XIX CONGRESSO NAZIONALE SIES 2026

Le CAR-T nei linfomi in Italia: dati dello studio CAR-T SIE

Michele Spina – Aviano

Firenze | 4-6 marzo 2026
Palazzo degli Affari

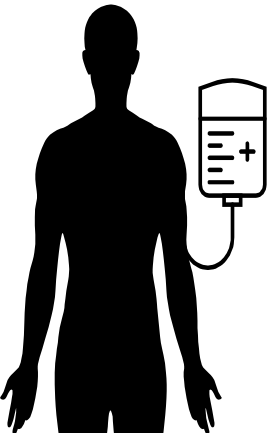
Disclosures of Michele Spina

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Gilead					x	x	
Servier					x	x	
Roche					x		
Novartis					x		
Incyte					x		
Istituto Gentili					x		
BeiOne					x		
AbbVie					x		
Sobi					x	x	
Astra Zeneca					x		

CAR T- cell therapy is more than one step

Leukapheresis

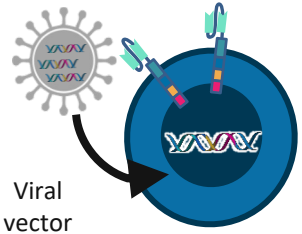
Collect patient's white blood cells

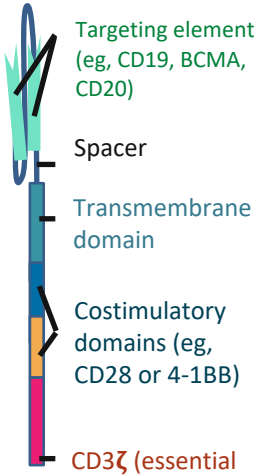


Manufacturing – Bridging therapy

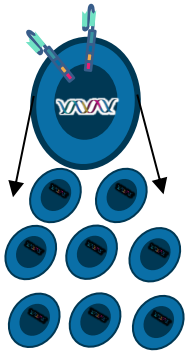
Isolate and activate T-cells

Engineer T-cells with CAR gene



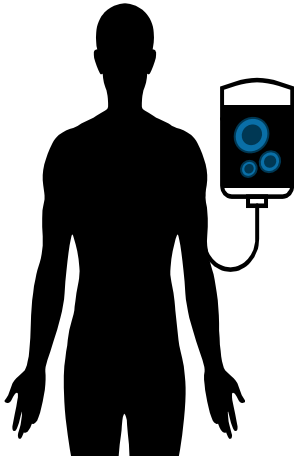


Expand CAR T-cells



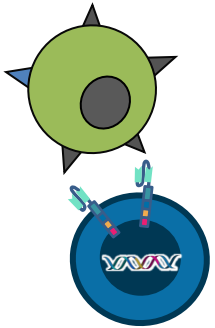
Infusion

Infuse same patient with CAR T-cells



Activity

CD19



Median manufacturing time: 17-28 days

Patients undergo lymphodepleting (and possibly salvage/bridging) therapy

CAR-T SIE update @ nov 2025

FONDAZIONE IRCCS ISTITUTO NAZIONALE DEI TUMORI

Società Italiana di Ematologia

2019-2025
1465 patients enrolled

Diagnosis missing in 12

PMBCL

105 enrolled

102 infused

99 evaluable for analysis

Axi n=95
Liso n=3
1 Brexu??

DLBCL/HGBL

1052 enrolled (249 2L)

939 infused (221 2L)

904 evaluable for analysis (204 2L)

Axi n= 574 (n=**192 2L)**
Liso n=22 (n=2 2L??)
Tisa n=304 (n=9 2L??)
4 missing??

FL

104 enrolled

88 infused

84 evaluable for analysis

Axi n=8
Tisa n=75
Liso n=1 ??

MCL

192 enrolled

173 infused

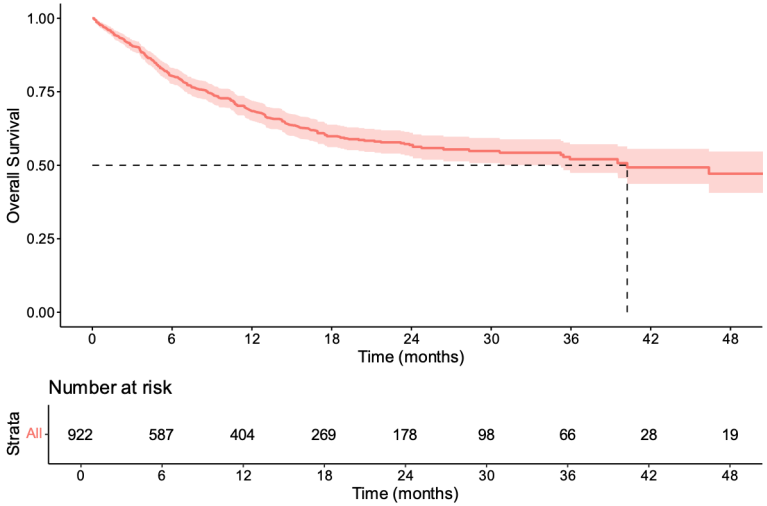
162 evaluable for analysis

Brexu n= 158
Tisa n=4??

OVERALL: 1249 patients (85%) are evaluable for analysis
(at least 1 follow-up recorded after CAR-T infusion)

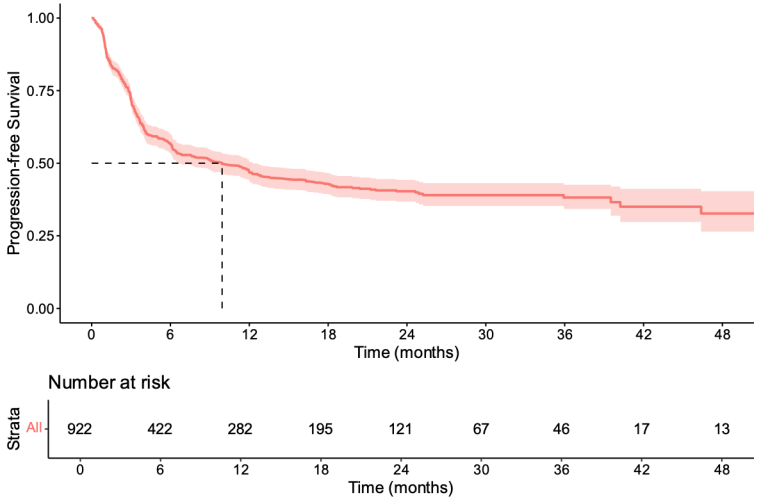
Response and Survival Outcomes – global cohort

