LINFOMI NEI PAZIENTI CON INFEZIONE DA HIV

DLBCL E IMMUNOTERAPIA (MoAB e IMMUNOCONIUGATI, AB BISPECIFICI, CAR-T)

MANUELA ZANNI
SCDU EMATOLOGIA di ALESSANDRIA

Milano, 29 maggio 2026

FONDAZIONE ITALIANA LINFOMI

BACKGROUND
Lymphomas in PWH (People living with HIV)

B-cell lymphomas are among the most common malignancies among people living with HIV and a a leading cause of death in PWH as they live longer on ART (1)

The most common histological types are diffuse large B-cell lymphoma (DLBCL; 37%), HL (26%) and Burkitt lymphoma (BL; 20%). (2)

The probability of developing lymphomas is markedly raised in people living with HIV with low CD4+ T-cell counts and prolonged HIV viraemia. (3)

The incidence of all AIDS-defining malignancies has significantly decreased in the ART era, but the risk remains significantly elevated. (3)

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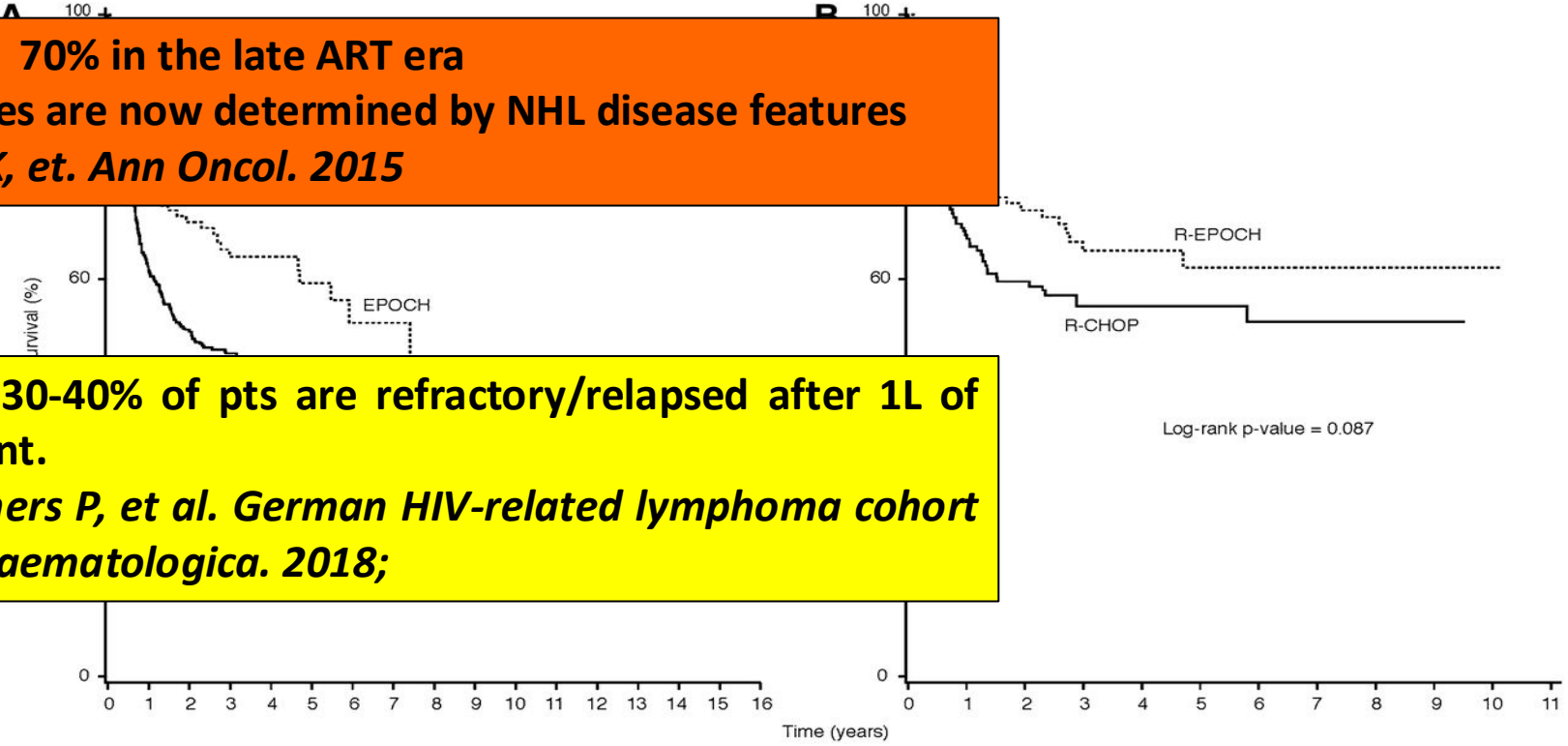
1) Odeny TA et al. Cancer in people living with HIV. Infect Dis Clin North Am. 2024
2) Carbone A., Hematologic cancers in individuals infected by HIV Blood. 2022
3) Hernández-Ramírez RU, et al. Lancet HIV. 2019;

OS for HIV-pos DLBCLs treated with EPOCH vs CHOP and R-EPOCH vs R-CHOP

5 yrs-OS 70% in the late ART era
Outcomes are now determined by NHL disease features
Barta SK, et. Ann Oncol. 2015

Around 30-40% of pts are refractory/relapsed after 1L of treatment.
Schommers P, et al. German HIV-related lymphoma cohort study. Haematologica. 2018;



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Stefan K. Barta,, Treatment factors affecting outcomes in HIV-associated non-Hodgkin lymphomas: a pooled analysis of 1546 patients, Blood, 2013,

American Society of Hematology
Helping hematologists conquer blood diseases worldwide

Salvage treatments in HIV-positive relapsed/refractory lymphomas

More intensive chemotherapy and peripheral stem cell rescue are feasible the safety and efficacy of this treatment strategy in HIV-positive lymphomas

ASCT:

- ✓ Comparable survival between HIV+ and HIV−

José L. Díez-Martín, et al. Blood, 2009;

- ✓ HIV status does not affect the outcome of autologous stem cell transplantation (ASCT) for non-Hodgkin lymphoma (NHL

Palmer JM, et al. Biol Blood Marrow Transplant. 2010;

ALLO-SCT:

- ✓ Allogenic stem cell transplantation has also been successfully performed in patients with HIV with refractory lymphoma

Ambinder RF,et al. Biol Blood Marrow Transplant. 2019

-SCT

Arslan S, et al. Biol Blood Marrow Transplant. 2019;

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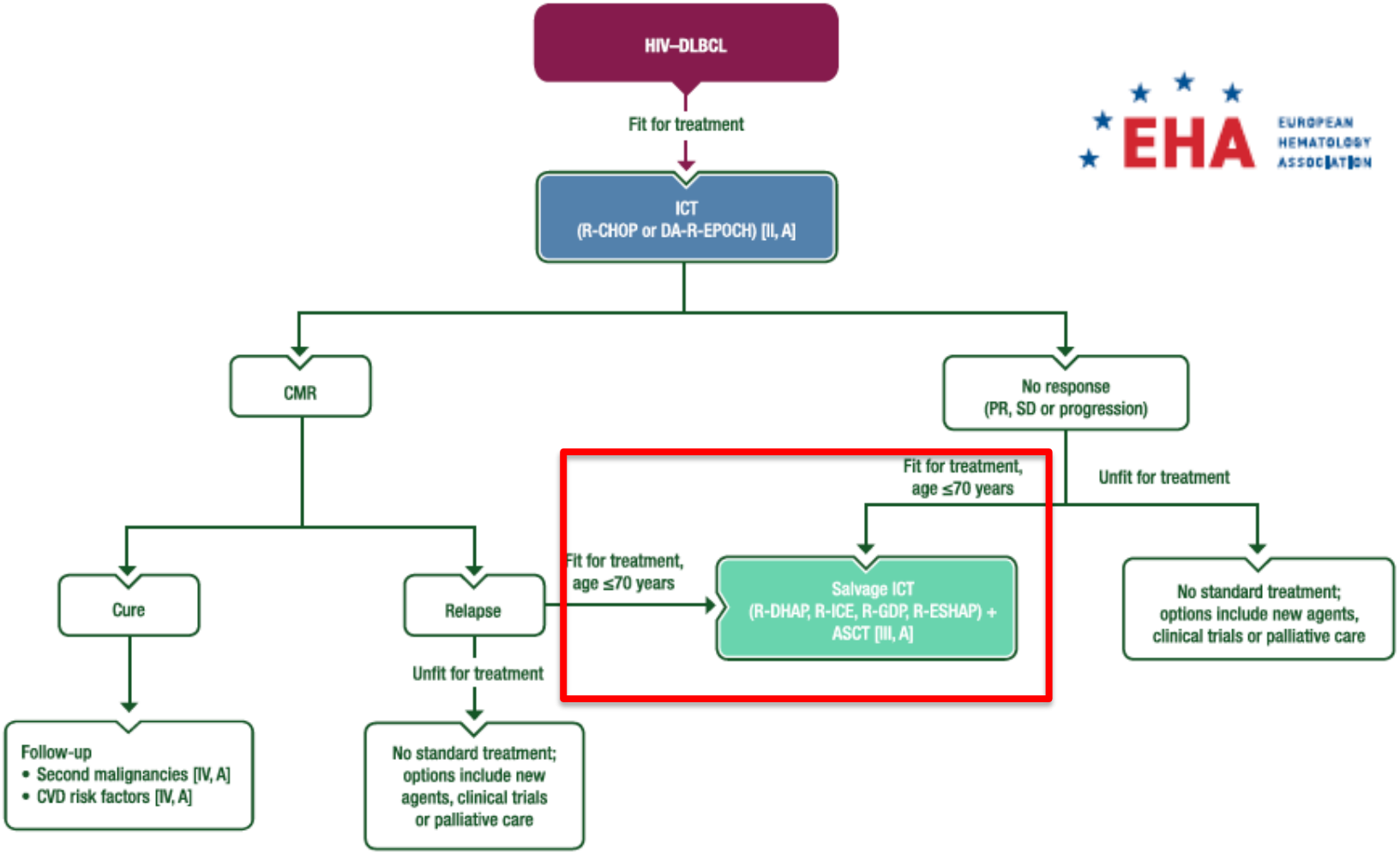
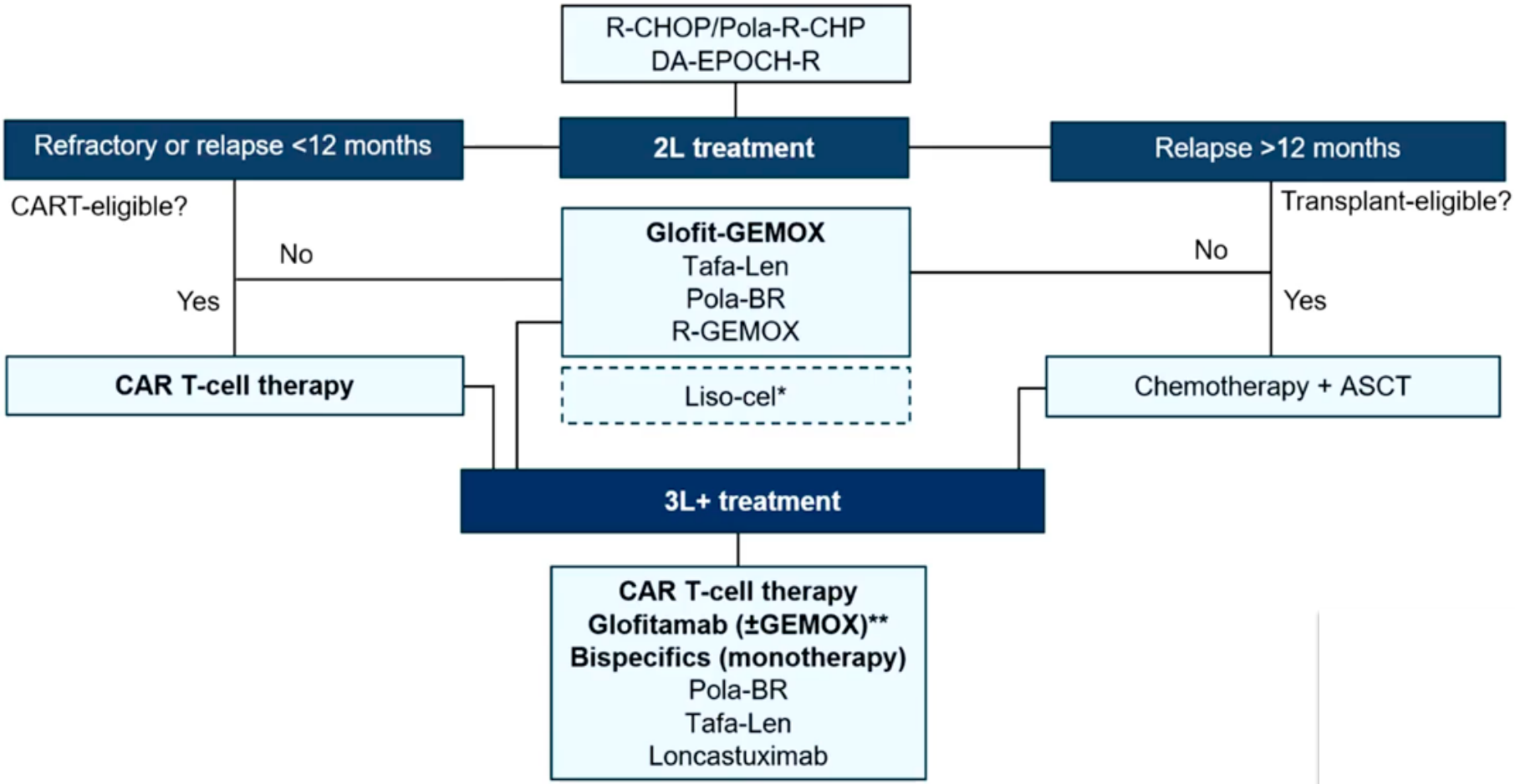
HIV-associated Lymphomas: EHA–ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up (2024)



