CORSO EDUCAZIONALE

GRUPPO LINFOMI IN PAZIENTI CON IMMUNODEFICIT

Milano, UNAHOTELS Galles

23 maggio 2025

Update della terapia nei linfomi HIV-associati

Luisa Verga

Ematologia Monza

Fondazione IRCCS San Gerardo dei Tintori

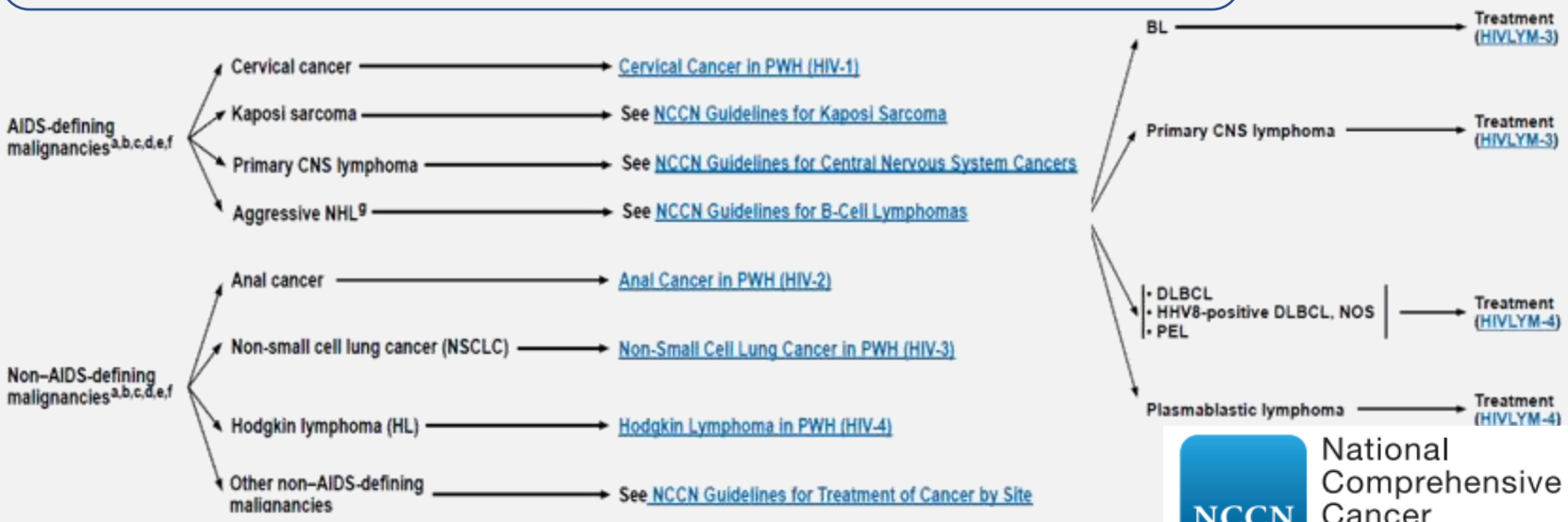
Sistema Socio Sanitario Regione Lombardia

Disclosures of Name Surname

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
Sobi					x		
Pfizer					x		

LYMPHOMA AND PLWH: what we must know

NCCN Guidelines Version 2.2024
Cancer in People with HIV



NCCN Guidelines Version 1.2025
Cancer in People with HIV

Aggressive NHL[g]	See NCCN Guidelines for B-Cell Lymphomas
Anal cancer	Anal Cancer in PWH (HIV-1)
Cervical cancer	Cervical Cancer in PWH (HIV-2)
Hodgkin lymphoma (HL)	Hodgkin Lymphoma in PWH (HIV-3)
Kaposi sarcoma	See NCCN Guidelines for Kaposi Sarcoma
Non-small cell lung cancer (NSCLC)	Non-Small Cell Lung Cancer in PWH (HIV-4)
Primary CNS lymphoma	See NCCN Guidelines for B-Cell Lymphomas
Other malignancies	See NCCN Guidelines for Treatment of Cancer by Site

LYMPHOMA AND PLWH: what we must know

Longitudinal trends in causes of death among adults with HIV on antiretroviral therapy in Europe and North America from 1996 to 2020: a collaboration of cohort studies

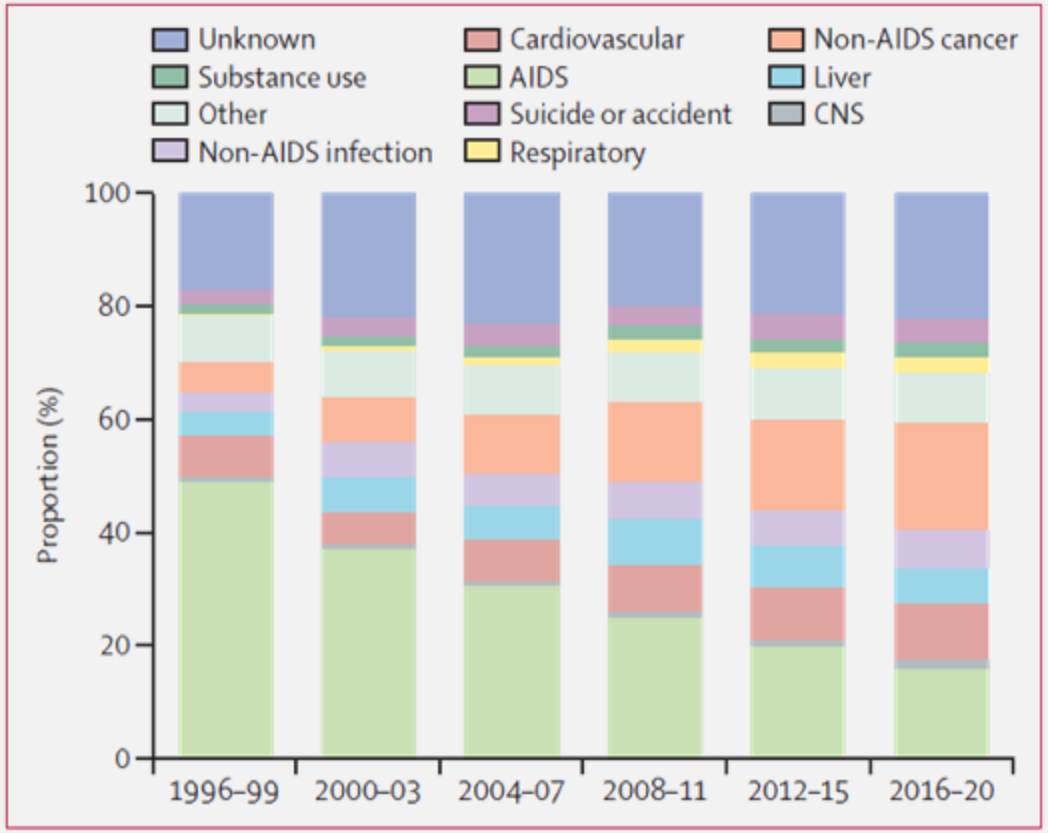
Adam Trickey, Lancet HIV,2024

189.301 PLWH followed up for 1 519 200 person-years

The median age at initiation of ART: 35 years 1996–99
38 years 2016–20.

Participants' median age: 37 years on Jan 1, 2000
43 years on Jan 1, 2008
47 years on Jan 1, 2016

Proportion PLWH with CD4 counts of 0–199:
42·6% at the start of the 1996–99
7·6% at the start of the 2016–20



LYMPHOMA AND PLWH: what we must know

Cancer Treatment Disparities in People With HIV in the United States, 2001-2019

McGee-Avila, JK, JCO2024

Characteristic	Adults With HIV (n = 16,334), No. (%)	Adults Without HIV (n = 2,880,955), No. (%)	*P*
Cancer type			**<.0001**
Cervix	558 (3.4)	49,474 (1.7)	
Diffuse large B-cell lymphoma	3,053 (18.7)	71,729 (2.5)	
HL	1,278 (7.8)	30,540 (1.1)	
Lung	3,561 (21.8)	634,437 (22.0)	
Anus	2,219 (13.6)	19,518 (0.68)	
Prostate	2,987 (18.3)	795,348 (27.6)	
Colon	1,428 (8.7)	462,585 (16.1)	
Breast	1,250 (7.7)	817,324 (28.4)	
Cancer stage			**<.0001**
Local	6,695 (41.0)	1,591,973 (55.3)	
Regional	3,899 (23.9)	743,109 (25.8)	
Distant	5,740 (35.1)	545,873 (19.0)	

Adults W HIV: 16,334; Adults W/H HIV 2,880,955

Cancer Type	PWH Not Receiving Cancer Treatment, No. (%)	People Without HIV Not Receiving Cancer Treatment, No. (%)	aOR[a]	95% CI
Overall aOR			**1.37**	1.32 to 1.44
Cancer type				
Cervix	52 (10.2)	2,961 (6.0)	**2.03**	1.52 to 2.70
DLBCL	531 (17.4)	10,616 (14.8)	**1.53**	1.38 to 1.70
HL	229 (17.9)	4,334 (14.2)	**1.39**	1.19 to 1.63
Lung	923 (25.9)	120,349 (19.0)	**1.79**	1.65 to 1.93
Anus	104 (4.7)	1,032 (5.3)	0.85	0.68 to 1.08
Prostate	705 (23.6)	141,297 (17.8)	**1.32**	1.21 to 1.44
Colon	137 (9.6)	23,964 (5.2)	**1.73**	1.43 to 2.08
Breast	71 (5.7)	27,730 (3.4)	**1.38**	1.07 to 1.77

LYMPHOMA AND PLWH: what we must know

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McGee-Avila, JK, JCO2024

	Calendar Year Periods			
	2001-2007	2008-2013	2014-2019	
Cancer Type	aOR[a] (95% CI)	aOR[a] (95% CI)	aOR[a] (95% CI)	*P* Interaction[b]
Overall aOR	**1.69 (1.55 to 1.84)**	**1.41 (1.32 to 1.51)**	**1.14 (1.06 to 1.23)**	**<.0001**
Cancer types				
Cervical cancer	**2.27 (1.34 to 3.86)**	**2.07 (1.28 to 3.35)**	**1.84 (1.12 to 3.01)**	.5720
DLBCL	**1.78 (1.49 to 2.12)**	**1.48 (1.26 to 1.75)**	**1.32 (1.07 to 1.63)**	.0872
HL	**1.53 (1.16 to 2.02)**	**1.42 (1.11 to 1.81)**	1.20 (0.88 to 1.63)	.1662
Lung cancer	**2.09 (1.80 to 2.43)**	**1.80 (1.59 to 2.03)**	**1.54 (1.33 to 1.77)**	**.0090**
Anal cancer	1.35 (0.85 to 2.15)	0.77 (0.52 to 1.13)	0.71 (0.48 to 1.04)	.1024
Prostate cancer	**1.74 (1.39 to 2.18)**	**1.42 (1.24 to 1.63)**	1.12 (0.98 to 1.28)	**.0048**
Colon cancer	**1.95 (1.31 to 2.93)**	**2.05 (1.55 to 2.70)**	1.31 (0.95 to 1.80)	.0509
Breast cancer	**2.63 (1.62 to 4.26)**	**1.54 (1.02 to 2.32)**	0.91 (0.60 to 1.34)	**.0008**

Association between HIV and lack of treatment

attenuated over time for many cancer types

HIV remained associated with the lack of treatment for
cervical cancer
DLBCL
lung cancer

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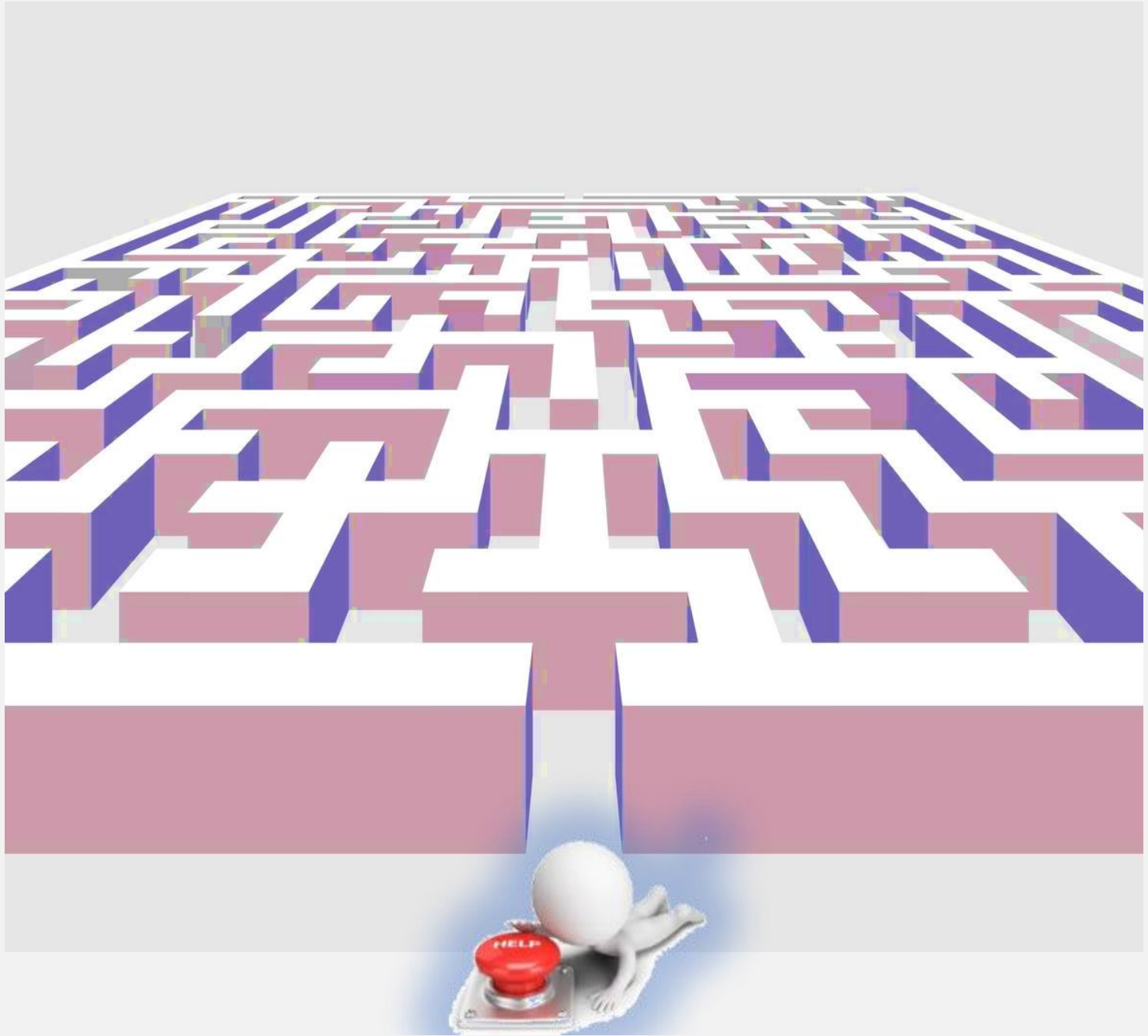
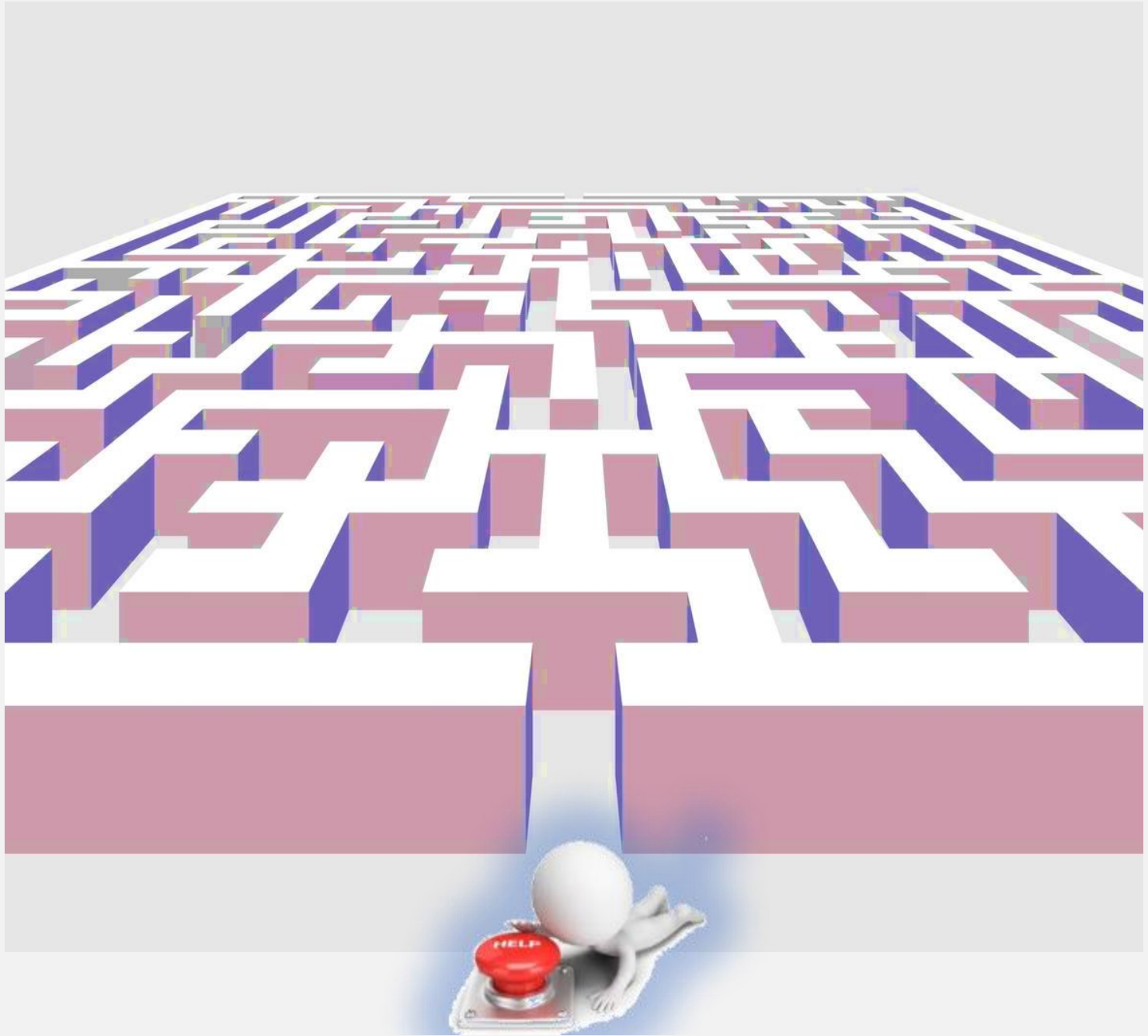
Associations between HIV status and lack of standard treatment by cancer type