2-year OS 56.9% (95% CI 53–61.1%)



Median OS: 40.2 months (95% CI 3.23-NR)

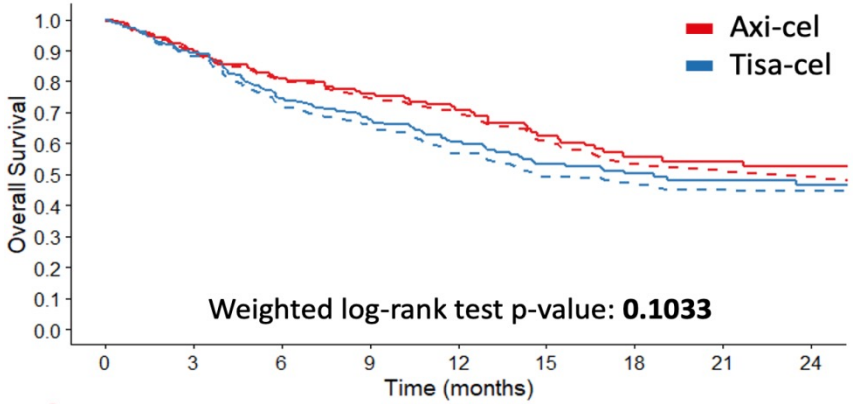
2-year PFS 40.3% (95% CI 36.8–44.3%)

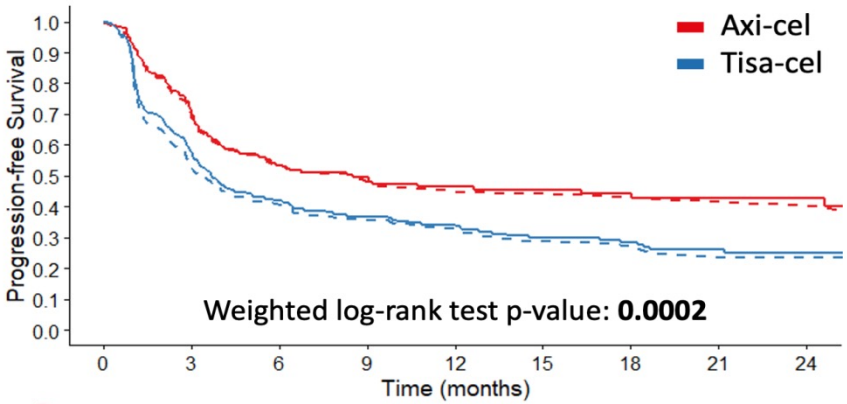


Median PFS: 9.9 months (95% CI 6.6-12.2)

A Multicenter Real-life Prospective Study of Axicabtagene Ciloleucel versus Tisagenlecleucel Toxicity and Outcomes in Large B-cell Lymphomas

Federico Stella; Annalisa Chiappella; Beatrice Casadei; Stefania Bramanti; Silva Ljevar; Patrizia Chiusolo; Alice Di Rocco; Maria C. Tisi; Matteo G. Carrabba; Ilaria Cutini; Massimo Martino; Anna Dodero; Francesca Bonifazi; Armando Santoro; Federica Sorà; Barbara Botto; Anna M. Barbui; Domenico Russo; Maurizio Musso; Giovanni Grillo; Mauro Krampera; Jacopo Olivieri; Marco Ladetto; Federica Cavallo; Massimo Massaia; Luca Arcaini; Martina Pennisi; Pier L. Zinzani; Rosalba Miceli; Paolo Corradini

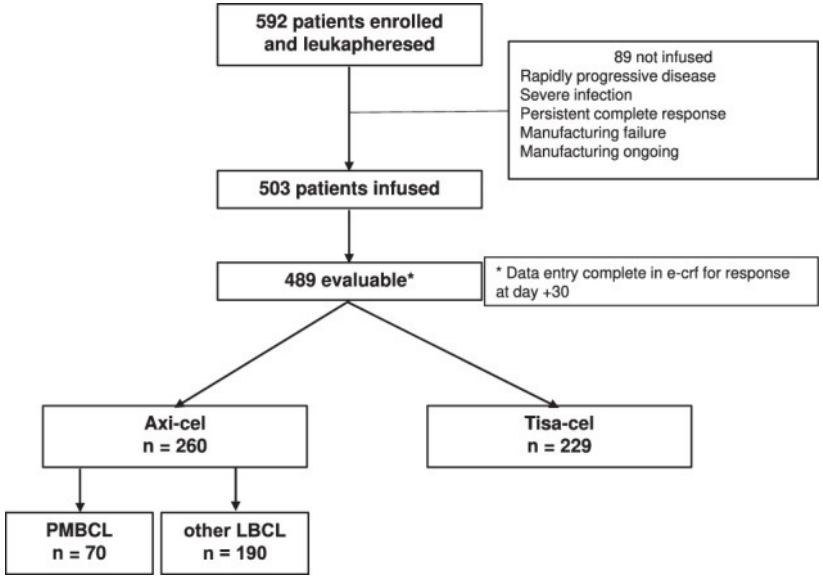


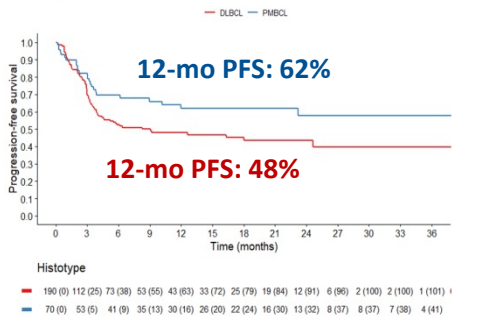


Blood Cancer Discovery 2024

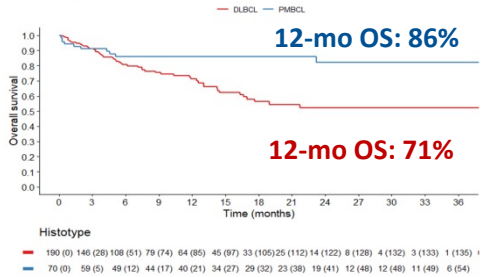
Axicabtagene ciloleucel treatment is more effective in primary mediastinal large B-cell lymphomas than in diffuse large B-cell lymphomas: the Italian CART-SIE study