K. Hübel, et al . Ann Oncol, 2024

Treatment algorithm of large B-cell lymphoma



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Eyre T.A. et al. Annals of Oncology 2025

CAR-T in HIV+ lymphoma

POTENTIAL CONCERNS REGARDING CAR-T IN HIV-LYMPHOMA

Interactions
direct influence of combined ART on CAR-T cells

Target dose of CAR T-cells (low CD4+)

Low-level viraemia and blips

Lentiviral vectors

Only gamma-retroviral-based CAR T-cells can be recommended

Side effects
Higher IL-6 levels of PWH might be associated with an increased risk for CRS.

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Hattenhauer ST et al, HIV Med, 2023

CAR-T in HIV+ lymphoma (anti CD19)

PWH have been excluded based on HIV status

from pivotal trials leading to FDA and EMA approval of all currently available CD19-directed CAR-T cell products for the management of relapsed or refractory B cell lymphomas

Limited data on CAR-T are available

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CAR-T in HIV+ lymphoma (anti CD19)

TABLE 1 Use of CAR T-cell therapy in patients with HIV ($n = 6$)

Case	References	Age (years)	Sex	Combined ART	$CD4^+$ T-cells (cells/μL)	T-cells (cells/μL)	Viral load (copies/mL)	Lymphoma	CAR product	Side effects (grade)/ therapy	Response (follow up)
1	[33]	47	m	Yes	52	n.s.	67	DLBCL	Axicabtagene ciloleucel	CRS (grade 2)/ tocilizumab, steroid ICANS (grade 3)/ steroid	CR (1 year)
2	[33]	n.s.	m	Bictegravir/ emtricitabine/ tenofovir alafenamide	127	n.s.	Undetectable	DLBCL	Axicabtagene ciloleucel	no CRS no ICANS	CR (at least 28 days)
3	[31]	n.s.	n.s.	n.s.	127	n.s.	Undetectable	DLBCL	Axicabtagene ciloleucel	n.s.	CR (n.s.)
4	[32]	49	m	Yes	170	847	Undetectable	DLBCL	Axicabtagene ciloleucel	CRS (grade 1)/steroid ICANS (grade 2)/ steroid	PR (PD after 2 months)
5	[36]	66	f	n.s.	629	n.s.	Undetectable	DLBCL	Axicabtagene ciloleucel	CRS (grade 1)/steroid ICANS (grade 2)/ steroid	PD (isolated CNS recurrence after 4 months with systemic CR)
6	[34]	53	m	Yes	n.s.	n.s.	n.s.	DLBCL	Axicabtagene ciloleucel	CRS (grade 1)/ anakinra, steroid ICANS (grade 3)/ anakinra, steroid	PD (after 15 days)

Abbreviations: ART, antiretroviral therapy; CAR, chimeric antigen receptor; CNS, central nervous system; CR, complete response; CRS, cytokine releasing syndrome; DLBCL, diffuse large B-cell lymphoma; f, female; ICANS, immune effector cell-associated neurotoxicity syndrome; m, male; n.s., not stated; PD, progressive disease (including recurrent disease); PR, partial response.

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Hattenhauer ST et al, HIV Med, 2023

CONSORTIUM FOR
Advancing
Management and Prevention of
Cancer in People with HIV

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AMC-113: CD19-Directed CAR T-Cell Therapy for B-Cell Lymphoid Malignancies Is Safe and Effective in People Living with HIV (PWH) – A Matched Cohort Analysis by the Center for International Blood and Marrow Transplant Research (CIBMTR) and the AIDS Malignancy Consortium (AMC)

Stefan K. Barta, Ariela Noy, Kwang Woo Ahn, Jinalben Patel, Tiffany Hunt, Uroosa Ibrahim, Robert Biaocchi, Deukwoo Kwon, Marcelo C. Pasquini, Richard F. Ambinder

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Barta SK, et al. ASH meeting 2025