During 2014-2019, HIV and lack of standard cancer treatment
DLBCL
cancers of the cervix
lung



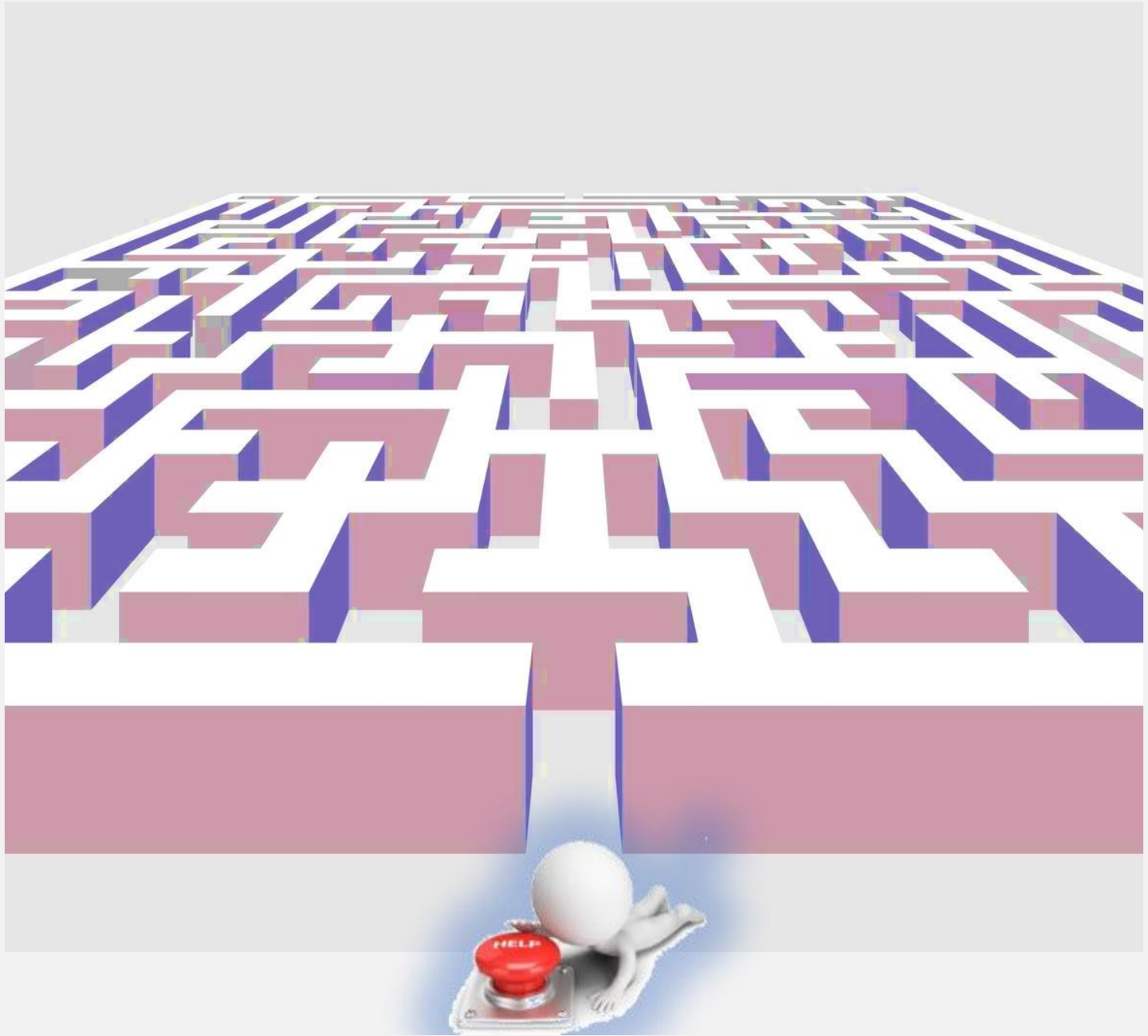
Burning issues:

- What types of lymphomas should I know about?
- Is the risk of infectious toxicity still high today? Are there any other significative toxicities? What about viral factors?
- what about staging? what role does the PET scan play?
- what are the clinical presentations today?
- Is the risk of CNS recurrence increased compared to the general population?



Burning issues:

- What do we know about the biology of these lymphomas?
- Are there any guidelines?



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WHO Classification of Tumors of Hematologic and Lymphoid Tissues

WHO classification, 5th edition 2022	WHO classification, revised 4th edition, 2016	
Hyperplasia arising in immune deficiency/ dysregulation distincted in - Follicular proliferation - interfollicular and paracortical proliferations Plasma-cell hyperplasia Mononucleosis-like hyperplasia - T-cell and histiocytic proliferations	Non-destructive forms distincted in: - Florid follicular hyperplasia - Plasmacytic hyperplasia - Infectious mononucleosis	**In contrast to the past, WHO 5 subclassifies these lesions based on pathologic features, as in immunocompetent patients, rather than clinical setting.**
KSHV/HHV8 Multicentric Castleman disease (also included in tumor-like lesion with B-cell predominance)	Multicentric Castleman disease	
Lymphomas arising in immune deficiency/ dysregulation	Monomorphic B and T cell neoplasms, cHL **Lymphomas associated with HIV infection** Other iatrogenic immunodeficiency-associated LPDs	
In born error of immunity-associated lymphoid proliferations and lymphomas	Lymphoproliferative disease associated with primary immune disorders	

LYMPHOMA AND PLWH: The viral cooperation

DEFINITION: a mechanism by which different viruses coinfecting human tissue have synerigstic or regulatory effects on carcinogenesis

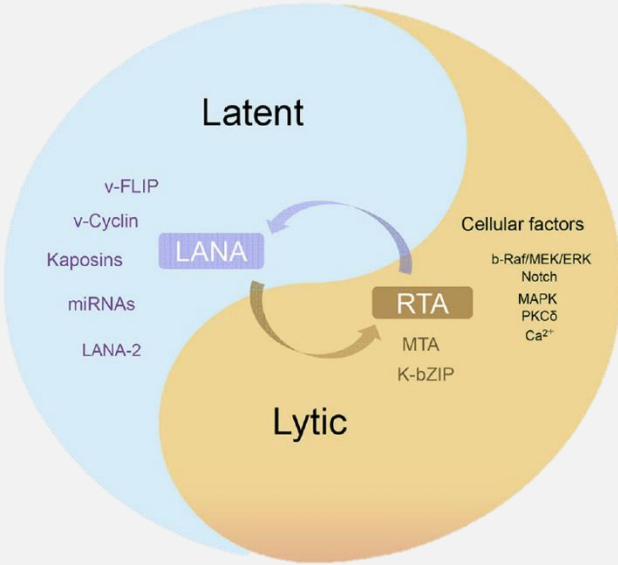
EBV

originally identified in 1964 by Sir Anthony Epstein and co-workers in Burkitt's lymphoma;

KSHV/HHV8

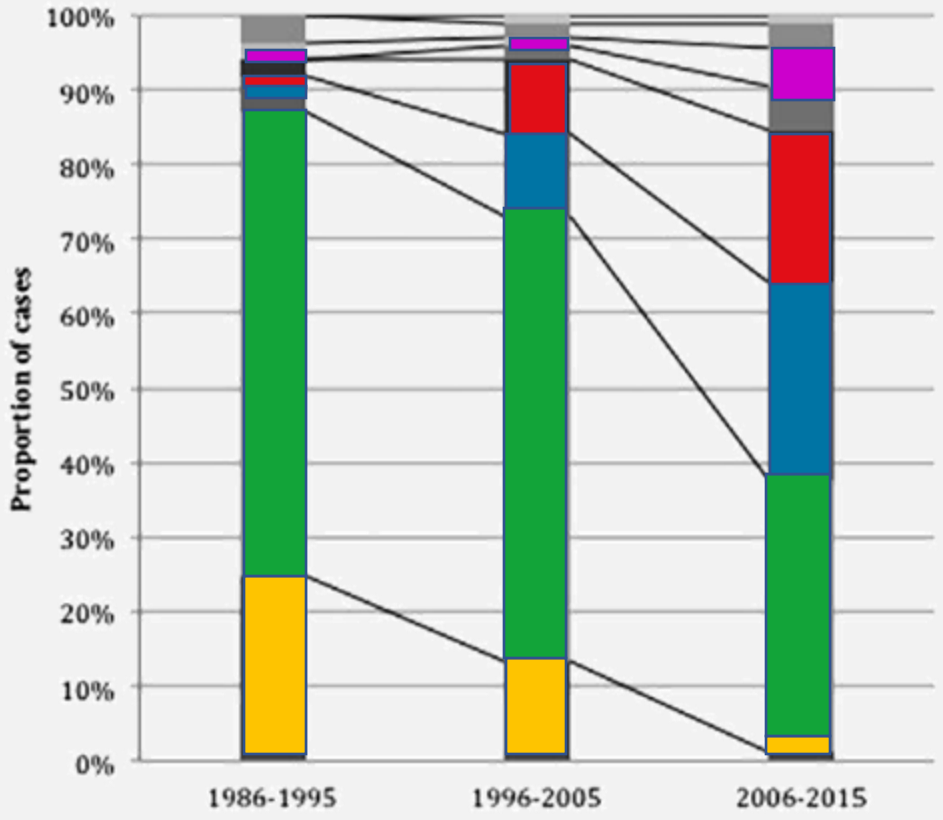
Molecular identification in KS in 19 an oncogenic double-stranded DNA virus