Annalisa Chiappella[1✉], Beatrice Casadei[2], Patrizia Chiusolo[3], Alice Di Rocco[4], Silva Ljevar[5], Martina Magni[1], Piera Angelillo[6], Anna Maria Barbui[7], Ilaria Cutini[8], Anna Dodero[1], Francesca Bonifazi[2], Maria Chiara Tisi[9], Stefania Bramanti[10], Maurizio Musso[11], Mirko Farina[12], Massimo Martino[13], Mattia Novo[14], Giovanni Grillo[15], Francesca Patriarca[16], Giulia Zacchi[17], Mauro Krampera[18], Martina Pennisi[1], Eugenio Galli[3], Maurizio Martelli[4], Andrés J. M. Ferreri[6], Silvia Ferrari[7], Riccardo Saccardi[8,21], Anisa Bermema[1], Anna Guidetti[1,19], Rosalba Miceli[5], Pier Luigi Zinzani[2,20] and Paolo Corradini[1,19]





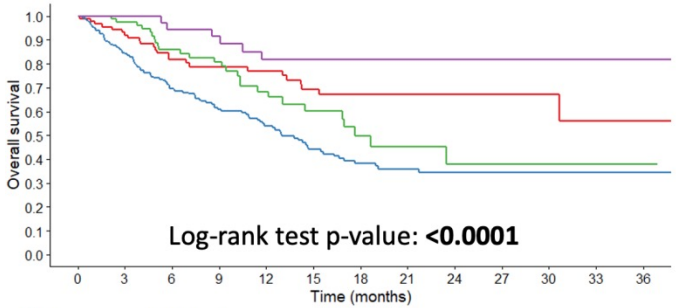
p 0.0386

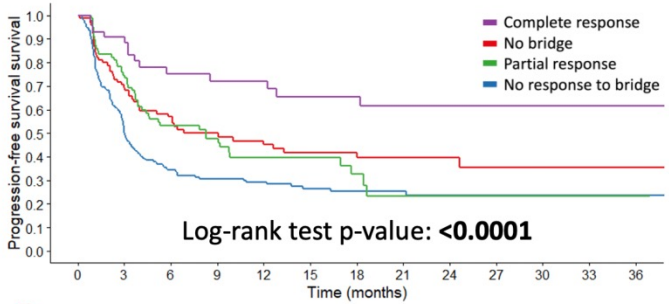


p 0.0034

Leukemia 2024

The role of bridging treatment



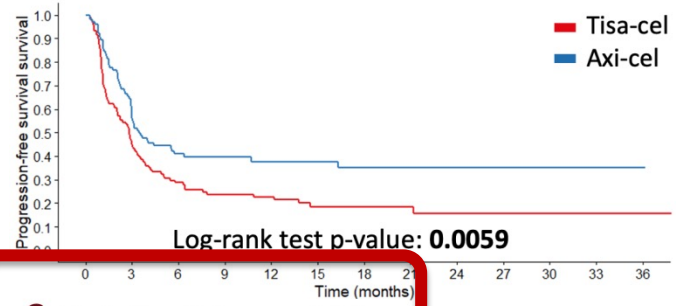


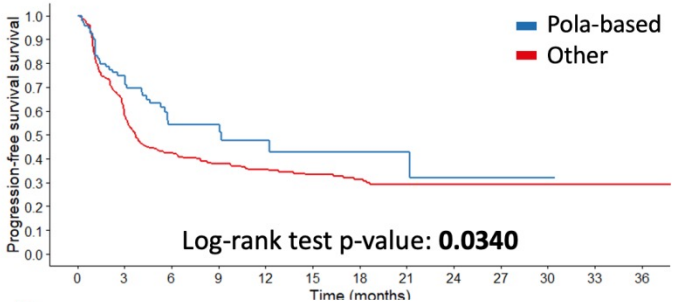
A Response to bridging therapy

	92 (0)	78 (7)	61 (16)	48 (27)	44 (30)	31 (39)	25 (44)	22 (47)	18 (51)	7 (62)	6 (63)	4 (64)	2 (66)
	225 (0)	172 (19)	129 (34)	88 (61)	68 (72)	47 (82)	38 (85)	27 (94)	17 (103)	11 (109)	6 (114)	6 (114)	3 (117)
	82 (0)	74 (6)	56 (16)	44 (25)	31 (32)	20 (40)	12 (45)	7 (49)	1 (54)	1 (54)	1 (54)	1 (54)	1 (54)
	44 (0)	42 (2)	34 (8)	30 (11)	25 (13)	22 (16)	19 (19)	13 (25)	10 (28)	5 (33)	4 (34)	3 (35)	1 (37)

B Response to bridging therapy

	92 (0)	58 (7)	42 (13)	31 (19)	28 (20)	21 (24)	19 (26)	15 (29)	13 (31)	4 (39)	3 (40)	3 (40)	2 (41)
	225 (0)	105 (12)	67 (18)	46 (33)	36 (41)	26 (48)	22 (51)	15 (58)	9 (63)	6 (66)	4 (68)	4 (68)	2 (70)
	82 (0)	58 (4)	37 (9)	26 (17)	16 (23)	12 (27)	8 (29)	4 (31)	1 (34)	1 (34)	1 (34)	1 (34)	1 (34)
	44 (0)	38 (2)	26 (8)	24 (9)	22 (11)	18 (13)	16 (15)	12 (18)	9 (21)	4 (26)	3 (27)	2 (28)	1 (29)





C Axi-cel vs Tisa-cel in No response to bridge

	119 (0)	51 (4)	32 (5)	22 (10)	19 (12)	11 (17)	10 (18)	7 (23)	4 (23)	3 (24)	2 (25)	2 (25)	1 (26)
	106 (0)	54 (8)	35 (13)	24 (23)	17 (29)	15 (31)	12 (33)	8 (37)	5 (40)	3 (42)	2 (43)	2 (43)	1 (44)

D Bridging therapy: Pola-based vs Other

	298 (0)	166 (10)	117 (15)	91 (29)	72 (43)	57 (54)	45 (63)	31 (74)	20 (85)	11 (94)	8 (97)	8 (97)	5 (100)
	95 (0)	58 (15)	30 (30)	17 (43)	11 (47)	6 (51)	6 (51)	4 (53)	2 (54)	1 (55)	1 (55)	0 (56)	0 (56)

Outcomes of CAR T-cell therapy in high-grade B-cell lymphomas compared to DLBCL: a weighted comparison analysis

A Dodero,G Ceparano,B Casadei,P Angelillo,S Bramanti,MC Tisi,S Ljevar,F Stella,A Chiappella,B Botto,I Cutini,G Zanirato,P Chiusolo,AM Barbui,M Farina,A Di Rocco,G Grillo,J Olivieri,M Krampera, M Ladetto,A Guidetti,PL Zinzani,C Carniti, P Corradini, Outcomes of CAR T-cell therapy in high-grade B-cell lymphomas compared to DLBCL: a weighted comparison analysis, Blood Adv, 2025,