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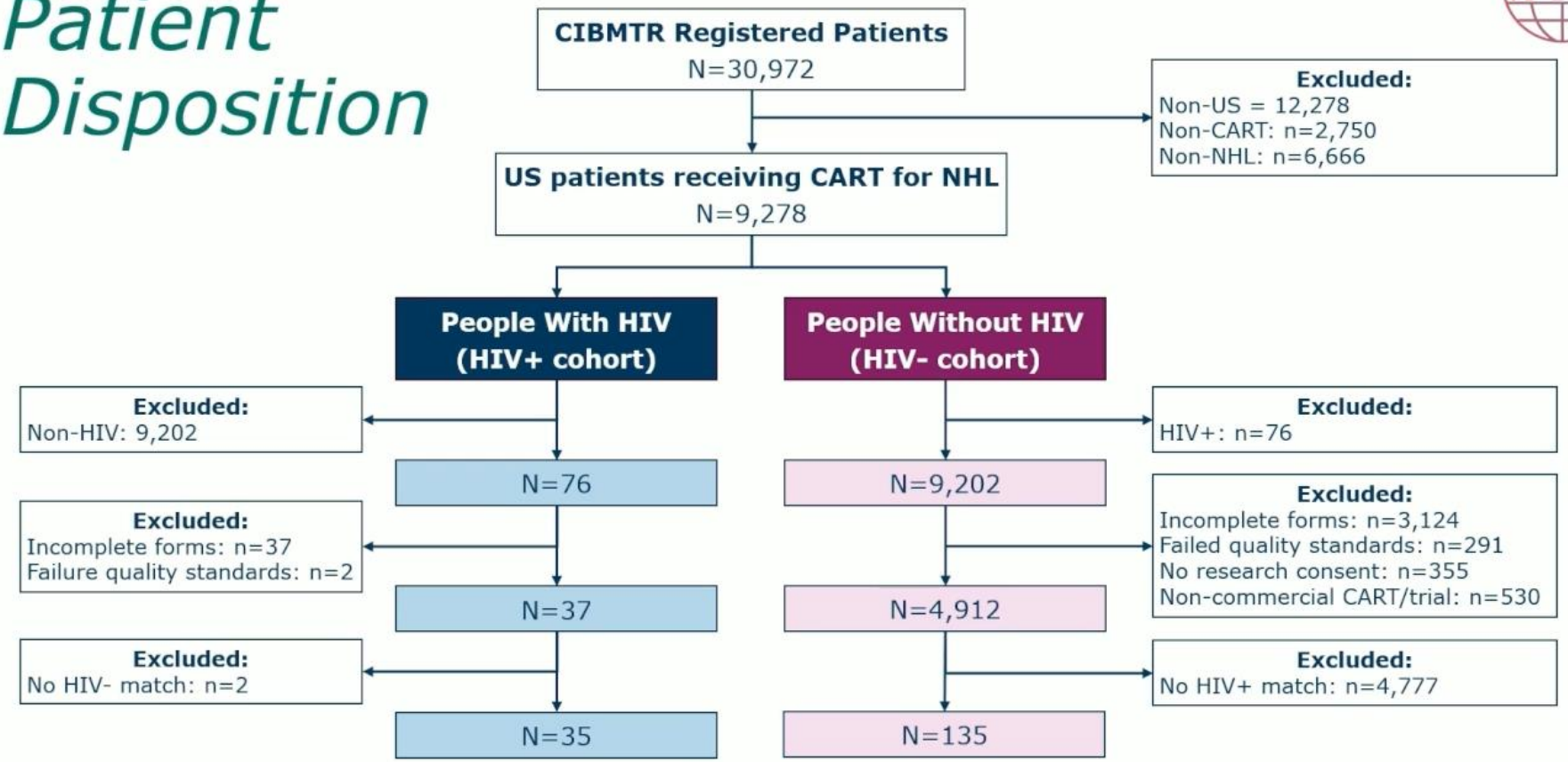
Patient Disposition



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Patient Demographics

Patient and Disease Characteristics		HIV+ N=35	HIV- N=135	P-value
Age, median (range)*		56 (29-70)	57 (24-73)	0.88
Gender, male (%)		31 (89)	75 (56)	<0.1
Race, n (%)				
	White	20 (57)	105 (78)	<0.01
	Black/AA	9 (26)	11 (8)	
	Asian	0 (0)	12 (9)	
	Unknown/Not reported	6 (17)	7 (5)	
Ethnicity, n (%)				
	Latinx	6 (17)	22 (16)	0.32
	Non-Latinx	26 (74)	109 (81)	
	Not reported	3 (9)	4 (3)	
Performance Status, n(%)*	*Karnofsky ≥80*	26 (74)	101 (75)	0.98
Histology, n (%)*	*DLBCL*	32 (91)	123 (91)	0.72
	Follicular (G1-3)	2 (6)	8 (6)	
	Mantle Cell	1 (3)	4 (3)	
LDH >ULN, n(%)		15 (43)	59 (44)	0.77
CART19 product, n (%)*				
	Axicabtagene ciloleucel	34 (97)	131 (97)	0.97
	Brexucabtagene autoleucel	1 (3)	4 (3)	
Prior HCT, n (%)		8 (23)	23# (17)	0.68

Patient and Treatment Characteristics		HIV+ N=35	HIV- N=135	P-value
Prior therapies, n (%)	*1*	5 (14)	11 (8)	0.42
	2	9 (26)	38 (28)	
	3+	20 (57)	80 (60)	
	Not reported	1 (3)	6 (4)	
Disease status at CART, n(%)*				0.90
	CR	1 (3)	4 (3)	
	PR	5 (14)	19 (14)	
	Relapse, resistant	22 (63)	82 (61)	
	Relapse, untreated	1 (3)	6 (4)	
	Relapse, chemo-sensitive	3 (9)	18 (13)	
	Relapse, sensitivity unknown	3 (8)	6 (4)	
Bridging therapy, n (%)*		22 (63)	65 (48)	0.22
Lymphodepletion n (%)				0.15
	Flu/Cy	28 (80)	120(89)	
	Bendamustine	6 (17)	12 (9)	
	Other$	1 (3)	3 (1)	

HIV viral load pre-CART, Copies/ml, median (range)	20 (0-10x10^6)
HIV VL < 200 copies/ml, n (%)^	21 (88)
CD4 count pre-CART, median (range)**	191 (0-252)

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* Matching parameters; # n=1/23 had a prior allo HCT; $ Fludarabine single agent, n=1; Fludarabine & cytarabine n=1; bendamustine & other n=2; ^ available for n=24; ** only available for n=7

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Adverse Events – CRS and ICANS