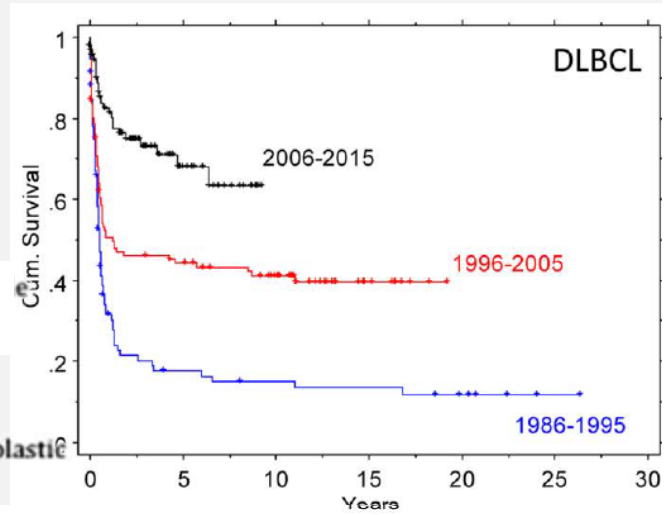
persists in human cells for a lifetime

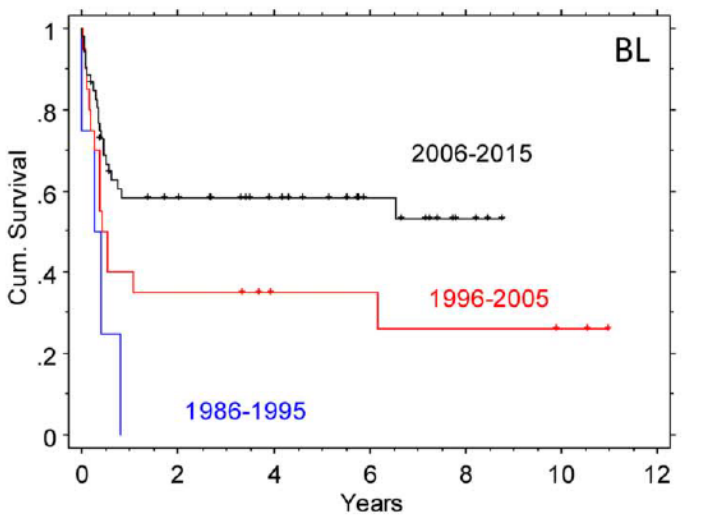


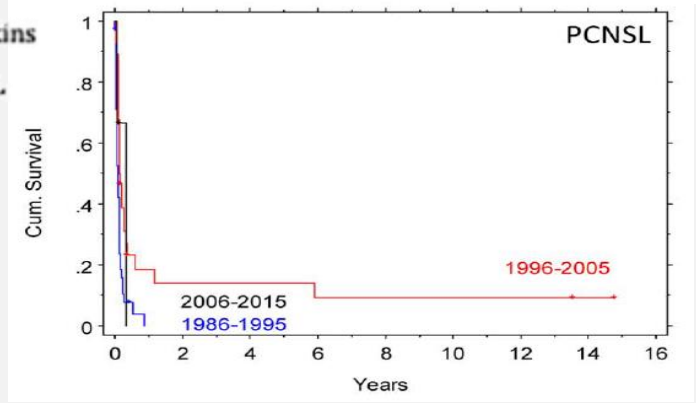
LYMPHOMA AND PLWH: changes over years

Evolution of HIV-Associated Lymphoma Over 3 Decades



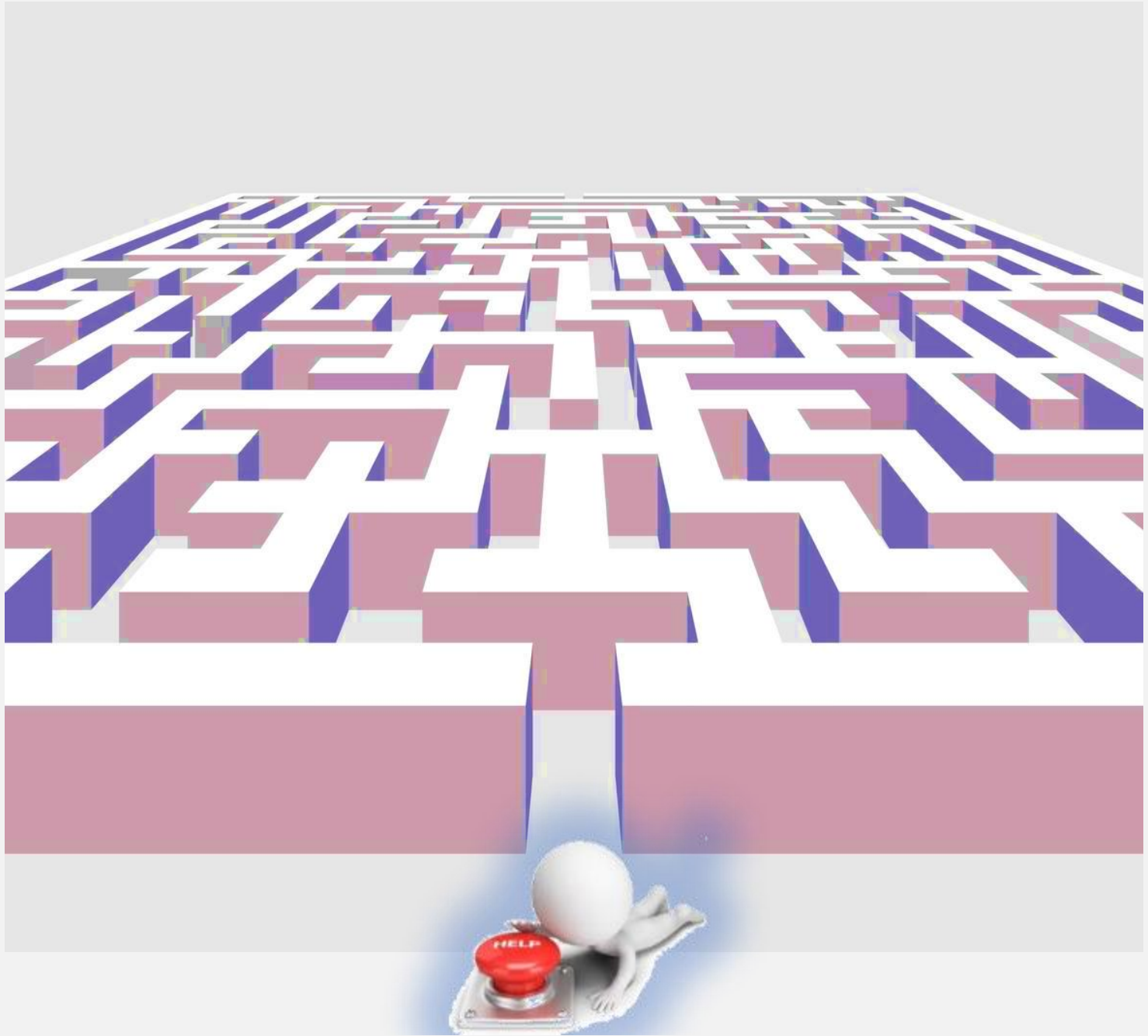






- use of cART,
- better focus on opportunistic infection prophylaxis
- improved chemotherapy
- Modern therapy!

Ramya Ramaswami et al, 2016



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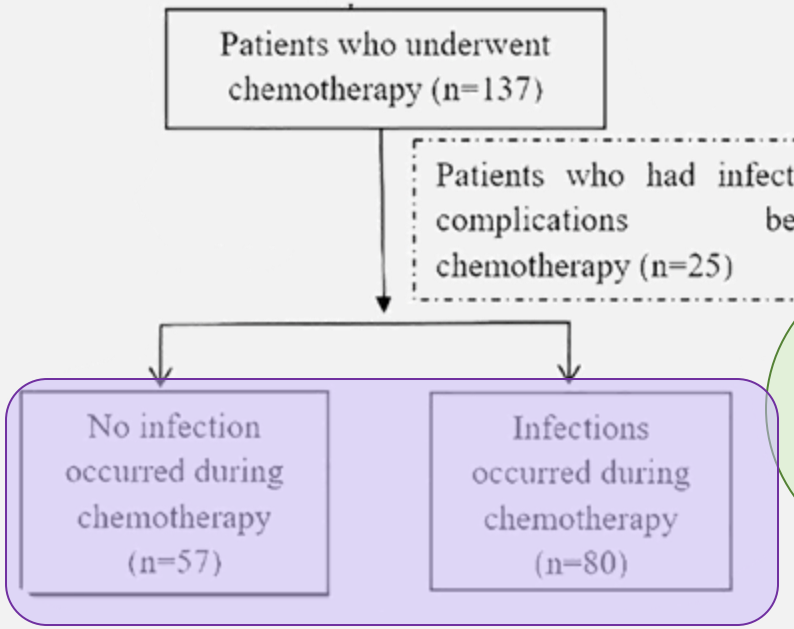
LYMPHOMA AND PLWH: Chemotherapy and excess of toxicity

Incidence and spectrum of infections among HIV/AIDS patients with lymphoma during chemotherapy
Wang Z. *Journal of infection and chemotherapy, 2022*

Characteristics	AIDS patients with lymphoma (n = 164)
Age (year)	
Median (interquartile range)	43 (34–55)
Range	8–81
Gender, n (%)	
Male	149 (90.9)
Female	15 (9.1)
Extranodal involvement, n (%)	106 (64.6)
B symptoms, n (%)	34 (20.7)
Serum LDH, n (%)	
Normal	50 (30.5)
>1-3 × ULN	74 (45.1)
>3 × ULN	40 (24.4)
Hemoglobin<100 g/L, n (%)	53 (32.3)
Serum albumin <35 g/L, n (%)	66 (40.2)
AIDS before lymphoma diagnosis, n (%)	78 (47.6)
HAART at lymphoma diagnosis, n (%)	62 (37.8)
CD4 count <200 cells/μL, n (%)	112 (68.3)



58.4% of pts experienced a total of 153 episodes of infection incidence rate (20.4%)

Lung infection and FN were the most frequent types of infection

Retrospective study,
164 HIV+ Lymphomas
56%: DLBCL
28% BL

1st line treat:
DLBCL: R-DA-EPOCH
R–CHOP

BL: R-hyper-CVAD
R-DA-EPOCH

Multivariate analysis of risk factors for infections during chemotherapy

Variables	OR	95% CI	*p*
Total number of chemotherapy cycles	1.225	1.043–1.439	0.014
Grade 4 decrease in neutrophil count (<500/mm3) (yes vs. no)	7.128	3.051–16.654	<0.001
Duration of HAART at lymphoma diagnosis (<6 months vs. ≥ 6 months)	3.520	1.432–8.653	0.006
Lymphoma type (DLBCL vs. non-DLBCL)	3.010	1.282–7.069	0.011

LYMPHOMA AND PLWH: Chemotherapy and excess of toxicity

Bandera A 15th EUROPEAN AIDS CONFERENCE October 21-24, 2015, Barcelona, Spain

Cohort pilot study, case-control, monocentric, retrospective

AIM:

- to evaluate the incidence of HEMATHOLOGICAL, NEUROLOGICAL, LIVER TOXICITY, FEBRILE NEUTROPENIA, INFECTIVE COMPLICATIONS AND MUCOSITIS related to the use of chemotherapeutic agents in *HIV-positive and HIV-negative patients* diagnosed with lymphoma from 2006 to 2014;
- to evaluate if HIV related factors are associated with an increased risk of toxicity
- to evaluate **clinical outcome** as **response to chemotherapy**, overall survival and disease free survival

	HIV+ (n=47)	Controls (n=50)	p
	N (%) or median (IQR)	N (%) or median (IQR)	
Age (years)	47 (39-51)	51 (46-56)	ns
Sex (M)	40 (85%)	38 (76%)	ns
HCV Ab pos	14 (37%)	2 (4%)	<0.001
Lymphoma type: **- DLBCL** **- Burkitt**	 34 (72%) 13 (28%)	 38 (76%) 12 (24%)	ns
Ann Arbor stage III-IV	36 (78%)	35 (73%)	ns
Extranodal sites n.	1 (0-2)	1 (0-2)	ns
ECOG 2-4	16 (35%)	14 (30%)	ns
Bulky mass	12 (29%)	16 (36%)	ns
CNS localization	10 (26%)	2 (7%)	0.05
IPI-aa score 3-4	11 (30%)	9 (18%)	0.03
ART use at diagnosis	28 (59%)	-	-
CD4+ T cell at diagnosis (cells/mmc)	220 (111-394)	-	-
HIV-RNA log10 at diagnosis	2.5 (1.6-5.0)	-	-

LYMPHOMA AND PLWH: Chemotherapy and excess of toxicity

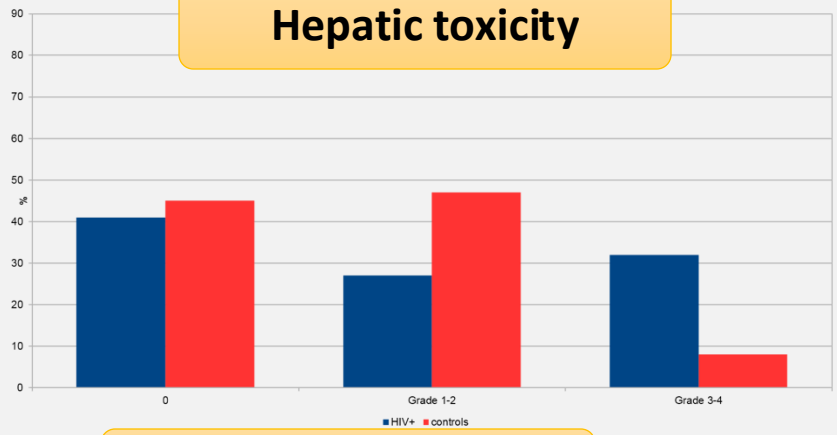
Bandera A 15th EUROPEAN AIDS CONFERENCE October 21-24, 2015, Barcelona, Spain

Results

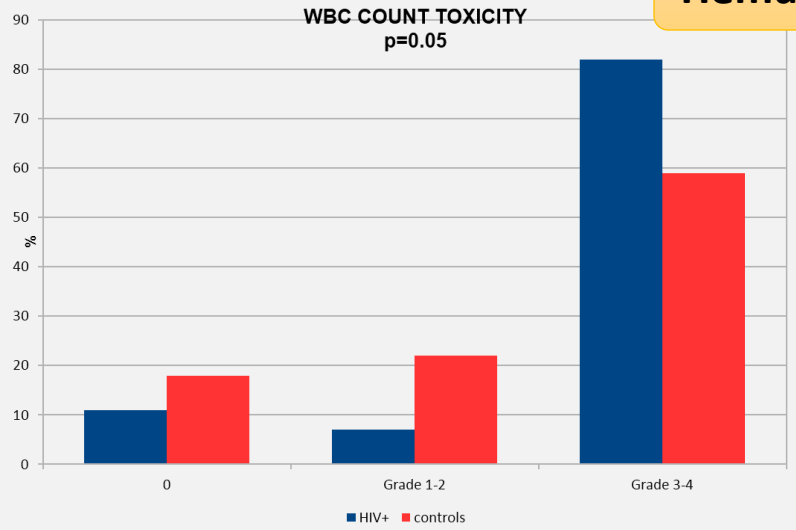
Tossicità di qualsiasi grado

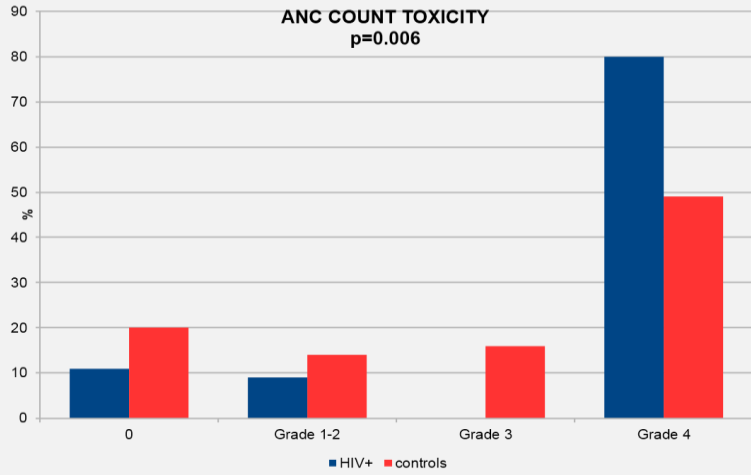
	Totale cicli (n=401)		Cicli dei casi (n=171)		Cicli dei controlli (n=230)		p value*
	N	%	N	%	N	%	
Tossicità ematologica	201/386	52.07	102/170	60.00	99/216	45.83	<0.01
Neurotossicità	14/394	3.55	5/164	3.05	9/230	3.91	ns
Neutropenia febbrile	22/390	5.64	18/161	11.18	4/229	1.75	<0.01
Complicanze infettive	66/399	16.54	39/169	23.08	27/230	11.74	<0.01
Epatotossicità	53/379	13.98	25/165	15.15	28/214	13.08	ns
Mucosite	35/397	8.82	18/167	10.78	17/230	7.39	ns