CD19 CAR T-cells Therapy in High-grade B-cell Lymphomas (HGBL) Compared To Diffuse Large B-Cell Lymphomas (DLBCL)

Objective and Study Population

Predictive value of subtype (HGBL versus DLBCL) using a weighted log-rank test and a weighted Cox model in pts treated with CD19 CAR T cells in third line or beyond

N = 432 pts
CD19 CAR T cells infused
Axicel (n = 210)
Tisacel (n = 222)

N = 78 HGBL

N = 354 DLBCL

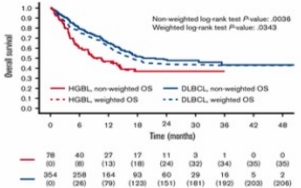
NRM and SPM

	NRM 12 months	NRM 24 months	*P*-value
HGBL	4.1% (1.1%-10%)	10% (1.9%-28%)	.631
DLBCL	4.9% (2.4%-8.7%)	11% (6.1%-19%)	

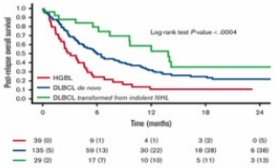
	Incidence SPM 12 months	Incidence SPM 24 months	*P*-value
HGBL	2.8% (0.20%-13%)	6.4% (1.1%-19%)	.844
DLBCL	6.1% (3.4%-9.7%)	11% (6.1%-17%)	

OUTCOMES

- Unweighted (solid line) versus weighted (dashed) Kaplan-Meier curves for OS



- Kaplan-Meier curves for OS following CAR T cells failure in different subtypes (Transformed DLBCL versus de novo DLBCL versus HGBL)



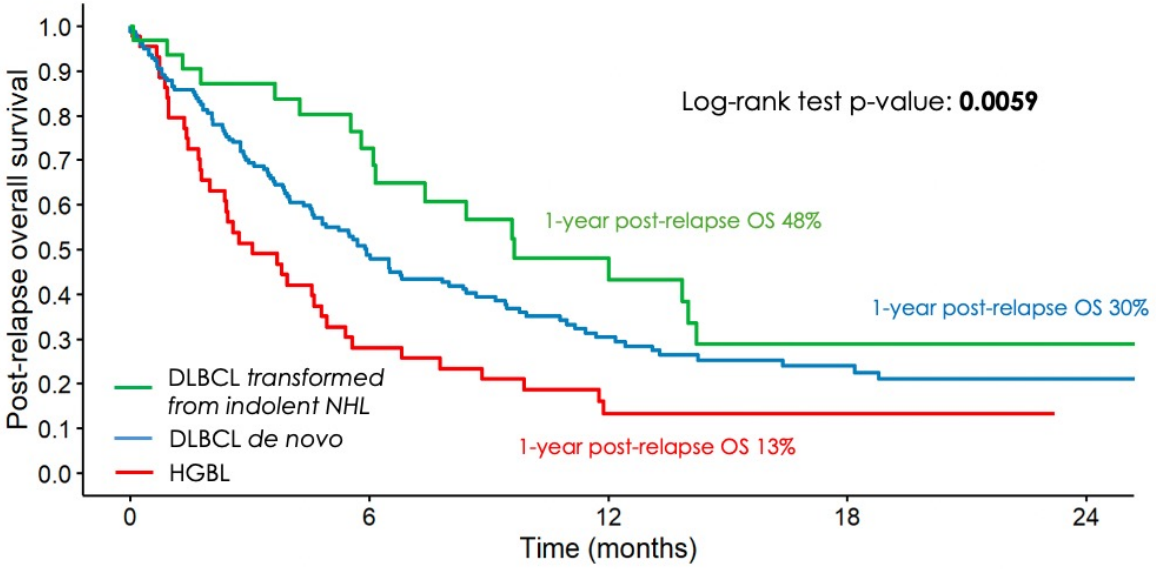
Conclusions: The 2-year OS difference between HGBL and DLBCL remained significant following weighted log-rank tests; this difference was related to inferior survival following CAR T cells failure in HGBL.

*Dodero et al. DOI: 10.1182/**bloodadvances**.2025016117*

blood advances Visual Abstract

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Not all LBCL are the same: outcome in different subtypes after CAR T-cells failure

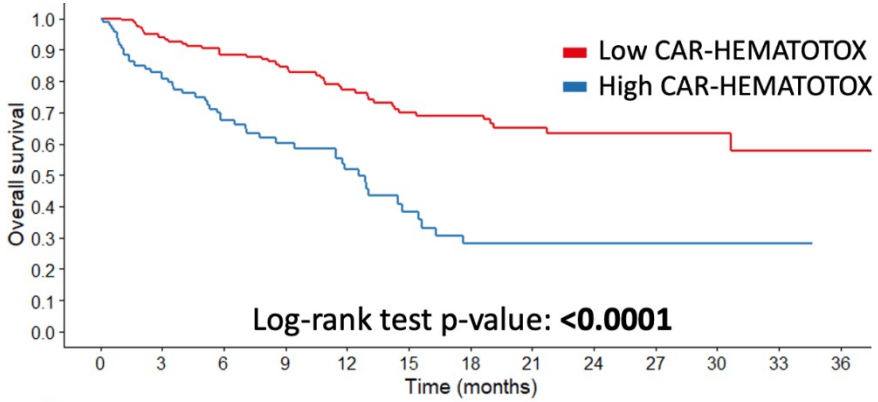


CAR – HEMATOTOX score in LBCL

Stella F et al, TCT 2025

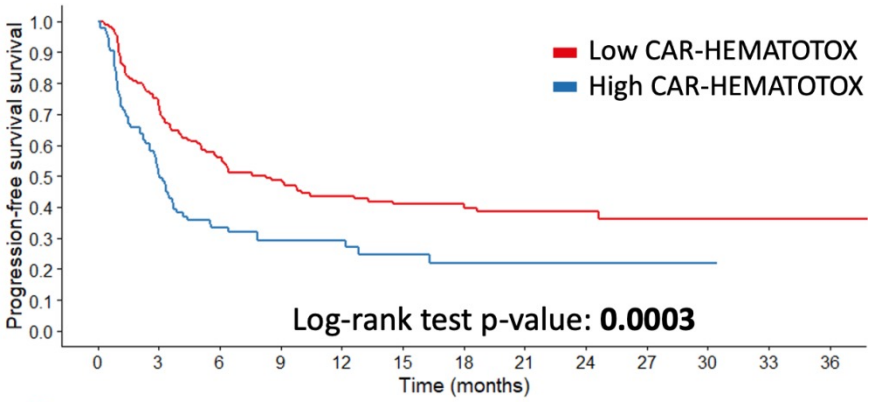
Baseline Features	0 Point	1 Point	2 Points
Platelet Count	> 175,000/μl	75,000 – 175,000/μl	< 75,000/μl
Absolute Neutrophil Count (ANC)	> 1200/μl	< 1200/μl	-
Hemoglobin	> 9.0 g/dl	< 9.0 g/dl	-
C-reactive protein (CRP)	< 3.0 mg/dl	> 3.0 mg/dl	-
Ferritin	< 650 ng/ml	650 – 2000 ng/ml	> 2000 ng/ml
Low: 0-1	High: ≥ 2		

