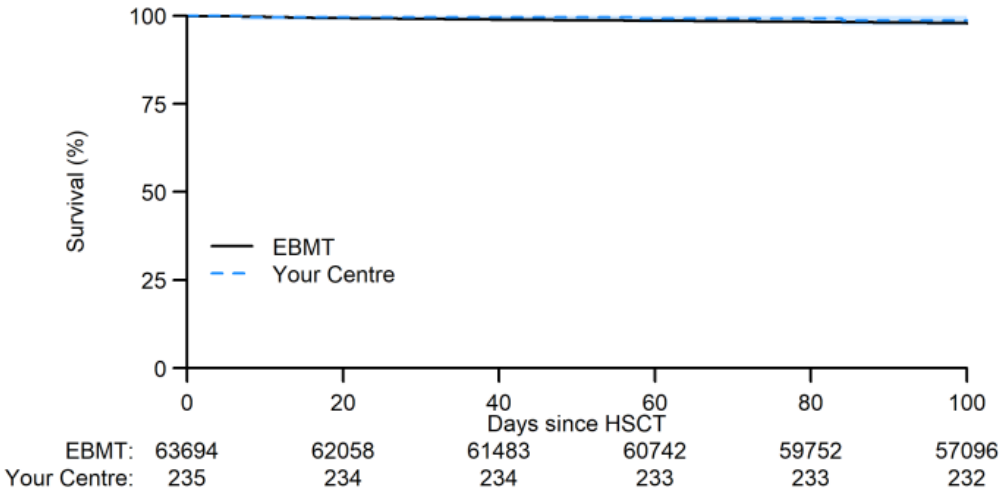
SOC: **56% crossover** to CAR-T (off-study)

Median FU: 47.2 months

HR for OS, axi-cel vs SOC: 0.73 (p = .03)

Westin et al. NEJM 2023

EBMT 2017-2021 autologous SCT benchmarking



	Day 100 Survival
EBMT	98% (98-98%)
Your Centre	99% (97-100%)

HSM, transplant unit
Median age (2019-2023),
ASCT for B-NHL: 59yrs (21-72)

HCT-CI	Total	68791 (93.3)
	Low	43056 (62.6)
	Intermediate	15839 (23.0)
	High	9896 (14.4)

Lisocabtagene maraleucel as second-line therapy in adults with relapsed or refractory large B-cell lymphoma who were not intended for haematopoietic stem cell transplantation (PILOT): an open-label, phase 2 study

Infused Patients, N	**61**
Median age, yrs - <70yrs (%) - 70-74yrs (%) - ≥75yrs (%)	74 (53-84) 13 (21) 20(33) 28(46)
ECOG 0-1, n (%) ECOG 2	45(74) 16(26)
- DLCO ≤60% - FE <50% - Creatinine clearance <60mL/min - ALT>2ULN	4(7) 1(2) 15(25) -
Primary REF, n (%)	33(54)
Median time from 1stL end to Liso, months	6.9 (3.5-16.4)
DH or TH, n (%)	20(33)

Transplant Not Intended (TNI) criteria, at least 1

- Age ≥70yrs
- ECOG 2
- DLCO ≤60%
- FE <50%
- Creatinine clearance <60mL/min
- ALT>2ULN

Adeguate organ function for CAR-T required
Secondary CNS lymphoma allowed

Primary EP: ORR

Sehgal et al. Lancet Onc 2022

PILOT trial

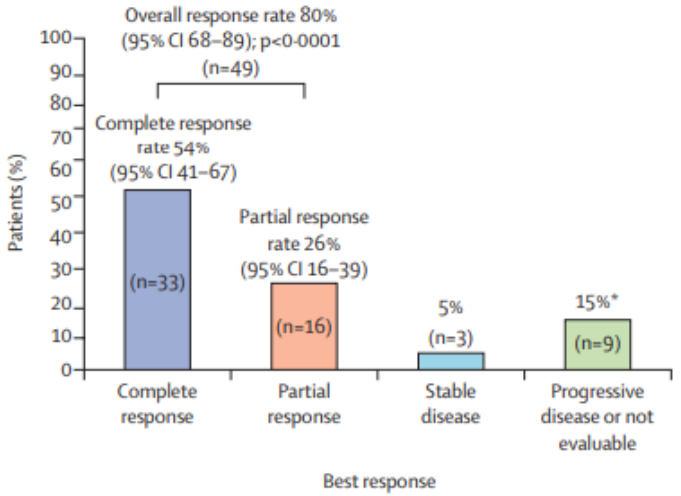
- median FU 13 months
- 52% received BT (IC)