Hepatic toxicity



Hematological toxicity





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Hematological toxicity

Neurotoxicity

Febrile neutropenia

Liver toxicity

Infectious complications

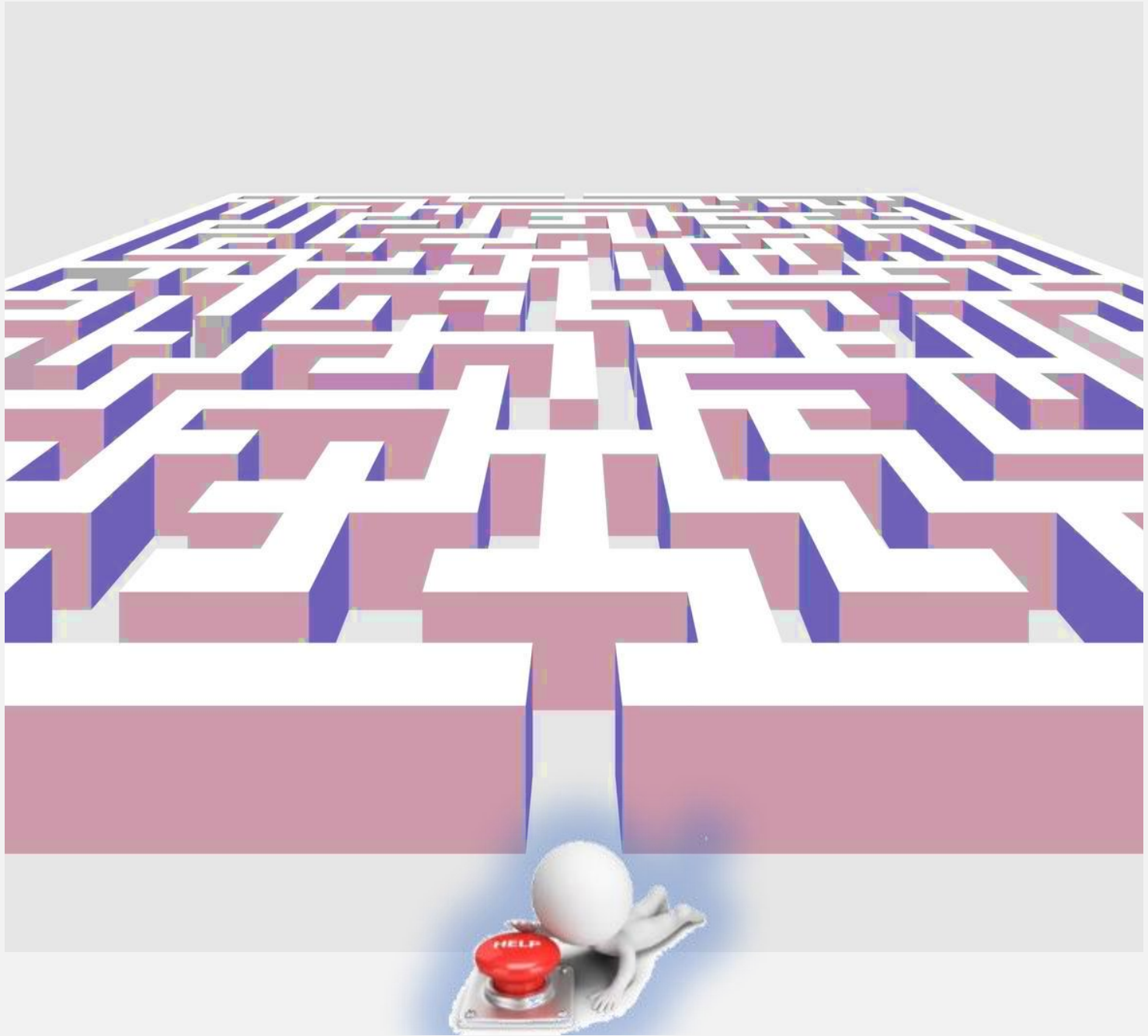
Mucositis

The association of the HIV-related variables respect to an increase in the occurrence of toxicity was assessed:

- **HIV viral load at lymphoma diagnosis**
- **Cd4 T cell count at lyphoma dg**
- **Percentage of CD4 + T lymphocytes at diagnosis**
- **ART at diagnosis**

None of these associations was significant

Opportunistic Infection	When to Prescribe Prophylaxis or Suppressive Therapy	Preferred Regimens
Pneumocystis jirovecii	$CD4^+$ T-cell count <200 cells/μL With any cytotoxic chemotherapy, radiation, or other cancer treatment with expected decline in $CD4^+$ count	Trimethoprim/sulfamethoxazole 800/160 mg orally three times per week or 400/80 mg orally once daily Atovaquone 1500 mg daily Both agents also provide prophylaxis against toxoplasmosis
Herpes simplex 1/2 and varicella zoster virus	History of recurrent HSV outbreaks With any cytotoxic chemotherapy, radiation, or other cancer treatment with expected decline in $CD4^+$ count as high risk of disseminated VZV when $CD4^+$ count <200 cells/μL	Valacyclovir 500 mg orally twice daily
Candida albicans	Recent history of mucosal candidiasis Consider if $CD4^+$ T-cell count <100 cells/μL Consider if cancer treatment will lead to prolonged neutropenia or if prolonged exposure to steroids	Fluconazole 200 mg orally once daily Nystatin oral suspension 5 mL 2-4 times daily (does not prevent esophageal candidiasis) Consider micafungin 100 mg intravenously once daily for short periods if DDI concerns with fluconazole
Mycobacterium avium complex	Consider if $CD4^+$ T-cell count <100 cells/μL, especially if HIV is uncontrolled and $CD4^+$ count expected to decline with treatment	Azithromycin 1,200 mg once per week To avoid drug resistance from single-agent treatment, rule out active infection before prescribing prophylaxis
Hepatitis B virus	Suppressive therapy should be given to anyone with HIV and HBV coinfection regardless of $CD4^+$ count or HBV viral load	Tenofovir disoproxil 300 mg orally once daily plus emtricitabine 200 mg orally once daily or lamivudine 300 mg orally once daily Tenofovir alafenamide 25 mg orally once daily plus emtricitabine 200 mg orally daily or lamivudine 300 mg orally once daily



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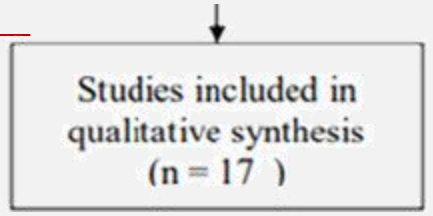
LYMPHOMA AND PLWH: LYMPHOMAS AND PET-CT

Recent advancements in ^{18}F-FDG PET/CT for the diagnosis, staging, and treatment management of HIV-related lymphoma
Soufi GJ, Am J Nucl Med Mol Imaging, 2024



Differentiating between benign lymphadenopathy and HIV-related lymphoma

Study	Year	Study type	Study population	Study groups		Parameters					
						SURmax	SUV_{LN}	SUV_{Marrow}	SUV_{Liver}	Number of lymph node involved areas	Maximum diameter of lymph nodes
Chen et al.	2022	Retrospective cross-sectional study	59	37 HIV-related lymphoma (35 B-cell lymphoma; 1 Hodgkin lymphoma; 1T-cell lymphoma)	22 HIV-infected patients with biopsy-proven inflammatory lymphadenopathy	AUC: 0.888 Cut-off: 3.1 Sensitivity: 68.2% Specificity: 91.9% *P*-value: 0.000*	AUC: 0.815 Cut-off: 8 Sensitivity: 63.6% Specificity: 89.2% *P*-value: 0.000*	AUC: 0.611 Cut-off: - Sensitivity: - Specificity: - *P*-value: 0.156	AUC: 0.567 Cut-off: - Sensitivity: - Specificity: - *P*-value: 0.393	AUC: 0.692 Cut-off: 5 Sensitivity: 62.2% Specificity: 72.7% *P*-value:	AUC: 0.768 Cut-off: 3.6 Sensitivity: 64.9% Specificity: 86.4%

malignant lymphoma colonized extra-lymphatic lesions more frequently (83.8% vs. 54.5%, P = 0.000)

the SURmax, SUVLN in malignant lymphoma were considerably greater (P = 0.000, 0.000)

SUVLN: the maximum standardized uptake value (SUVmax) of lymph nodes

SURmax : the ratio of the greatest SUVmax of an FDG-avid lesion to the SUVmax of the liver

Lymphoma patients demonstrated significantly higher quantitative PET measures than inflammatory lymphadenopathy patients (*p*-values = 0.001).

						Single SULmax	TLG	Single SULpeak	MTV	Sum SULpeak	Sum SULmax
Mhlanga et al.	2014	Retrospective study	41	19 had biopsy-proven untreated lymphoma (16 DLBCL, 3 HL)	22 with reactive adenopathy without malignancy	AUC: 0.971 Cut-off: 7.8 Sensitivity: 89% Specificity: 100% PPV: 100% NPV: 92%	AUC: 0.964 Cut-off: 173 Sensitivity: 89% Specificity: 100% PPV: 100% NPV: 92%	AUC: 0.964 Cut-off: 6.6 Sensitivity: 84% Specificity: 100% PPV: 100% NPV: 88%	AUC: 0.957 Cut-off: 53.8 Sensitivity: 84% Specificity: 100% PPV: 100% NPV: 88%	AUC: 0.935 Cut-off: 23.8 Sensitivity: 84% Specificity: 95% PPV: 94% NPV: 88%	AUC: 0.904 Cut-off: 28.4 Sensitivity: 84% Specificity: 82% PPV: 80% NPV: 86%

LYMPHOMA AND PLWH: LYMPHOMAS AND PET-CT

First Extensive Analysis of 18F-Labeled Fluorodeoxyglucose Positron Emission Tomography–Computed Tomography in a Large Cohort of Patients With HIV-Associated Hodgkin Lymphoma: Baseline Total Metabolic Tumor Volume Affects Prognosis. Louarn NMD, JCO 2022

AIM:
characteristics of **baseline 18F-FDG PET-CT**
its prognostic value
→ 109 patients with HIV-HL
→ a prospective ongoing cohort.

Total metabolic tumor volume (TMTV)
→ reflects the active tumor burden of HIV-HL pts

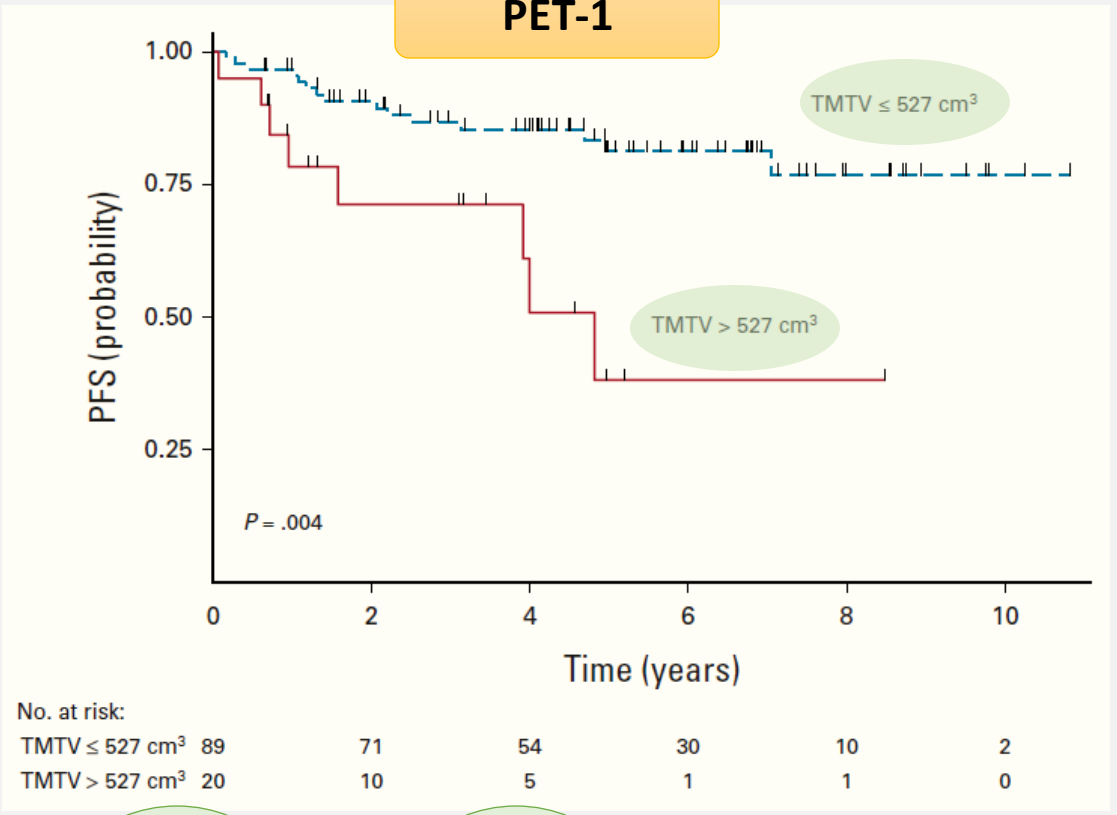
WHO:

109pts
79%: stage IIB-IV
104pts:ABVD

PET-1

Extranodal involvement	
Bone marrow	42 (39)
Liver	21 (19)
Lung	3 (3)
Pleura	4 (4)
Pericardium	1 (1)
Stomach	2 (2)
Muscle	1 (1)

PET-1



5-year OS
86.1%

HL:3;
NHL:2;
TRM: 3
AIDS: 1

LYMPHOMA AND PLWH: LYMPHOMAS AND PET-CT

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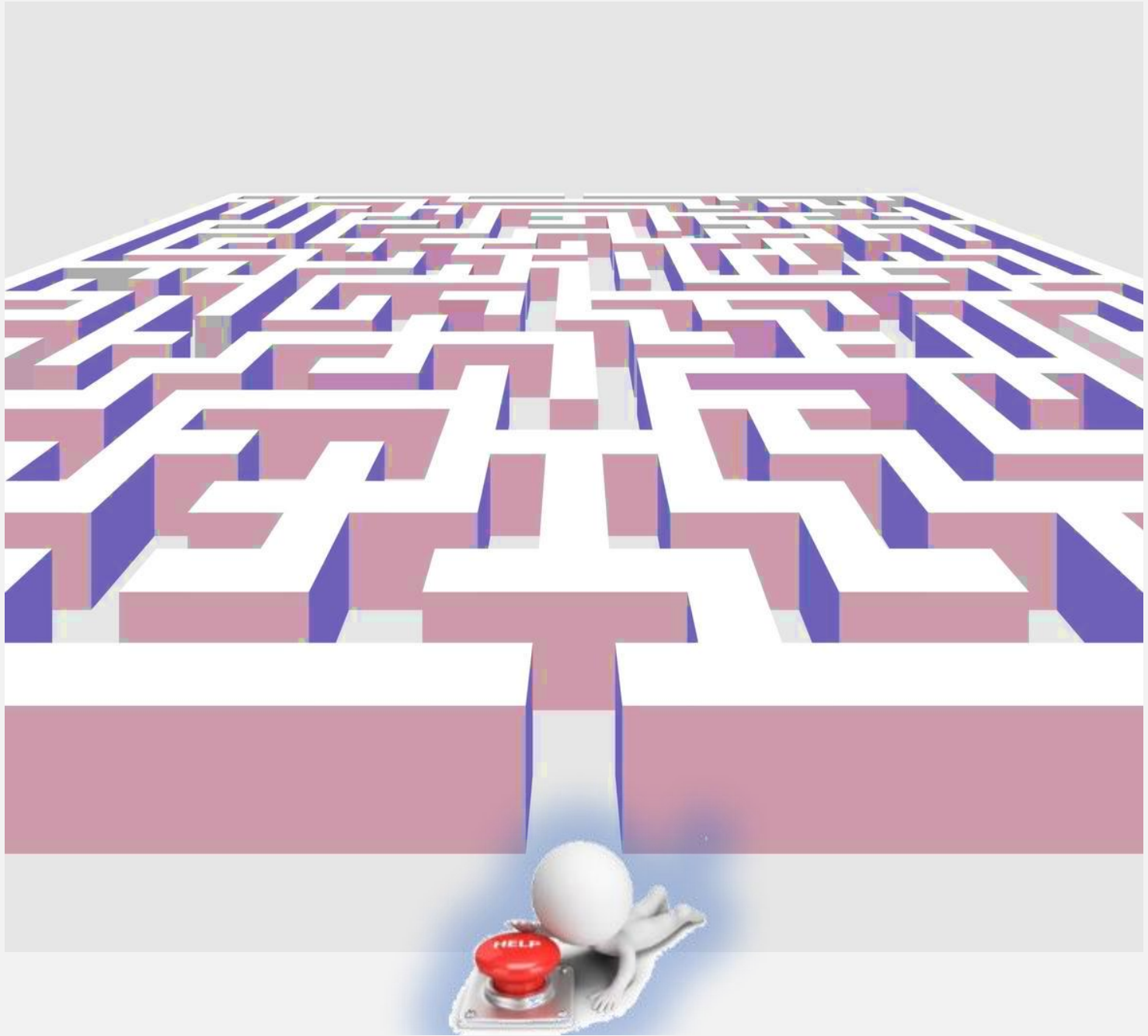
PROGNOSTIC ANALYSIS FOR PFS

In the 59 patients with detectable HIVRNA, the median TMTV value was similar to that observed in the 50 patients with undetectable viral load

After a 6.7-year follow-up, 40% of the patients with high TMTV relapsed or died compared with 17% in patients with low TMTV

Variable	Patients, No.	Univariate Analysis, HR (95% CI)	Multivariate Analysis, HR (95% CI)
SUVmax			
≤ 8.7	38	1	
> 8.7	71	3.03 (1.03 to 8.96)	NS
SUVpeak			
≤ 7.1	40	1	
> 7.1	69	3.14 (1.07 to 9.26)	NS
SUVmean			
≤ 5.1	37	1	
> 5.1	72	2.99 (1.02 to 8.86)	NS
TMTV, cm^3			
≤ 527	89	1	
> 527	20	3.62 (1.52 to 8.63)	2.70 (1.13 to 6.49)
TLG, cm^3			
≤ 230	25	1	
> 230	84	8.13 (1.09 to 60.64)	NS
IPS			
Low (reference)	55	1	
Intermediate	43	1.77 (0.70 to 4.49)	NS
High	11	4.01 (1.31 to 12.3)	NS
CD4, cells/μL			
≤ 200	37	1	
> 200	72	0.87 (0.37 to 2.06)	—
HIV-RNA, copies/mL			
Undetectable	50	1	
Detectable	59	0.83 (0.36 to 1.89)	—



Burning issues:

- What types of lymphomas should I know about?
- Is the risk of infectious toxicity still high today? Are there any other significative toxicities? What about viral factors?
- what about staging? what role does the PET scan play?
- what are the clinical presentations today?
- Is the risk of CNS recurrence increased compared to the general population?