CART-Associated Toxicities among patients with follow up (n=19)	All Grades, n (%)		G1, n (%)		G2 n (%)		G3, n (%)		G4 n (%)		G5, n (%)		P-value
	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	HIV+	HIV-	
Cytokine Release Syndrome (CRS)	24 (69)	111(82)	17 (49)	70 (52)	5 (14)	36 (27)	0 (0)	3 (2)	0 (0)	1 (1)	**2 (6)***	0 (0)	**0.04**
Median time to onset, median (range):	**HIV+:** 5 days (1-10);				**HIV-:** 5 days (1-354)								0.12
Median time to resolution, median (range):	**HIV+:** 4 days (1-13);				**HIV-:** 5 days (1-22)								0.51
Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)	8 (22)	60 (44)	0 (0)	16 (12)	1 (3)	12 (9)	3 (9)	19 (14)	3 (9)	5 (4)	0 (0)	2 (2)	**0.17**
Median time to onset, median (range):	**HIV+:** 8 days (4-11);				**HIV-:** 7 days (2-20)								0.82
Median time to resolution, median (range):	**HIV+:** 7 days (4-11);				**HIV-:** 4 days (1-27)								

** Concurrent G5 bacterial sepsis, n=1, and PD n=1*

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Adverse Events – Infections & Hematologic

Infections by 100 days	HIV+	HIV-	P-value
Bacterial infection, n(%)	10 (29)	14 (10)	<0.01
Fungal infection, n(%)	2 (6)	1 (1)	0.05
Viral infection, n(%)	6 (17)	26 (19)	0.78
Parasitic infection, n(%)	0 (0)	0 (0)	N/A
Other specified infection, n(%)	2 (6)	6 (4)	0.75

Hematological Toxicity	HIV+	HIV-	P-value
Neutrophil recovery, n(%)	29 (83)	106 (79)	0.39
ANC≥ 500/mm^3 x3			
@100 days, % (95%CI)	91 (78-99)	96 (92-99)	0.39
Platelet recovery, n(%) ≥ 20 × 10^9/L	27 (77)	122 (91)	0.13
@100 days, % (95%CI)	77 (61-90)	91 (85-95)	0.06

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Efficacy – Response

Response Rate			
	HIV+	HIV-	P-value
Best Response @ 100 days, n(%)			**0.003**
CR	11 (32)	75 (56)	
PR	3 (9)	14 (10)	
SD	2 (6)	6 (4)	
PD	16 (46)	32 (24)	
Dead	2 (6)	4 (3)	
Not assessed	1 (3)	4 (3)	
Best Response @ 6 months, n(%)			**0.003**
CR	12 (34)	78 (58)	
PR	2 (6)	13 (10)	
SD	2 (6)	7 (5)	
PD	16 (46)	31 (23)	
Dead	3 (9)	4 (3)	
Not assessed	0 (0)	2 (2)	
Best Response @ 1 year, n(%)			**0.003**
CR	12 (34)	80 (59)	
PR	2 (6)	13 (10)	
SD	2 (6)	5 (4)	
PD	16 (46)	33 (24)	
Dead	3 (9)	4 (3)	

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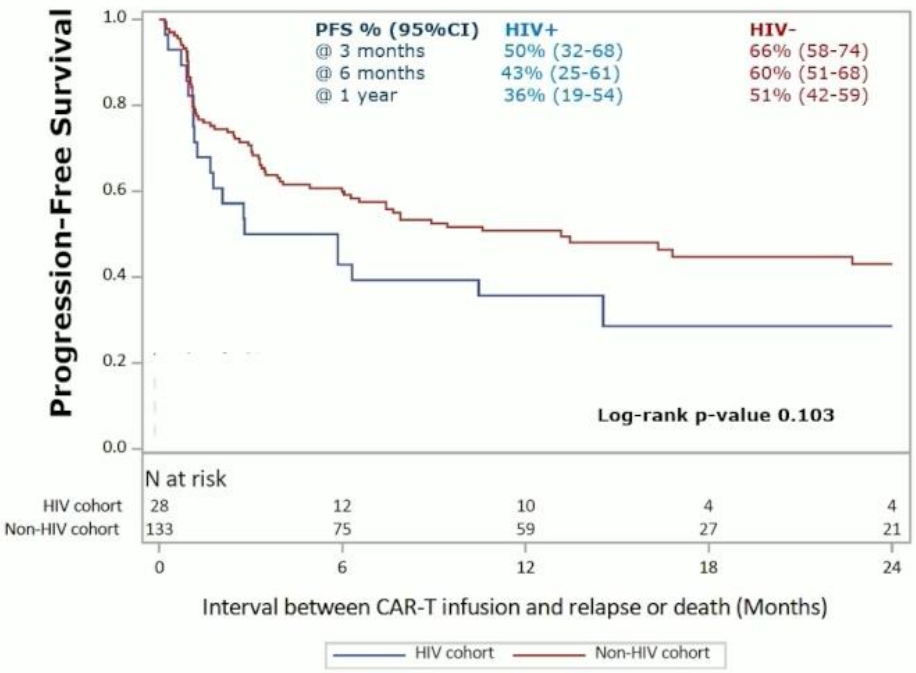
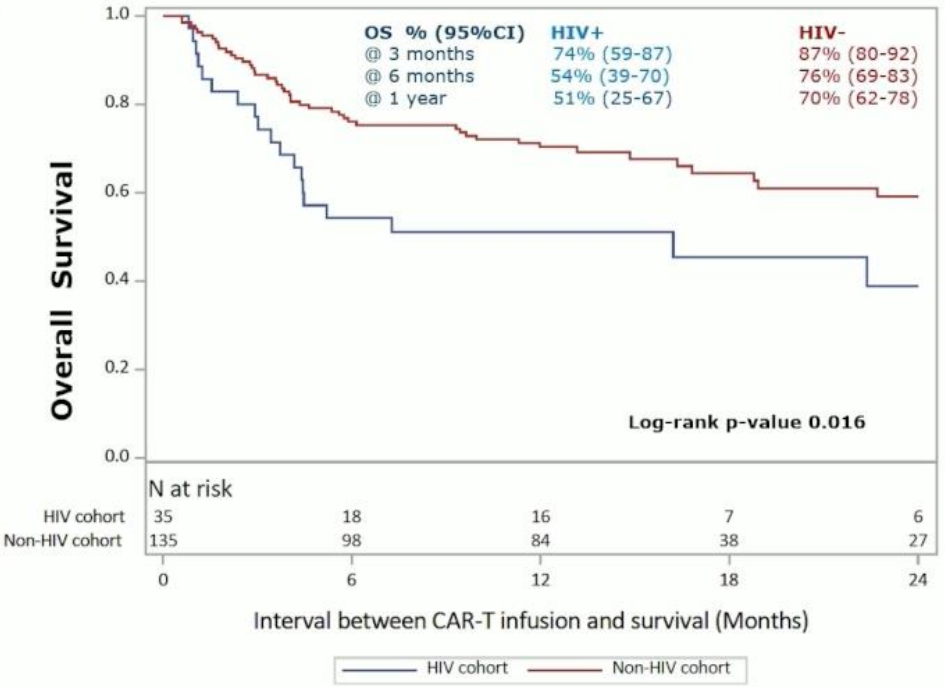
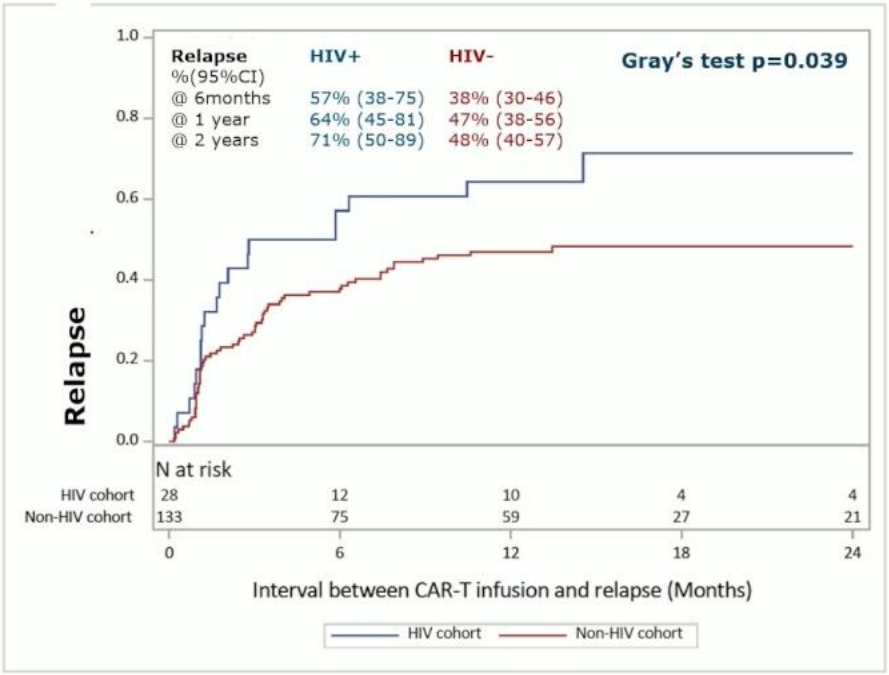
Outcomes - Survival