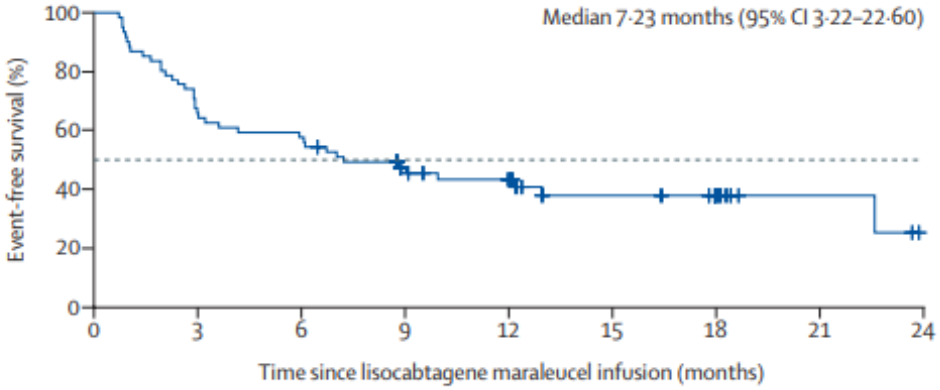
- 38% CRS, 2% Gr. 3-4
- 31% NE, 5% Gr. 3-4

- Toci, steroids, both for CRS: 26%
- Steroids for NT: 13%

- 80% ORR, 54% CR
- Median EFS 7.23months
- Median OS NR

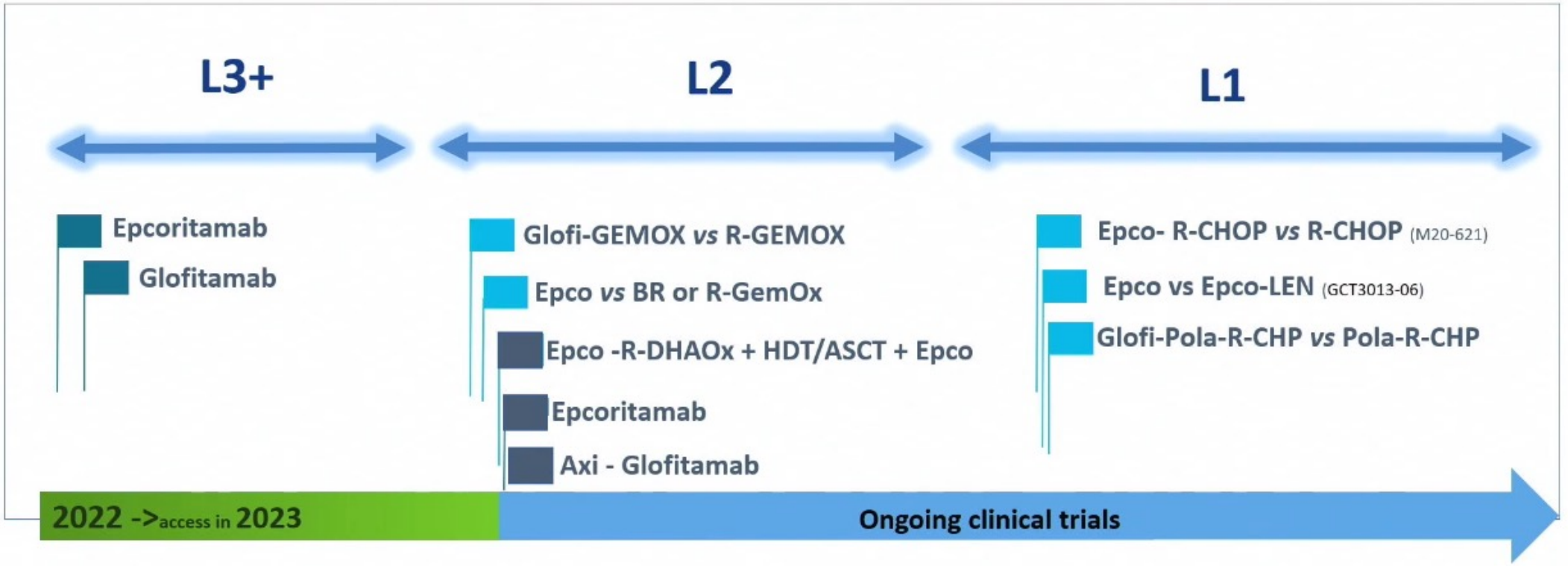
NRM: 3.3% (COVID, >1month)





Sehgal et al. Lancet Onc 2022

DLBCL



Thieblemont. EBMT2024, adapted

Conclusions

NRM -> relatively low rates; prophylaxis, frails and neutropenic

Secondary active CNS involvement -> time for inclusion

Primary CNS lymphoma -> encouraging data

Richter’s transformation -> still debated

Second-line CAR-T according to frailty -> feasible