LYMPHOMA AND PLWH: clinical presentation

HIV Infection and Survival of Lymphoma Patients in the Era of Highly Active Antiretroviral Therapy 2004-15

HIV HL: 1,729/36,521 (4.7%), HIV DLBCL: 4,424/81,534 (5.4%) HIV BL: 1,348/4,684 (28.8%)

Xuesong Han, 2016

	HL			DLBCL			BL			PTCL			FL		
	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]
Stage															
I	5,911 (17)	214 (12.4)	<0.0001	21,537 (27.9)	996 (22.5)	<0.0001	683 (20.5)	190 (14.1)	<0.0001	3,754 (32.2)	79 (19.9)	<0.0001	11,906 (26.9)	87 (20)	<0.0001
II	15,573 (44.8)	384 (22.2)		15,833 (20.5)	619 (14)		518 (15.5)	141 (10.5)		1,561 (13.4)	55 (13.9)		7,591 (17.1)	58 (13.3)	
III	7,321 (21)	405 (23.4)		13,539 (17.6)	785 (17.7)		361 (10.8)	164 (12.2)		2,308 (19.8)	90 (22.7)		11,386 (25.7)	121 (27.8)	
IV	5,987 (17.2)	726 (42)		26,201 (34)	2,024 (45.8)		1,774 (53.2)	853 (63.3)		4,042 (34.7)	172 (43.4)		13,402 (30.3)	169 (38.9)	
Initial treatment															
No treatment	2,773 (8)	271 (15.7)	<0.0001	8,672 (11.2)	718 (16.2)	<0.0001	281 (8.4)	111 (8.2)	0.69	2,160 (18.5)	98 (24.7)	<0.0001	11,060 (25)	95 (21.8)	0.005
Other/unknown	1,508 (4.3)	48 (2.8)		2,891 (3.7)	344 (7.8)		50 (1.5)	16 (1.2)		1,836 (15.7)	31 (7.8)		5,542 (12.5)	37 (8.5)	
Chemotherapy	30,511 (87.7)	1,410 (81.6)		65,547 (85)	3,362 (76)		3,005 (90.1)	1,221 (90.6)		7,669 (65.7)	267 (67.4)		27,683 (62.5)	303 (69.7)	
Days to initial treatment, d															
No treatment	2,773 (8)	271 (15.7)	<0.0001	8,672 (11.2)	718 (16.2)	<0.0001	281 (8.4)	111 (8.2)	0.055	2,160 (18.5)	98 (24.7)	<0.0001	11,060 (25)	95 (21.8)	<0.0001
0–14	6,699 (19.3)	371 (21.5)		22,639 (29.4)	1,497 (33.8)		1,660 (49.8)	732 (54.3)		2,537 (21.7)	113 (28.5)		5,447 (12.3)	90 (20.7)	
15–30	10,466 (30.1)	429 (24.8)		21,061 (27.3)	968 (21.9)		792 (23.7)	302 (22.4)		2,333 (20)	86 (21.7)		8,132 (18.4)	78 (17.9)	
31–60	9,197 (26.4)	376 (21.7)		15,369 (19.9)	711 (16.1)		359 (10.8)	119 (8.8)		2,335 (20)	45 (11.4)		10,500 (23.7)	100 (23)	
>60	4,330 (12.4)	225 (13)		6,157 (8)	342 (7.7)		124 (3.7)	37 (2.7)		1,752 (15)	35 (8.8)		7,187 (16.2)	58 (13.3)	
Missing	1,327 (3.8)	57 (3.3)		3,212 (4.2)	188 (4.2)		120 (3.6)	47 (3.5)		548 (4.7)	19 (4.8)		1,959 (4.4)	14 (3.2)	

LYMPHOMA AND PLWH: clinical presentation

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Xuesong Han, 2016

Xuesong Han, 2016

+B Symptoms
Extranodal sytes

	HL			DLBCL			BL			PTCL					
	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	HIV-infected, *n* (%)	*P*[a]	HIV-uninfected, *n* (%)	infected, *n* (%)	*P*[a]
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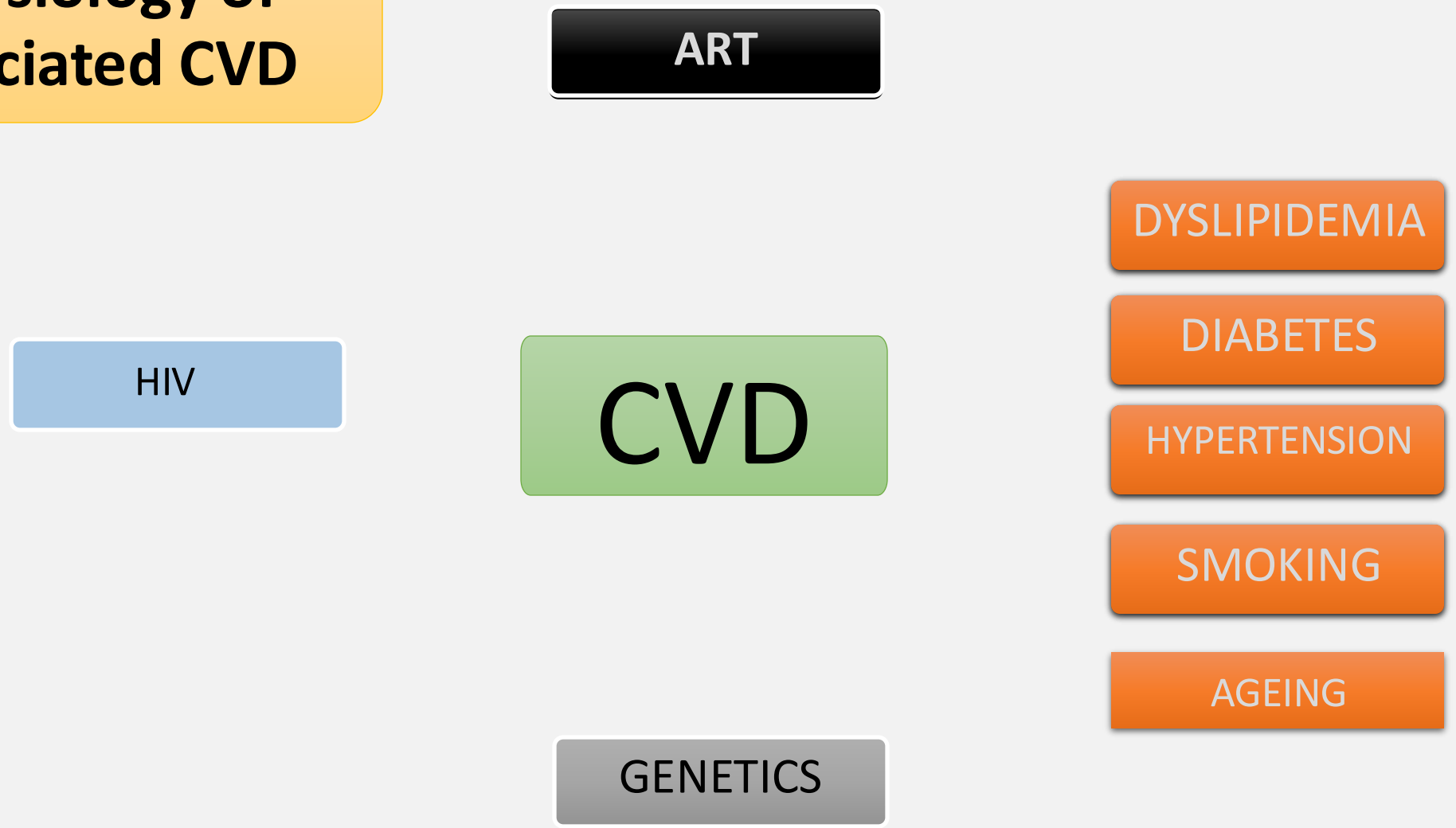
LYMPHOMA AND PLWH: cardiovascular and metabolic risk

Pathophysiology of HIV-Associated CVD



Thanks to Dr Squillace

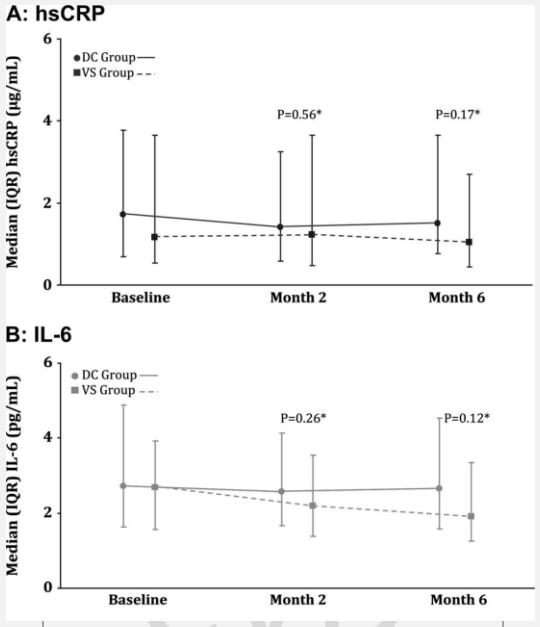
LYMPHOMA AND PLWH: cardiovascular and metabolic risk

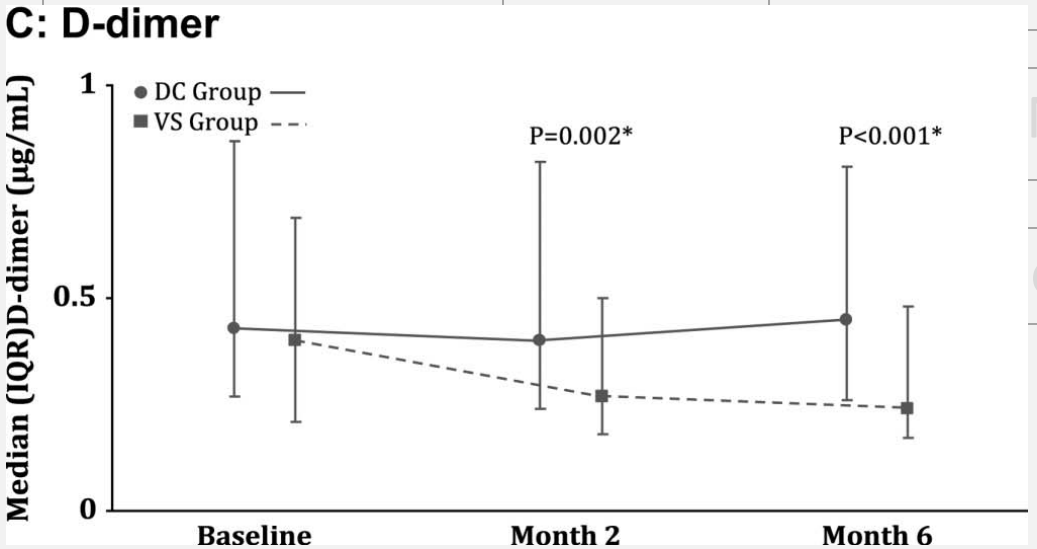
Pathophysiology of HIV-Associated CVD

HIV

is an indipendent risk factor for:

- Myocardial Infarction
- Stroke
- Peripheral Artery Disease





Changes in inflammatory and coagulation biomarkers: a randomized comparison of immediate versus deferred antiretroviral therapy in patients with HIV infection.
J Acquir Immune Defic Syndr. 2011;

DYSLIPIDEMIA

DIABETES

HYPERTENSION

Thanks to Dr Squillace

LYMPHOMA AND PLWH: cardiovascular and metabolic risk

Pathophysiology of HIV-Associated CVD

ART

Associations between integrase strand-transfer inhibitors and cardiovascular disease in people living with HIV: a multicentre prospective study from the RESPOND cohort consortium

Bastian Neesgaard, Lauren Greenberg, Jose M Miró, Katharina Grabmeier-Pfistershammer, Gilles Wandeler, Colette Smith, Stéphane De Wit, Ferdinand Wit, Annegret Pelchen-Matthews, Cristina Mussini, Antonella Castagna, Christian Pradier, Antonella d'Arminio Monforte, Jörg J Vehreschild, Anders Sönnerborg, Alain V Anne, Andrew Carr, Loveleen Bansi-Matharu, Jens D Lundgren, Harmony Garges, Felipe Rogatto, Robert Zangerle, Huldrych F Günthard, Line D Rasmussen, Coca Necsoi, Marc van der Valk, Marianna Menozzi, Camilla Muccini, Lars Peters, Amanda Mocroft, Lene Ryom