Società Italiana di Ematologia



A HEMATOTOX

169 (0)	149 (10)	127 (24)	100 (46)	82 (56)	67 (64)	57 (73)	44 (83)	32 (94)	17 (109)	11 (115)	9 (116)	4 (121)	
94 (0)	74 (2)	54 (11)	38 (22)	29 (26)	15 (34)	10 (35)	7 (38)	3 (42)	2 (43)	2 (43)	1 (44)	0 (45)	



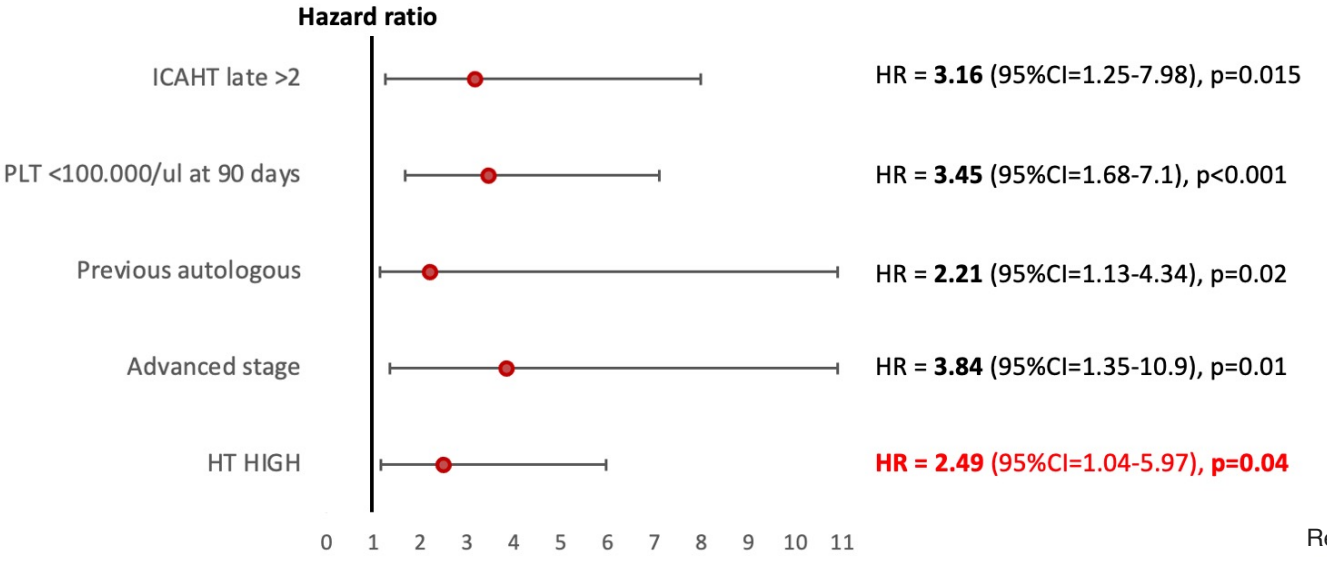
B HEMATOTOX

169 (0)	119 (5)	84 (13)	61 (26)	49 (32)	43 (35)	38 (40)	28 (48)	21 (55)	10 (65)	7 (68)	7 (68)	4 (71)	
94 (0)	46 (2)	27 (6)	18 (12)	16 (14)	8 (20)	7 (20)	5 (22)	2 (25)	1 (26)	1 (26)	0 (27)	0 (27)	

CAR HEMATOTOX and SPM

From univariable Fine and Gray models, a **high CAR HEMATOTOX score** was found to be associated with **higher risk** for occurrence of **SPM**.

The relative rarity of events prevented us from performing multivariate analyses.



Rejeski K et al. Blood 2021

BJHaem
BRITISH JOURNAL OF HAEMATOLOGY

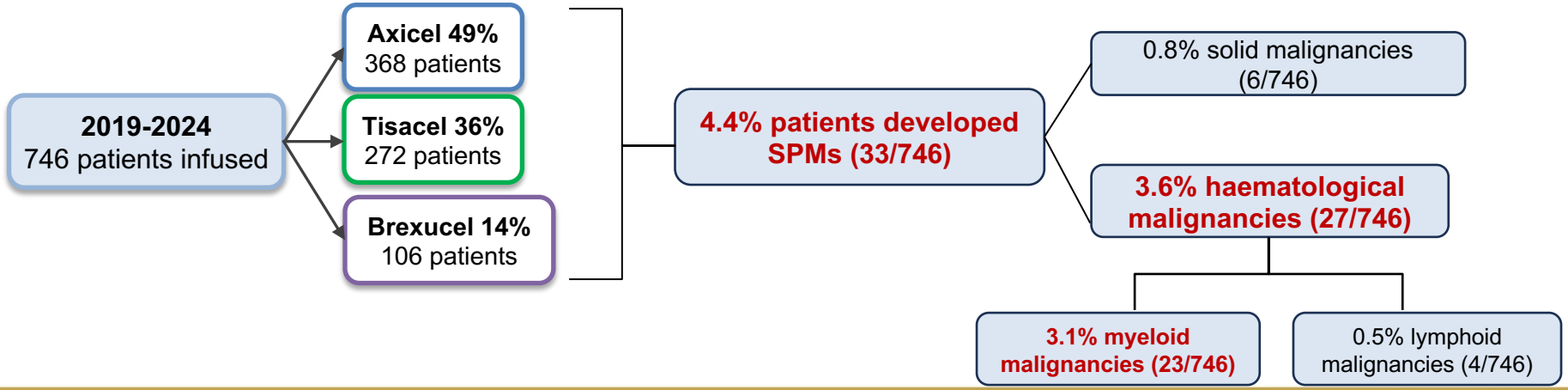
SHORT REPORT

Haematological Malignancy – Clinical

Secondary primary malignancies after CD-19 directed CAR-T-cell therapy in lymphomas: A report from the Italian CART-SIE study