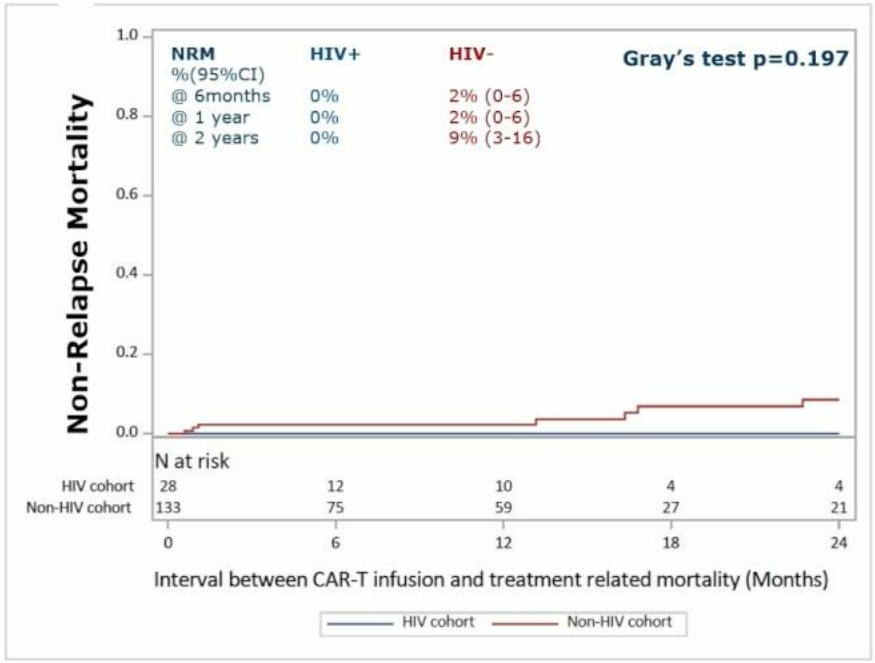




Barta SK, et al. ASH meeting 2025

Risk of Relapse & Non-Relapse Mortality





Reported Primary Cause of Death, N (%) **p=0.81**

	HIV+	HIV-
Primary Disease	18 (95)	34 (74)
Bacterial infection	1 (5)	3 (7)
Others	0 (0)	9 (19)

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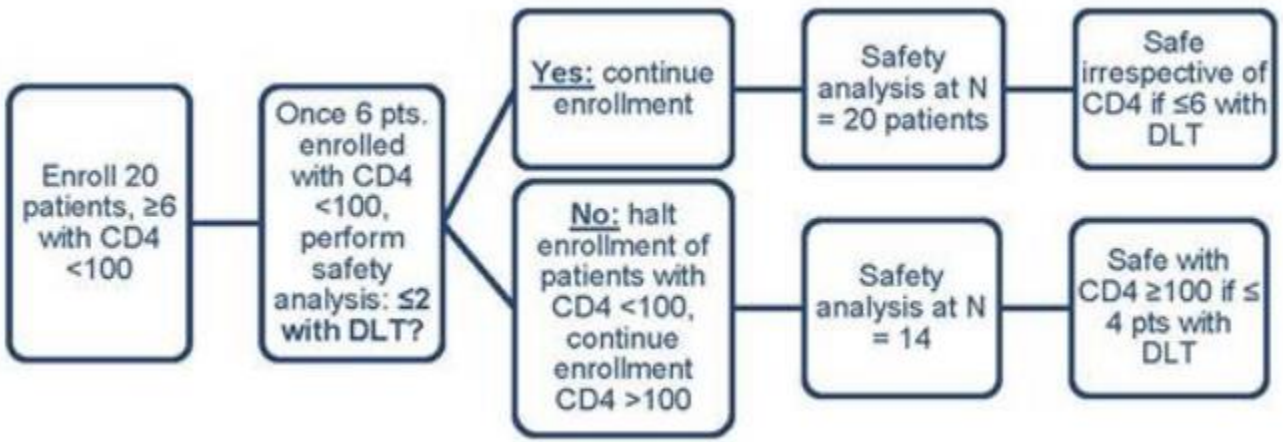
Trial-in-Progress: AMC 112: Axicabtagene Ciloleucel in Relapsed or Refractory HIV-Associated Aggressive B-Cell Non-Hodgkin Lymphoma (NCT05077527)