Lancet HIV 2022; 9: e474–85

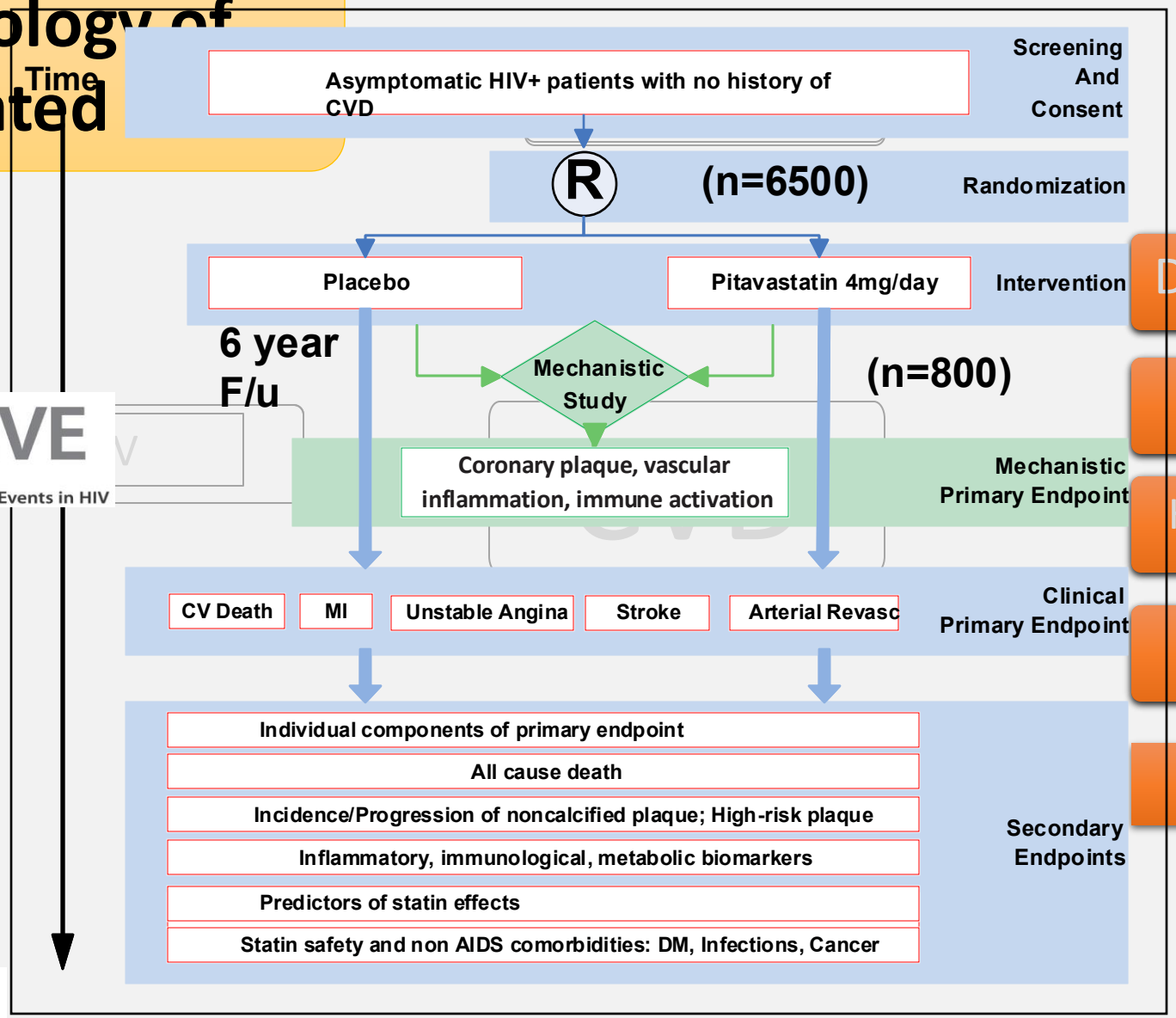
Published Online June 7, 2022 https://doi.org/10.1016/S2352-3018(22)00094-7

Summary

Background Although associations between older antiretroviral drug classes and cardiovascular disease in people living with HIV are well described, there is a paucity of data regarding a possible association with integrase strand-transfer inhibitors (INSTIs). We investigated whether exposure to INSTIs was associated with an increased incidence of cardiovascular disease.

LYMPHOMA AND PLWH: cardiovascular and metabolic risk

Pathophysiology of HIV-Associated



REPRIEVE
Randomized Trial to Prevent Vascular Events in HIV

DYSLIPIDEMIA

DIABETES

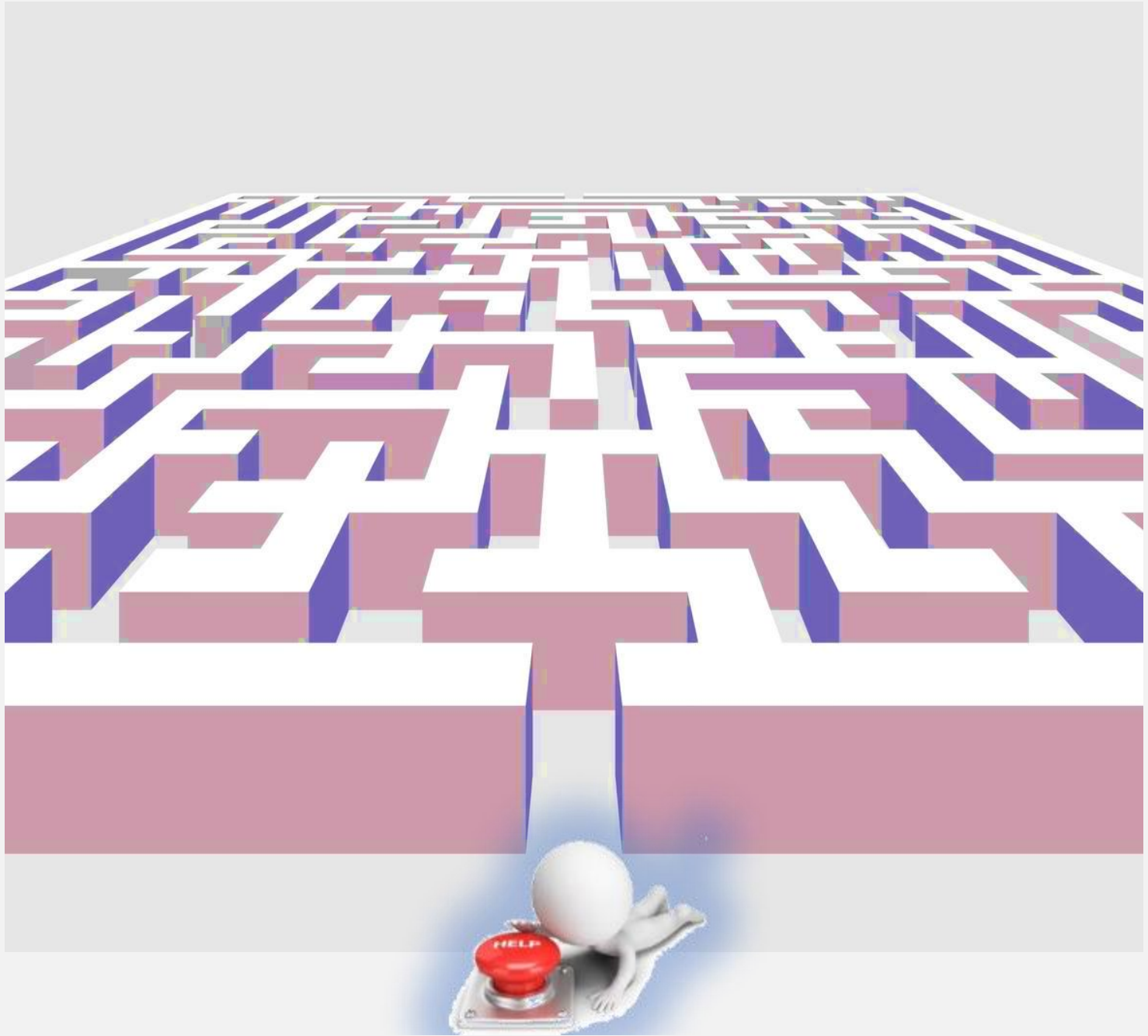
HYPERTENSION

SMOKING

AGEING

REPRIEVE

Thanks to Dr Squillace



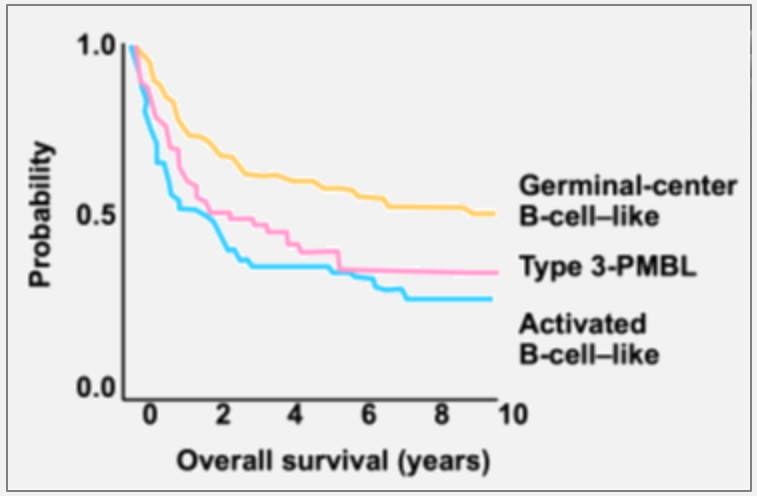
Burning issues:

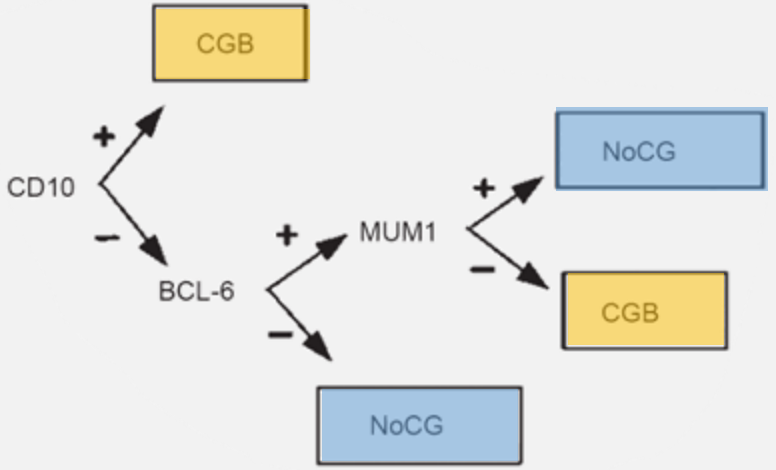
- What do we know about the biology of these lymphomas?
- Are there any guidelines?

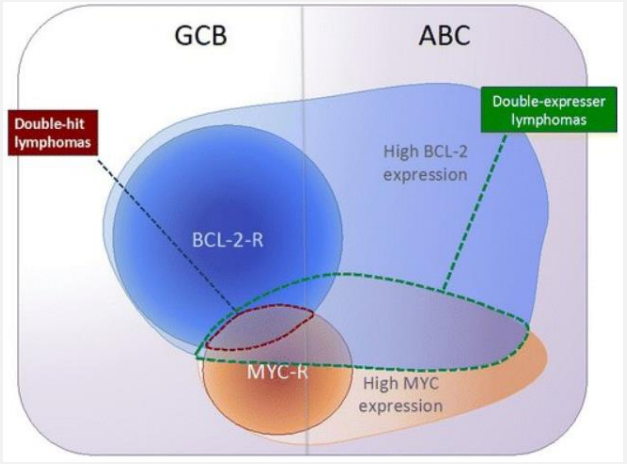
(D)LBCL

LYMPHOMA AND general population: DLBCL and COO

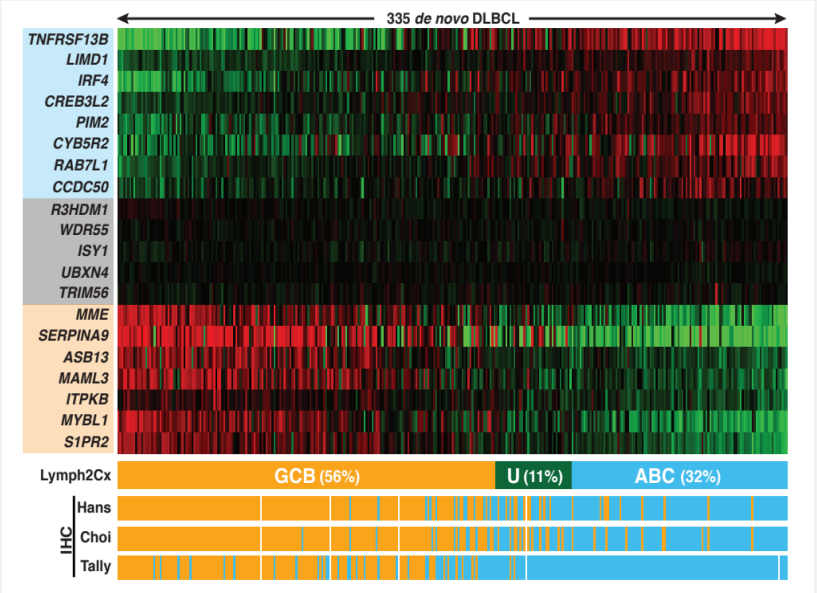
Distinct types of diffuse large B-cell lymphoma identified by gene expression profiling.
Alizadeh AA. Nature, 2000







- First definition of COO using **Lymph2Cx model- Nanostring**
  - RNA based Gene expression assay
  - Suitable for FFPE samples
- Based on differential gene expression, cases classified as "**ABC**" vs "**GCB**" vs "**Unclassifiable**

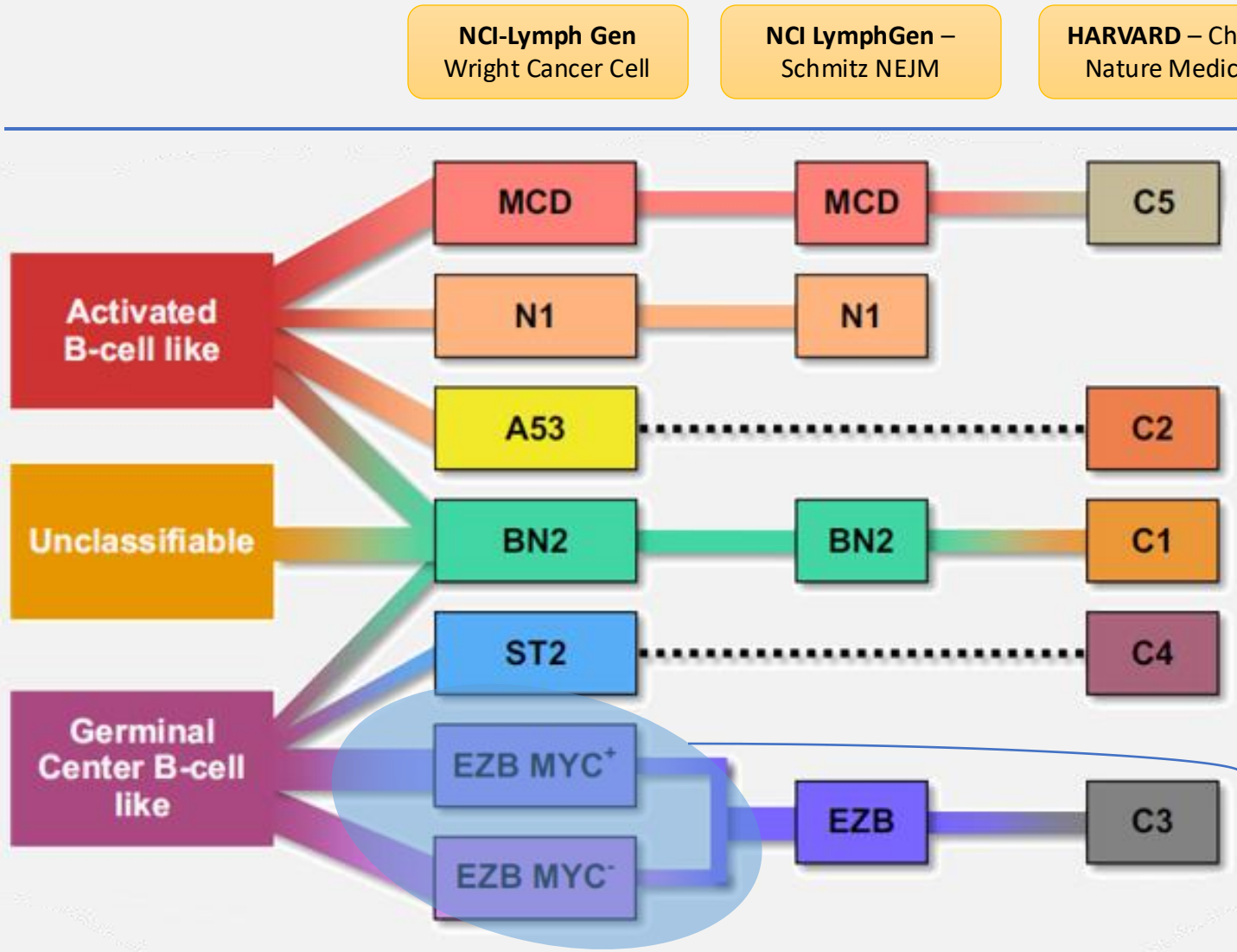


In *Germinal Center-type* → mutations of BCL6, Histone Acetyltransferases and EZH2 lead to a repressed transcriptional state.