Angelica Barone[1] | Annalisa Chiappella[2] | Beatrice Casadei[3] | Stefania Bramanti[4] | Silva Ljevar[5] | Patrizia Chiusolo[6] | Alice Di Rocco[7] | Maria Chiara Tisi[8] | Anna Maria Barbui[9] | Mirko Farina[10] | Lucia Brunello[11] | Maria Chiara Di Chio[2] | Mattia Novo[12] | Maurizio Musso[13] | Jacopo Olivieri[14] | Gentiana Elena Trotta[15,2] | Anna Dodero[2] | Antonella Aiello[16] | Paolo Corradini[1,2]

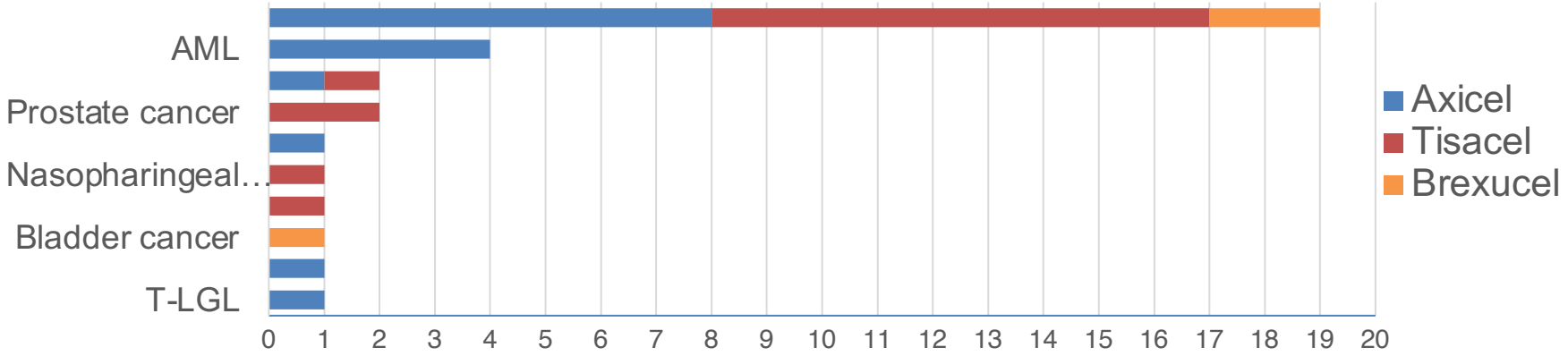
Società Italiana di Ematologia



Secondary primary malignancies in CART-SIE

- Median follow-up 14.9 months (IQR: 6.68-24.47)
- Median time to diagnosis: 12.6 months (range 1-40)
- **Very low incidence of T-NHL: 0.26%**
- **AML and MDS represented 70% of all SPMs (3.1%)**
- 12 deaths were observed, of which 7 were related to SPMs

Risk factors for occurrence of myeloid malignancies were Ann Arbor stage III-IV, previous ASCT, ICAHT, platelets count < 100.000/microliter at day 90 after infusion and neutrophils count < 500/microL before lymphodepletion.



2-year cumulative incidence of SPMs was 9.9% (95% CI: 6.5-14)
2-year cumulative incidence of myeloid malignancies was 6.7% (95% CI 4-10)

Incidence and timing of NRM

- **47 (5%) NRM events in our cohort**
- Early NRM (≤ 30 days) in 19 patients (40% of NRM deaths)
- Late NRM (30-90 days after infusion) in 11 patients (23% of NRM deaths)
- Very late mortality (beyond 90 days after infusion) in 17 patients (36% of NRM deaths)

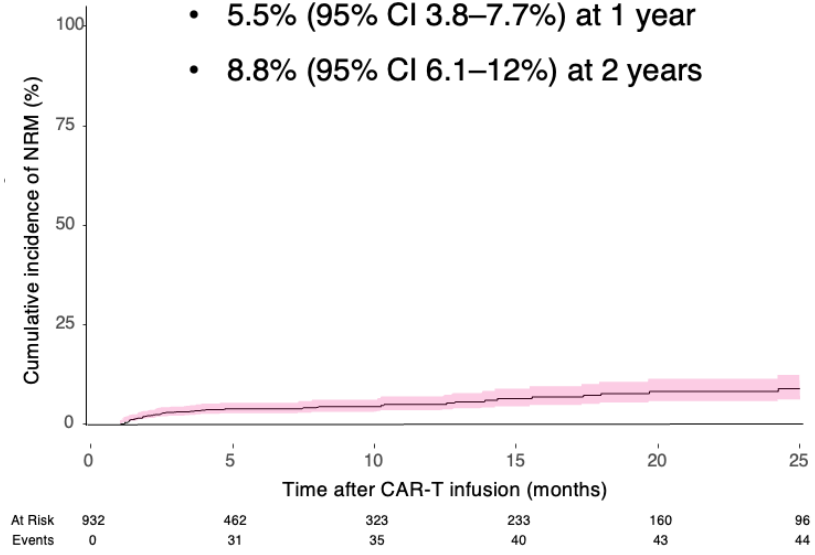
Overall, most patients died beyond day 30

Cumulative incidence of NRM:

- ***5.5% (95% CI 3.8–7.7%) at 1 year***
- ***8.8% (95% CI 6.1–12%) at 2 years***

Cumulative incidence of NRM:

- 5.5% (95% CI 3.8–7.7%) at 1 year
- 8.8% (95% CI 6.1–12%) at 2 years

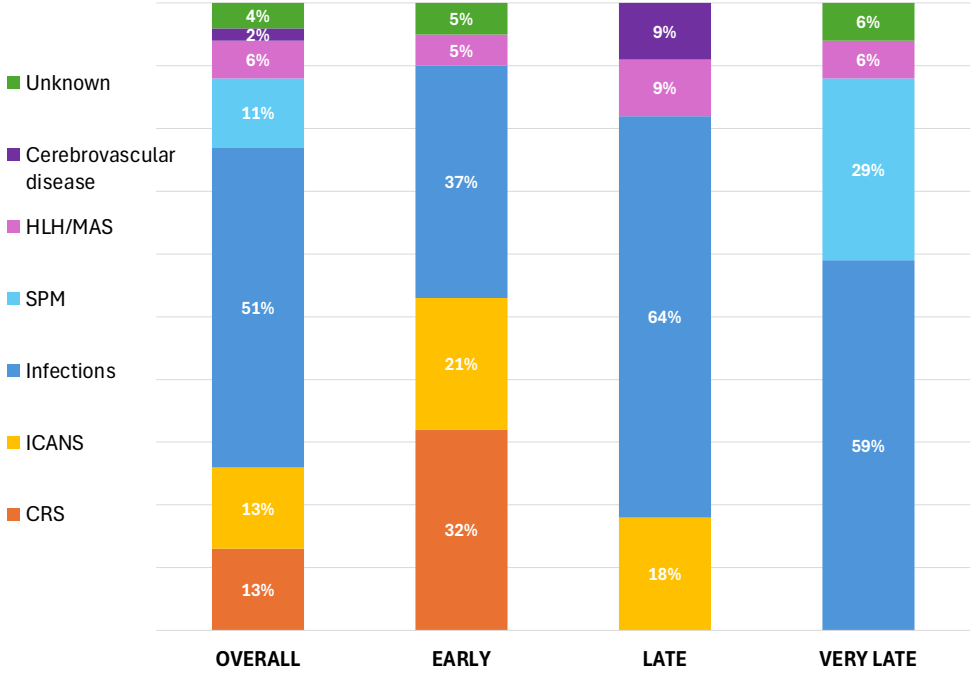


Infections are the main driver of NRM

- **NRM was mainly due to infections (n=24, 51%), followed by CRS (n=6, 13%), ICANS (n=6, 13%) and second primary malignancies (n=5, 11%).**

- Causes of infectious death included:
  - ✓ Septic shock (n=15)*
  - ✓ Sars-CoV-2-related infection (n=5)
  - ✓ Invasive Aspergillosis (n=1)
  - ✓ P. jirovecii pneumonia (n=1)
  - ✓ Pneumonia of unknown etiology (n=1)
  - ✓ Fournier's gangrene (n=1)

- **Only 1 comorbidity-related related death (=stroke)**



* *K. Pneumoniae* [n=5], *E. Coli* [n=1], *S. maltophila* [n=1], unidentifid [n=8]

Received: 30 May 2023 | Accepted: 9 August 2023

DOI: 10.1111/bjh.19057

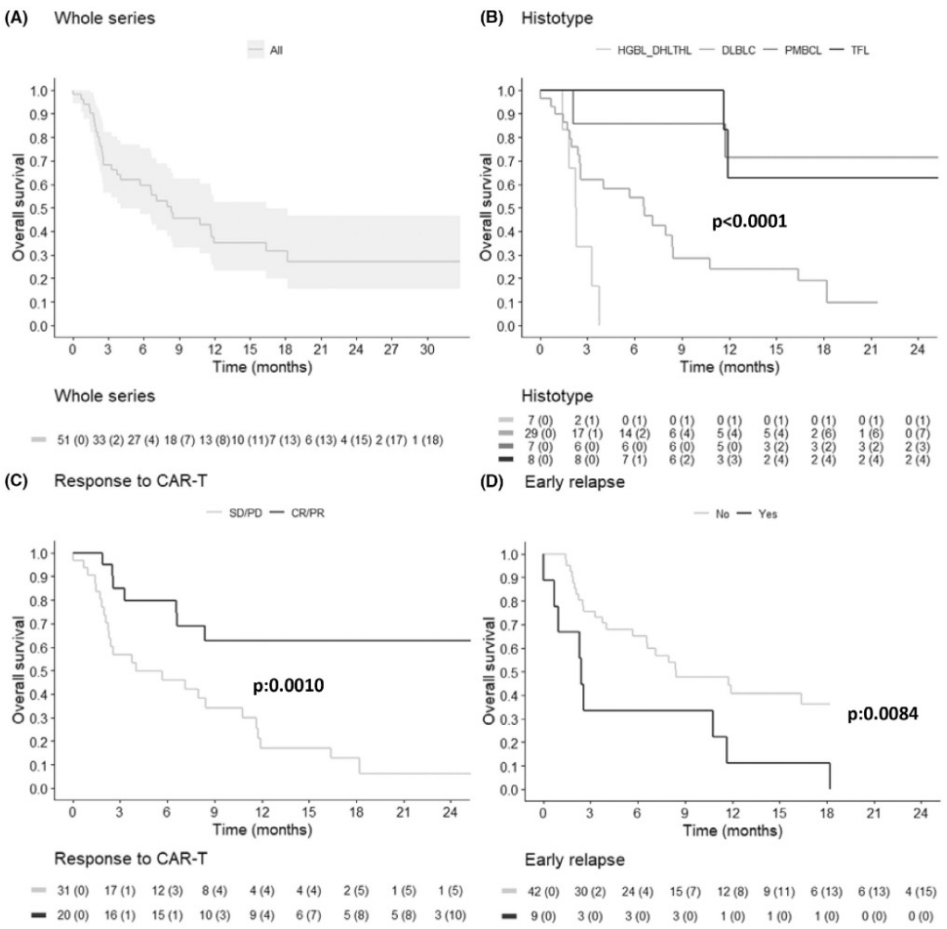
ORIGINAL PAPER

Outcome after chimeric antigen receptor (CAR) T-cell therapy failure in large B-cell lymphomas

Anna Dodero[1] | Stefania Bramanti[2] | Martina Di Trani[2] | Martina Pennisi[1] | Silva Ljevar[3] | Annalisa Chiappella[1] | Massimo Magagnoli[2] | Anna Guidetti[1,4] | Francesco Corrado[5] | Paulina Maria Nierychlewska[6] | Alice Di Rocco[7] | Daniele Lorenzini[8] | Daoud Rahal[9] | Chiara De Philippis[2] | Armando Santoro[2,5] | Carmelo Carlo-Stella[2,5] | Paolo Corradini[1,4]

Reported outcomes after CART-cell failure in large B-cell lymphomas (LBCL) are poor, with **median overall survival of ~ 8 months.**

The main salvage option is currently represented by CD3xCD20 bispecific antibodies (BsAb): durable responses are reported also in patients failing CAR-T cells .