Zachary D. Epstein-Peterson, Jeannette Y Lee, Stefan K. Barta, M. Lia Palomba, Ariela Noy



INCLUSION CRITERIA

- HIV viral load <50 copies/mL;
- diagnosis of R/R DLBCL, HG- DLCBL,PMBCL, FL grade 3B;
- post 2 prior lines of therapy or refractory/relapsed within 12 months of frontline treatment;

FONDAZIONE ITALIANA LINFOMI

Blood (2022) 140 (Supplement 1): 12788–12789.

Real-life (DESCAR-T registry): PLWH pts with R/R lymphoma treated with commercial CAR T therapy in France (24 pts in 15 centers)

- **DLBCL 84%,** FL 8%, T-FL 4%, GZL 4%
- **Median age 55 years (35-75),** 29% aged >60 yrs
- Stage III-IV 90%
- **median number of PTL 3 (1-4);** Prior ASCT 17%
- Median time from HIV diagnosis to CAR T 136 ms (11-342)
- HIV viral load undetectable in all available cases (11/24 pts)

- **Bridging therapy**:
  - 63% of pts (CT-based 37% of pts)
  - 73% (n=11) were NR
- **At time of CAR T infusion**:
  - 4 (17%) ECOG PS ≥2
  - 15 (63%) elevated LDH
  - 10 (42%) elevated ferritin

OUTCOME

- **ORR at 90 days (M3) 50%; CRR 42%**
- Median f-up of 10.5 ms
- **PFS 40% and OS 55% at 12 ms** (f-up 10.5 ms)
- Ten deaths:
  - 8 PD; 1 Pseudomonas; 1 PML not related to CAR T

TOXICITY

- **CRS**: 21 pts (88%) [1 grade ≥3]
  - median onset 3 days (1-15)
  - complete resolution in all cases after 6 ds (1-10)
- **ICANS**: 8 pts (33%) [3 grade ≥3]
  - median onset 5.5 days (1-29)
  - complete resolution in all cases after 5.5 ds (2-10)

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Michele Clerico, et al. ASH meeting 2024

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Studio CAR-T_PWH

- Studio osservazionale retrospettivo multicentrico

(Pol Gemelli, Univ Milano, AOU Alessandria, AOR Cervello, Palermo, Cuneo)

- PWH adulti con linfoma refrattario/recidivato trattati con CAR-T
- Obiettivo primario: sicurezza a breve termine (CRS, ICANS, infezioni)
- Obiettivi secondari: HIV-RNA/CD4, risposta oncologica precoce, mortalità 30–90 gg
- Campione: ~6 casi – analisi descrittiva
- Rilevanza: supporto all'uso equo delle CAR-T nelle PWH

FONDAZIONE ITALIANA LINFOMI

PI: Antonella Cingolani

BiTE in HIV+ lymphoma (CD20xCD3)

Case report of two patients with refractory HIV-related B-cell lymphoma treated with the monoclonal antibody glofitamab for secondary central nervous system involvement

Yueru Ji, Jing Gao, Tong Wei, Miaowang Hao and Weiwei Qin*

Department of Hematology, Tangdu Hospital, The Fourth Military Medical University, Xi'an, China

LEUKEMIA & LYMPHOMA
2025, VOL. 66, NO. 5, 969–972
https://doi.org/10.1080/10428194.2024.2444470

Taylor & Francis
Taylor & Francis Group

Check for updates

LETTER TO THE EDITOR

Glofitamab in patients with HIV-associated B-cell lymphoma

Jose Tinajero[a], Tanya Markary[a], Dat Ngo[a], Swetha Kambhampati Thiruvengadam[b], Sabarish Ayyappan[c] and Matthew Mei[b]

[a]Department of Pharmacy, City of Hope, Duarte, CA, USA; [b]Department of Hematology and Hematopoietic Stem Cell Transplant, City of Hope, Duarte, CA, USA; [c]Department of Hematologic Malignancies, City of Hope, Atlanta, GA, USA

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BiTE in HIV+ lymphoma (CD20xCD3)

Table 1. Treatment course of patients receiving glofitamab with a concurrent diagnosis of HIV or AIDS

Age (current or age at death) / Sex	Concurrent ART / HIV Diagnosis Year	Previous Therapies	CG/FISH	NGS	Glofitamab Treatment	Current Status	CD4 count (cells/uL)/ HIV VL (copies/ mL) at Start
39/M	Biktarvy (bictegravir/ emtricitabine/ tenofovir alafenamide) / 2022	R-EPOCH (2C) R-CHOP (4C) Brentuximab vedotin (5C) R-GEMOX (3C) Axi-cel Pembrolizumab (2C)	BCL6 rearrangement	NA	With obinutuzumab pre-treatment Cycles completed = 5	CR	88 / 50
64/M	Biktarvy (bictegravir/ emtricitabine/ tenofovir alafenamide) / 2022	R-CHOP (1C) R-EPOCH (6C) with IT MTX HD MTX R-HyperCVAD part B (1C) WBRT Axi-cel XRT x5 sessions to L2-S2 and T2-T4	BCL2+/MYC+ (double expressor) Negative for MYC/ BCL2/ BCL6 rearrangement	NA	With obinutuzumab pre-treatment with concurrent acalabrutinib Cycles completed = 6	Deceased	227 / <30
59/M	Biktarvy (bictegravir/ emtricitabine/ tenofovir alafenamide) / 2020	R-CHOP (6C) Axi-cel Polatuzumab vedotin (1C)	MYC rearrangement	Negative	With obinutuzumab pre-treatment Cycles completed = 3	PD	160 / not detected
44/M	Biktarvy (bictegravir/ emtricitabine/ tenofovir alafenamide) / 2023	R-EPOCH (6C) with IT MTX	MYC rearrangement	NA	With obinutuzumab pre-treatment Cycles completed = 3	PD	288 / not detected