In *ABC-type* → mutations in the B-cell Recepter Pathway lead to unchecked activation of NFkB.

LYMPHOMA AND general population: DLBCL and COO

Diffuse Large B-Cell Lymphoma (DLBCL): Early Patient Management and Emerging Treatment Options
P. Vodicka, OncoTargets and Therapy 2022



New algorithms have further expanded the concept of "COO"
Incresed heterogeinity within established groups (GCB, ABC, U)

Specific subtypes have different
- gene expression profiles
- microenvironmental features
- outcomes

reflects germinal center dark vs light zone origin
and MYC target gene expression.

LYMPHOMA AND PLWH: DLBCL and COO

A digital gene expression assay based on the expression of 20 genes (Lymph2Cx, Nanostring Technologies,FFPE

Using the Lymph2Cx assay for assessing cell-oforigin subtypes of HIV-related diffuse large B-cell
Maria Joao Baptista, Leukemia and Lymphoma, 2018

Aim:

- to study a series of HIV-DLBCL uniformly treated with RCHOP
- **to investigate the prognostic impact of COO subtypes**
- to compare the results with those obtained with Hans algorithm

WHO:

47 pts treated with R –CHOP

42 DLBCL
3 HGBL NOS
2 HGBL, DH

		Lymph2Cx assay				Hans algorithm		
Characteristic	Whole series N = 47	GCB N = 30	ABC N = 9	UNC N = 8	p Value[a]	GC N = 18	Non-GC N = 27	p Value[b]
Age years, median [range]	44 [27–63]	44.5 [30–63]	44 [36–58]	42.5 [27–61]	.618	43.5 [30–62]	44 [33–63]	.951
Male, N (%)	39 (83%)	25 (83%)	7 (78%)	7 (88%)	.520	16 (89%)	21 (78%)	.295
ECOG ≥2, N (%)	23 (49%)	13 (43%)	8 (89%)	2 (25%)	**.019**	5 (28%)	17 (63%)	**.021**
B-symptoms, N (%)	19 (40%)	6 (20%)	8 (89%)	5 (63%)	**<.001**	5 (28%)	14 (52%)	.109
Extranodal disease, N (%)	23 (49%)	16 (53%)	4 (44%)	3 (38%)	.465	10 (56%)	12 (44%)	.465
Bulky disease, N (%)	7 (15%)	4 (13%)	1 (11%)	2 (25%)	.676	5 (28%)	2 (7%)	.078
LDH increased, N (%)	29 (62%)	16 (53%)	6 (67%)	7 (88%)	.377	10 (56%)	17 (63%)	.619
B2M increased, N (%)	30/34 (88%)	18/21 (86%)	9 (100%)	3/4 (75%)	.328	11/14 (79%)	18/19 (95%)	.193
Ann Arbor III or IV, N (%)	35 (75%)	20 (67%)	9 (100%)	6 (75%)	**.047**	11 (61%)	23 (85%)	.069
IPI ≥2, N (%)	21 (45%)	12 (40%)	6 (67%)	3 (38%)	.153	5 (28%)	15 (56%)	.066
HBV, N (%)	9/38 (24%)	6/24 (25%)	2 (22%)	1/5 (20%)	.626	5/17 (29 %)	4/21 (19%)	.357
HCV, N (%)	14/38 (37%)	8/23 (35%)	4 (44%)	2/6 (33%)	.454	7/17 (41%)	7/21 (33%)	.618
History of previous AIDS, N (%)	22/45 (49%)	13/29 (45%)	6/8 (75%)	3 (38%)	.133	5/17 (29%)	16/26 (62%)	**.039**
History of OI, N (%)	18/36 (50%)	12/22 (55%)	4/8 (50%)	2/6 (33%)	.574	6/15 (40%)	11/19 (58%)	.300
Previous cART, N (%)	29/46 (63%)	18/29 (62%)	7 (78%)	4 (50%)	.329	10/17 (59%)	18 (67%)	.598
Detectable HIV-load, N (%)	29/44 (66%)	15/27 (56%)	8 (89%)	6 (75%)	.076	11/17 (65%)	17/25 (68%)	.824
CD4 counts <100/μL, N (%)	19/46 (41%)	10/29 (35%)	5 (56%)	4 (50%)	.228	6/18 (33%)	13/26 (50%)	.272
Diagnosis, N								
DLBCL	42	27	9	6	.614	15	25	.051
HGBL, DH	2	1	0	1		0	2	
HGBL, NOS	3	2	0	1		3	0	
CR achievement, N (%)	32 (68%)	22 (73%)	7 (78%)	3 (38%)	.581	14 (78%)	18 (67%)	.420
CD10, N (%)	15/45 (33%)	14/29 (48%)	0 (0%)	1/7 (14%)	**.008**	15 (83%)	0 (0%)	**<.001**
BCL6, N (%)	29/44 (66%)	21/28 (75%)	4 (44%)	4/7 (57%)	.100	17/17 (100%)	12 (44%)	**<.001**
MUM1, N (%)	26/44 (59%)	13/28 (46%)	7 (78%)	6/7 (86%)	.103	4/17 (24%)	22 (82%)	**<.001**
EBER, N (%)	10/44 (23%)	5/28 (18%)	4 (44%)	1/7 (14%)	.178	2/17 (12%)	8 (30%)	.271

LYMPHOMA AND PLWH: DLBCL and COO

Still Far to Go With Characterisation of Molecular and Genetic Features of Diffuse Large B-Cell Lymphoma in People Living With HIV: A Scoping Review
Manyau CP, Oncology Reviews,2024

COO

The distributions of COO varied widely between studies

Of the 12 studies which assessed **the impact of COO** on survival, only two found statistically significant association with survival (**BETTER FOR GC**)

Risk factors were more frequent in NGC-DLBCL.
- Lower CD4+ cell counts
- EBV positivity
- CNS involvement

TUMOR MARKERS

Pathway	Marker	Frequency	Prognosis/ (citation)
Cell cycle promoters	MYC	14%–58%	↔ [23, 32, 45, 50] ↑ [49]
B-cell activators/ differentiation	BCL6	28%–87%	↔ [32]
	FOXP1	37%–62%	↔ [30, 32]
	CD10	20%–53%	↔ [32] ↓ [38]
	CD138/ syn1	0%–16%	↔ [53]
	MUM1	14%–75%	↔ [32, 53]
	Blimp1	10%–28%	↔ [30, 32]
Apoptotic regulators	BCL2	16%–60%	↔ [30, 32, 40] ↑ [48, 50]
	p53	12%–64%	↔ [40] ↓ [32]
Other	CD20	74%–99%	↔ [32, 53] ↓ [38]
	Ki67	16%–85%	↔ [32, 48] ↑ [36] ↓ [30]
	DPE	10%–42%	↑ [23, 36] ↔
	LMO2	50–55	↔ [32]

Included

Studies included for review (n=24)

Total reports of included studies (n =32)

LYMPHOMA AND PLWH: DLBCL and MYC positivity

MYC rearrangements in HIV-associated large B-cell lymphomas: EUROMYC, a European retrospective study
C. Pagani, Blood Advances, 2023

WHO:
155 HIV pts who had received fluorescence in situ hybridization analysis for MYC

Retrospective study

AIM:
prevalence and prognostic impact of MYC rearrangements in HIV-associated LBCL

Pts with myc +: 43
DLBCL ,NOS: 129
DLBCL myc+: 25

HGBL,NOS :16
HGBL MYC +: 8

HGBL, DH/TH: 10
HGBL MYC+.10

LYMPHOMA AND PLWH: DLBCL and MYC positivity

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HGBL MYC +: 8

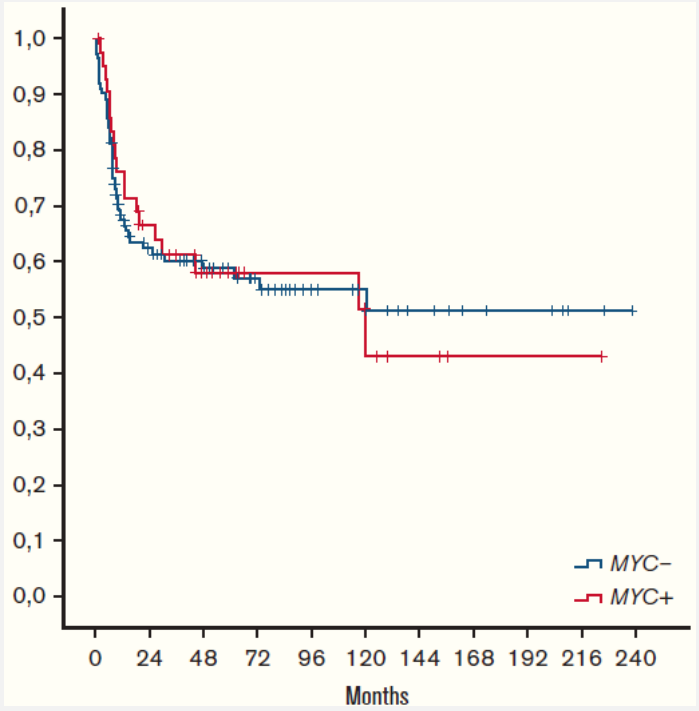
HGBL, DH/TH: 10
HGBL MYC+.10

	Patients with *MYC*+, n = 43	Patients with *MYC*–, n = 112	Total, N = 155	*P* valu
Median age (range), y	46 (26-74)	48 (23-83)	47 (23-83)	ns
Age >60 y	7 (16%)	14 (12%)	21 (14%)	ns
Male sex	37 (86%)	88 (79%)	125 (81%)	ns
Stage III-IV	40/43 (93%)	88/110* (80%)	128/155 (82%)	.05
B symptoms	22/43 (51%)	55/108* (51%)	77/151* (51%)	ns
Increased LDH	30/39* (77%)	70/104* (67%)	100/143* (70%)	ns
Extranodal sites				.05
≤ 2	19/38* (50%)	68/100* (68%)	87/138* (63%)	
> 2	19/38* (50%)	32/100* (32%)	51/138* (37%)	
CNS involvement	4/29* (14%)	2/64* (3%)	6/93* (6%)	.052
Kidney/adrenal gland involvement	8/29* (27%)	8/64* (12%)	16/93* (17%)	.074
ECOG performance status ≥2	19/34* (56%)	42/87* (48%)	61/121* (50%)	ns
IPI intermediate high-high	23/39* (64%)	49/92* (53%)	72/131* (55%)	ns
HCV seropositivity	11/38* (29%)	34/93* (36%)	45/131* (34%)	ns
Positive HBsAg	3/36* (8%)	8/89* (9%)	11/125* (9%)	ns
Median $CD4^+$ cell baseline (range), n/mmc	215 (32-1170)	198 (8-990)	198 (8-1170)	ns
$CD4^+$ cell <200/mmc	19/38* (50%)	51/100* (51%)	70/138* (51%)	ns
Detectable HIV load	24/40* (60%)	65/107* (61%)	89/147* (60%)	ns
AIDS before lymphoma diagnosis	5/41* (12%)	30/111* (27%)	35/152* (23%)	.054
cART before lymphoma diagnosis	20/42* (48%)	62/110* (56%)	32/152* (54%)	ns

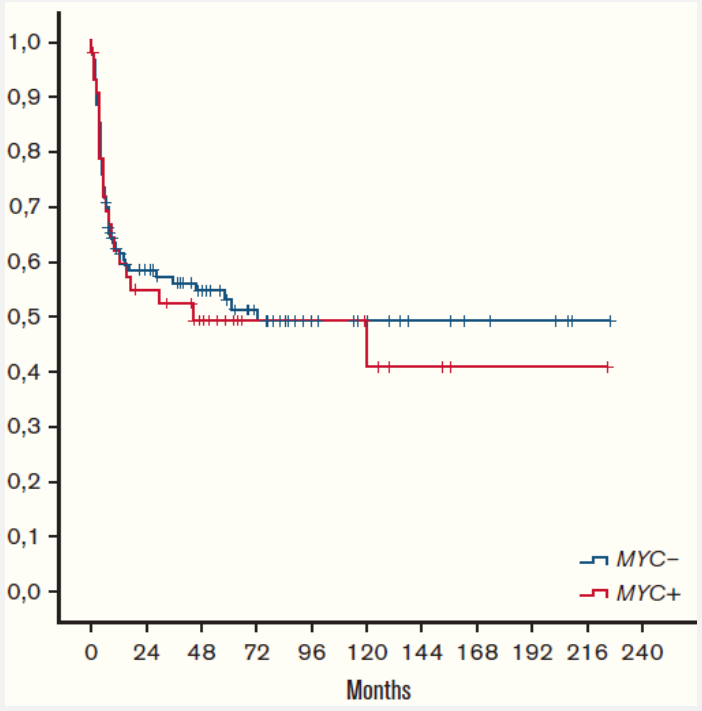
LYMPHOMA AND PLWH: DLBCL and MYC positivity

MYC rearrangements in HIV-associated large B-cell lymphomas: EUROMYC, a European retrospective study
C. Pagani, Blood Advances, 2023

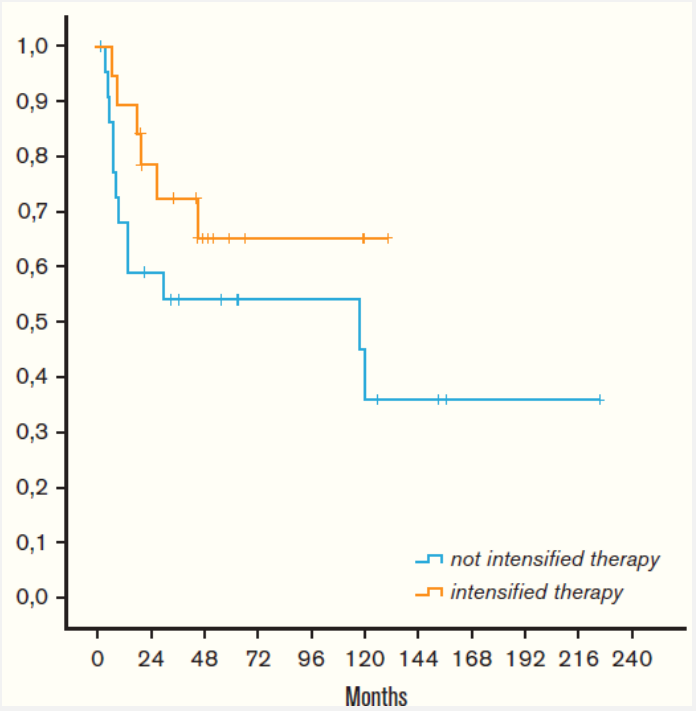
OVERALL SURVIVAL



PF SURVIVAL



OVERALL SURVIVAL MYC +



Whole population

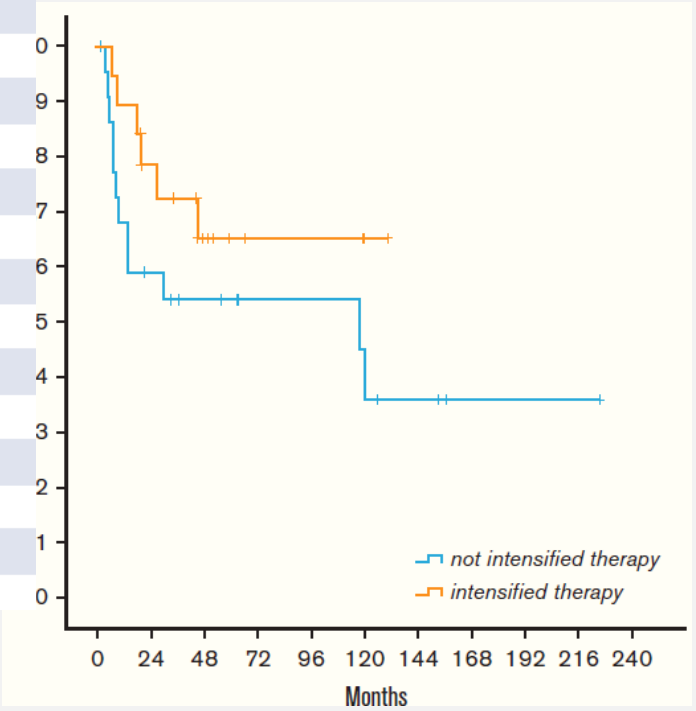
LYMPHOMA AND PLWH: DLBCL and MYC positivity