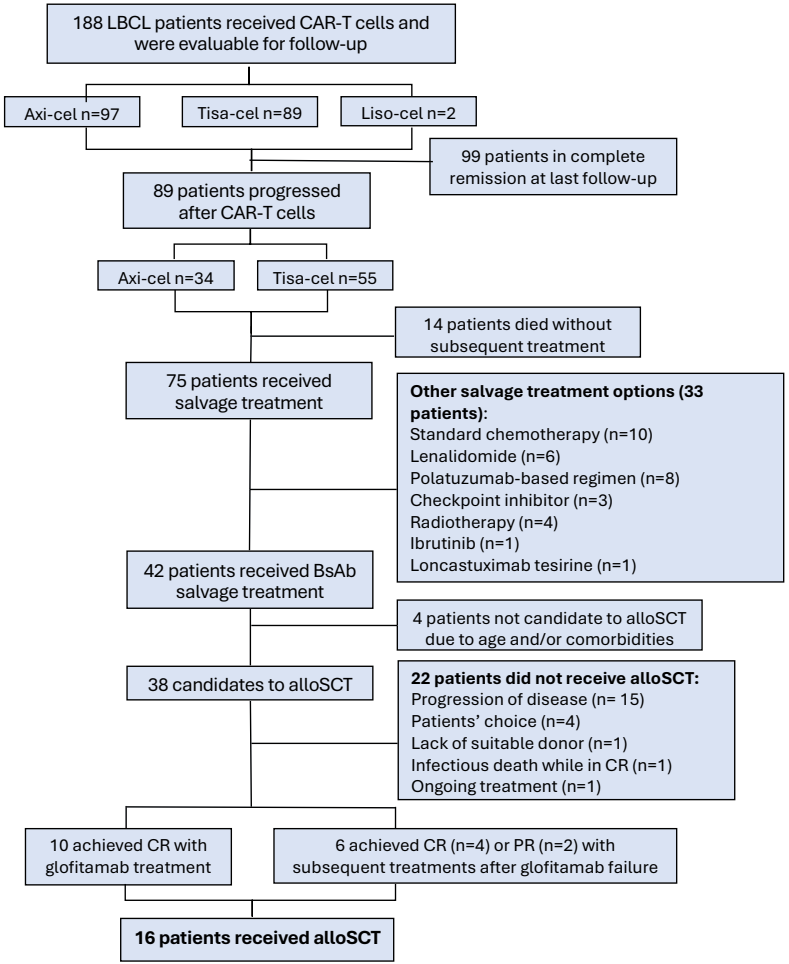


Multicenter Study > Br J Haematol. 2025 Sep;207(3):956-964. doi: 10.1111/bjh.70010.
Epub 2025 Jul 22.

Allogeneic transplantation after failure of chimeric antigen receptor–T cells and exposure to bispecific antibodies: Feasibility, safety and survival outcomes

Angelica Barone [1 2], Chiara De Philippis [3], Federico Stella [1], Anna Dodero [2], Barbara Sarina [3], Martina Pennisi [2], Armando Santoro [3 4], Carmelo Carlo-Stella [3 4], Anna Guidetti [1 2], Stefania Bramanti [3], Paolo Corradini [1 2]

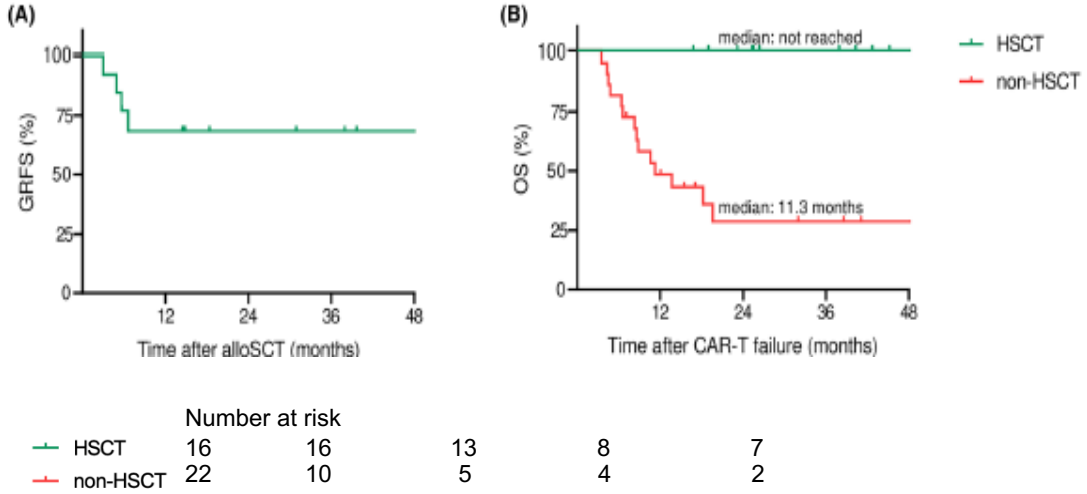
- From 2019 to 2025, **188 patients treated with CAR-T** cells and evaluable for follow-up (INT & Humanitas).
- Among **89 patients with progressive disease**, 38 (42%) received CD20xCD3 BsAb monotherapy (glofitamab in all patients) and were also candidates for up-front alloSCT consolidation.
- Among **38 alloSCT candidates**, 22 did not receive alloSCT, mainly because of progressive disease.
- Ultimately, **16 patients received alloSCT**; 15 were evaluable for post-transplantation outcomes.



Survival after CAR-T failure of allo-SCT vs non-alloSCT patients

At last follow-up:

- 1 (6%) infectious death in the alloSCT grou
- 15 (68%) deaths in the non-alloSCT group:
  - 14 due to progressive disease
  - 1 due to Sars-CoV-2 infection



2-years OS 93% vs 25%, p<0.001

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

UNIVERSITÀ
DEGLI STUDI
DI MILANO

Acknowledegments

All the Italian qualified centers for CAR-T treatment, the referral centers, patients, families and nurses.

Dept. of Hematology
Paolo Corradini
Federico Stella
Angelica Barone
Annalisa Chiappella
Anna Dodero
Anna Guidetti
Martina Pennisi
Lucia Farina

Lab and Pathology
Cristiana Carniti
Martina Magni
Giada Zanirato
Sadhana Jonnalagadda
Karishma Raulo
Eliana Irrigati
Daniele Lorenzini
Luca Agnelli

Research support and Statistics
Anisa Bermema
Stefano Marcandalli
Silva Lejvar
Rosalba Miceli

University of Bologna
Francesca Bonifazi
Pierluigi Zinzani

Humanitas Cancer Center
Stefania Bramanti
Chiara De Philippis
Carmelo Carlo Stella
Armando Santoro

fondazione GIMEMA onlus FRANCO MANDELLI

AIL ASSOCIAZIONE ITALIANA CONTRO LEUCEMIE LINFOMI E MIELOMA MILANO

LSH-TA Life Science Hub Terapia Avanzata
Research that improves therapies

Fondazione Regionale per la Ricerca Biomedica

60 AIRC

SIE Società Italiana di Ematologia