J. Tinajero, at al. Leukemia & Lymphoma, 2025

FONDAZIONE ITALIANA LINFOMI

International single-arm phase 2 trial addressing feasibility and efficacy of epcoritamab in HIV-positive patients with relapsed/refractory large B-cell lymphoma: EPICO STUDY

FONDAZIONE ITALIANA LINFOMI

Inclusion criteria:

- Adult (≥ 18 yo) HIV+ pts with CD20+ ***RR LBCL****
- ECOG PS score of 0-2
- ≥ 2 lines of anti-CD20 containing chemoimmunotherapy
- Failed or not eligible for HDT-ASCT
- HCV and/or HBV controlled infection are included

Exclusion criteria:

- CNS involvement
- Previous CD20xCD3 therapy
- Seizure disorder requiring anti-epileptic therapy
- Active infection

Sample size: 27 patients with RR HIV+ DLBCL

Sc Epcoritamab:

- *28-day cycles until PD or toxicity*

15 centers:

- **10 Italy**
- **4 Spain**
- **1 France**

PI: Andrés J.M. Ferreri, Alessandro Re, Michele Spina

CONCLUSIONS

Since PWH were not included in the pivotal trials, available data are limited about treatment of HIV+ DLBCL with new drugs.

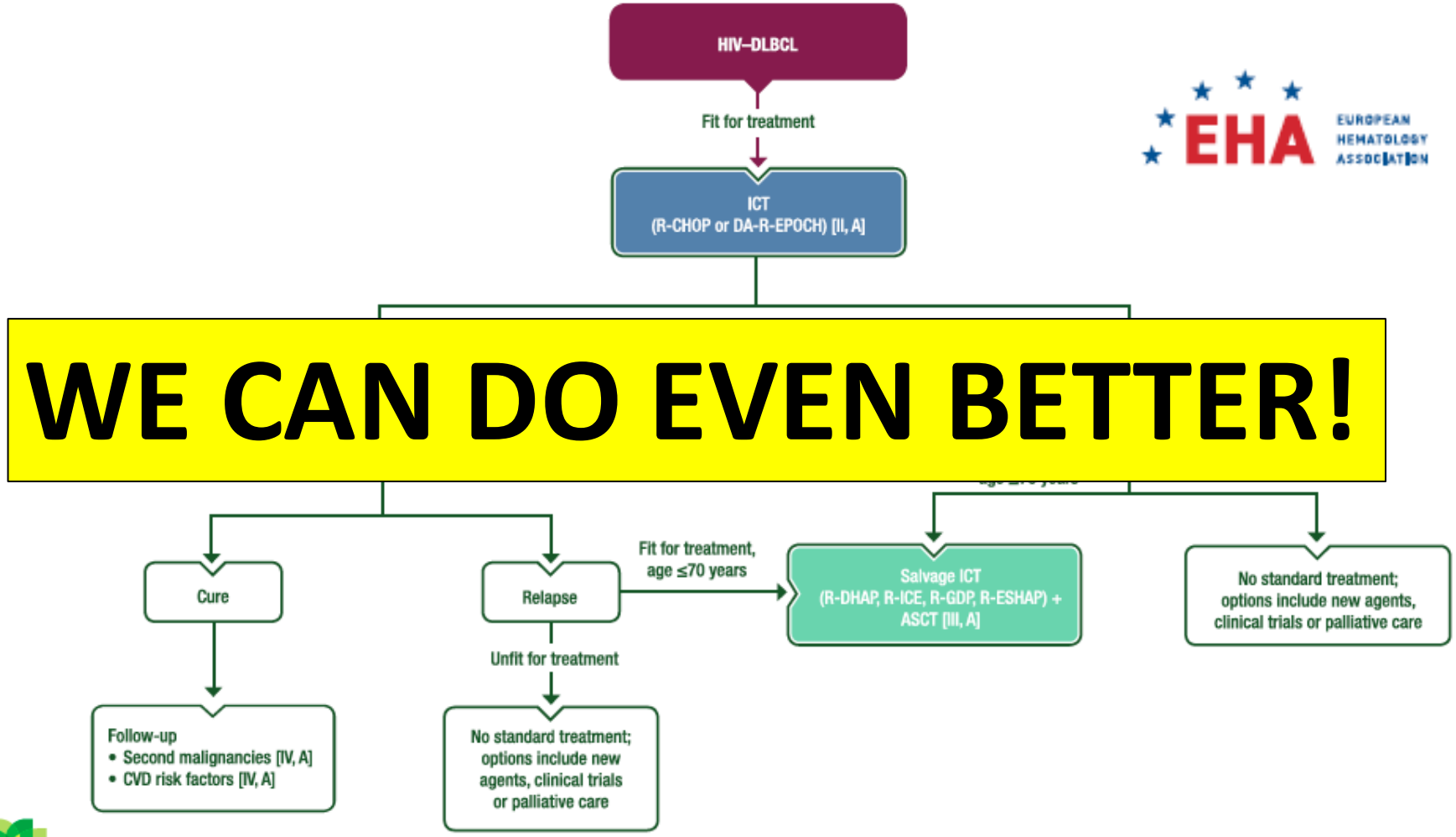
The emerging data revealed no clinical reasons for restrictions on the use of gamma-retroviral-based, CD19-targeted CAR T-cell therapy in PWH with r/r DLBCL.

Prospective clinical trials will be crucial to confirm the feasibility and safety of CAR-T e to define the role of BiTEs and other immunoconjugate antibodies.

The goal is to offer the same therapeutic standards of lymphoma therapy for people with and without HIV.

FONDAZIONE ITALIANA LINFOMI

HIV-associated Lymphomas: EHA–ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up (2024)



EHA EUROPEAN HEMATOLOGY ASSOCIATION

FONDAZIONE ITALIANA LINFOMI