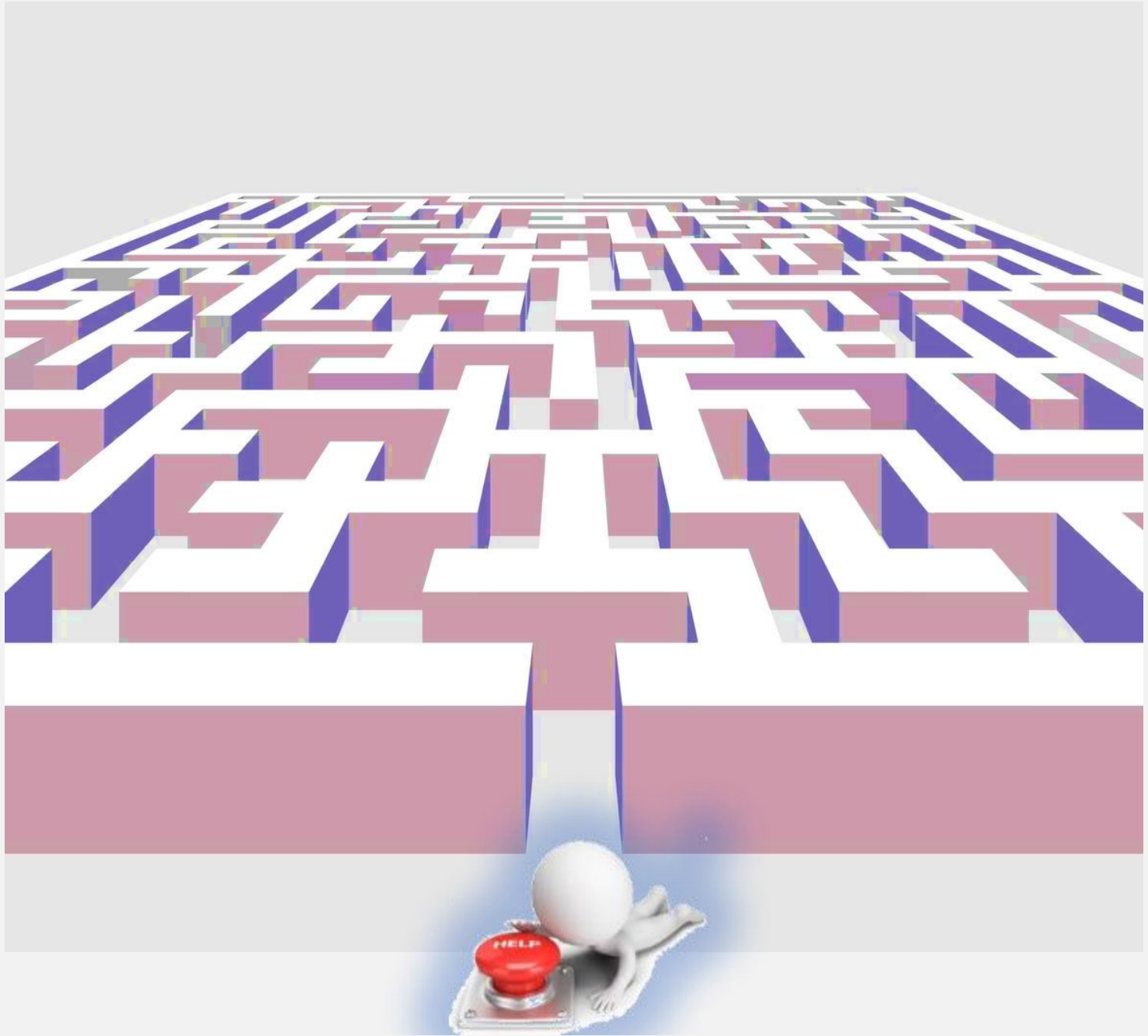
MYC rearrangements in HIV-associated large B-cell lymphomas: EUROMYC, a European retrospective study
C. Pagani, Blood Advances, 2023

	Patients with *MYC*+ n = 43	Patients with *MYC*– n = 112	Total N = 155	*P* value
Rituximab	41 (95%)	99 (88%)	140 (90%)	ns
CHOP/CHOP-like	15 (35%)	76 (68%)	91 (59%)	.0001
Infusional therapy	8 (19%)	9 (8%)	17 (11%)	.063
DA-EPOCH	6	6	12	
CDE	2	3	5	
iCT	19 (44%)	23 (20%)	42 (27%)	.003
CARMEN Regimen[28]	9	1	10	
GMALL	3	2	5	
CODOX IVAC	2	1	3	
CT* + ASCT consolidation	3	15	18	
Other†	2	4	6	
Palliative care	1 (2%)	4 (3%)	5 (3%)	ns
CNS prophylaxis	32/37‡ (86%)	62/94‡ (66%)	94/131‡ (72%)	.011
IT (MTX ± ARA-C)	24	55	79	
Iv MTX ± IT	8	7	15	
Radiotherapy	2 (5%)	9 (8%)	11 (7%)	ns

	OS		
	Hazard ratio	95% confidence interval	*P* value
ECOG PS ≥2	2.8	1.4-5.6	.003
Increased LDH	2.2	1.1-4.1	.018
Ki67>90%	0.56	0.3-0.96	.035

OVERALL SURVIVAL MYC +

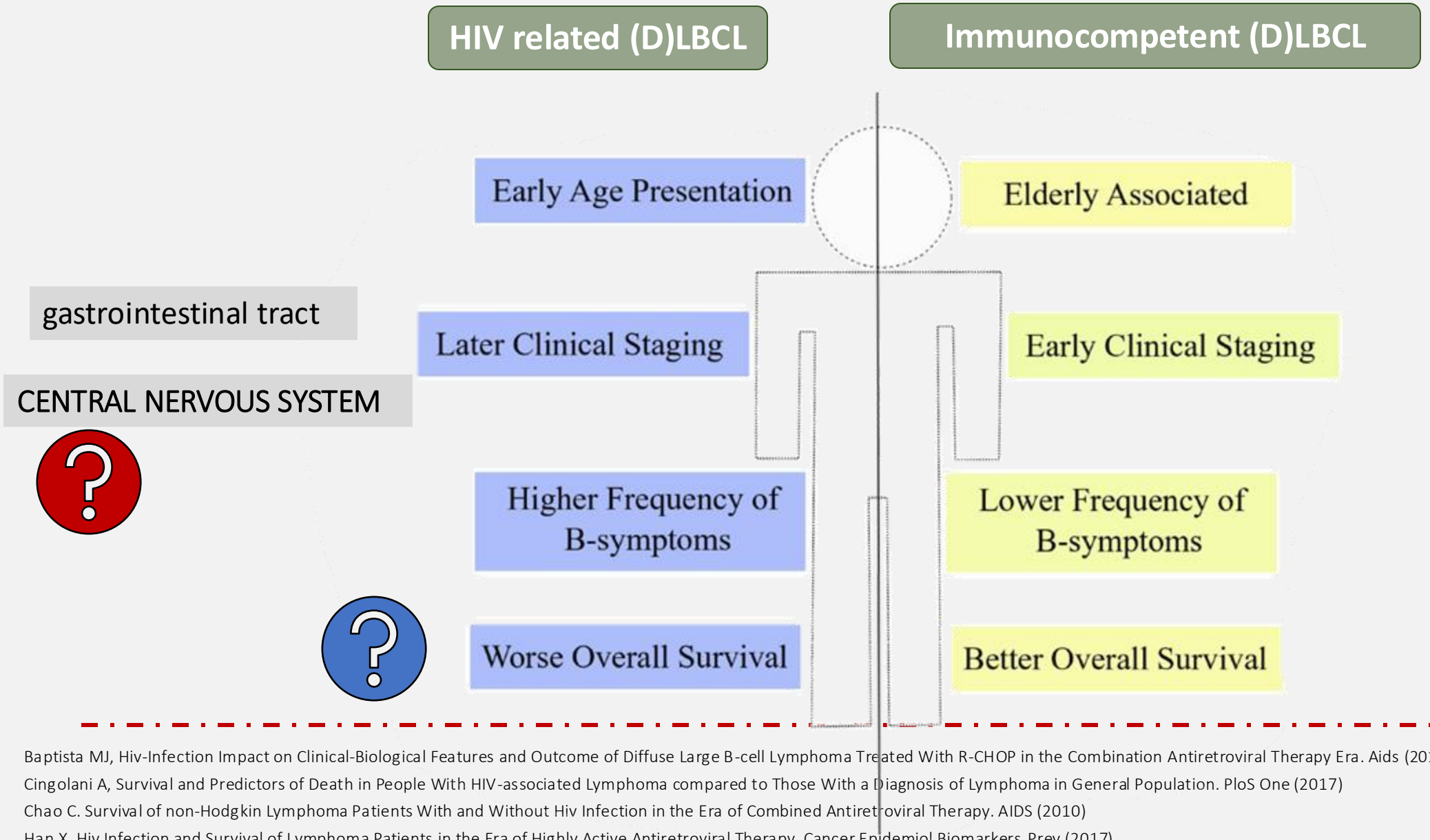




Burning issues:

- What types of lymphomas should I know about?
- Is the risk of infectious toxicity still high today? Are there any other significative toxicities? What about viral factors?
- what about staging? what role does the PET scan play?
- what are the clinical presentations today?
- Is the risk of CNS recurrence increased compared to the general population?

LYMPHOMA AND PLWH: Clinical Charactristics



Baptista MJ, Hiv-Infection Impact on Clinical-Biological Features and Outcome of Diffuse Large B-cell Lymphoma Treated With R-CHOP in the Combination Antiretroviral Therapy Era. Aids (2015)

Cingolani A, Survival and Predictors of Death in People With HIV-associated Lymphoma compared to Those With a Diagnosis of Lymphoma in General Population. PloS One (2017)

Chao C. Survival of non-Hodgkin Lymphoma Patients With and Without Hiv Infection in the Era of Combined Antiretroviral Therapy. AIDS (2010)

Han X, Hiv Infection and Survival of Lymphoma Patients in the Era of Highly Active Antiretroviral Therapy. Cancer Epidemiol Biomarkers Prev (2017)

Coutinho R, Hiv Status Does Not Impair the Outcome of Patients Diagnosed With Diffuse Large B-Cell Lymphoma Treated With R-CHOP in the cART Era. AIDS (2014)

LYMPHOMA AND PLWH: FACTORS ASSOCIATED WITH SURVIVAL

Outcomes for HIV-associated diffuse large B-cell lymphoma in the modern combined antiretroviral therapy era
Besson C, AIDS 2017

Prospective multicenter (22)
cohort study of HIV related L. 2008-2015

179 consecutive patients → **focus on 52 DLBCL;**
median age: 51

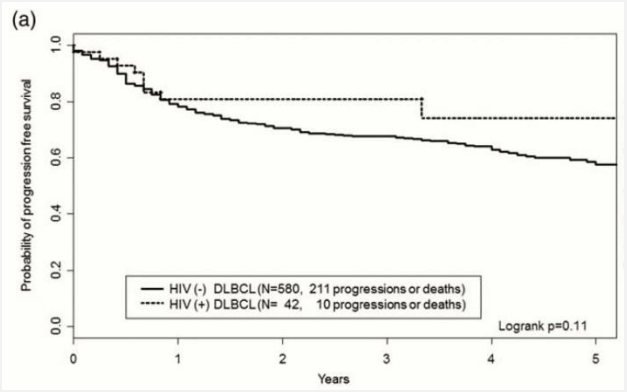
Median follow-up since diagnosis was 40 months

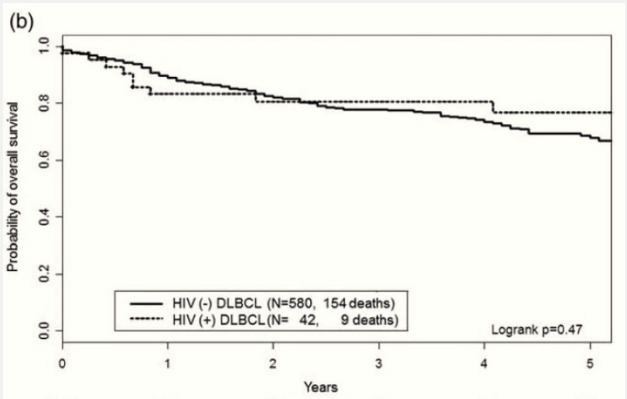
>Poor PS,
>more than one extranodal site
>advanced aaIPI
were associated with poorer PFS

COMPARISON WITH 52 DLBCL HIV NEG

	N = 52	(%)	Median (IQR)
Demographics			
Male sex	45	(87)	
Age (years)			51.5 (44.5–59)
Geographic origin[a]			
White	46	(92)	
Sub-Saharan	4	(8)	
HIV characteristics			
HIV transmission group[b]			
MSM	18	(42)	
Heterosexuals	12	(29)	
Intravenous drug users	12	(29)	
Year of HIV infection			
≤1995	25	(49)	
1996–2005	16	(31)	
≥2006	10	(20)	
Prior AIDS-defining illness	24	(46)	
$CD4^+$ T cell (nadir/μl)[c]			93.5 (44–200)
$CD4^+$ cell count/μl[a]			233 (105–406)
≤200	21	(42)	
HIV load (copies/ml)[a]			
<50	29	(57)	
≥50	21	(43)	80 173 (280–293 938)
cART at DLBCL diagnosis	41	(79)	
Length of cART therapy (years)[d]			11.4 (5.7–13.9)

Lymphoma characteristics		
Histologic subtype[e]		
GC	17	(47)
Non-GC	19	(53)
Extranodal sites[d]		
0	9	(19)
1	15	(29)
>1	27	(52)
Ann-Arbor stage		
I–II	8	(16)
III–IV	44	(84)
Performance status		
0–1	34	(65)
2–4	18	(35)
LDH above normal[a]	25	(50)
aaIPI[a]		
0–1	21	(42)
2–3	29	(58)





Changes in the influence of lymphoma- and HIV-specific factors on outcomes in AIDS-related non-Hodgkin lymphoma. Ann Oncol 2015.
Prognostic factors in HIV-related diffuse large-cell lymphoma: before versus after highly active antiretroviral therapy. Lim ST J Clin Oncol 2005
The role of tumor histogenesis, FDG-PET, and short-course EPOCH with dose-dense rituximab (SC-EPOCHRR) in HIV-associated diffuse large B-cell Lymphoma. Dunleavy K. Blood 2010

LYMPHOMA AND PLWH: CENTRAL NERVOUS SYSTEM INVOLVEMENT

2008

	HAART before lymphoma n=31	No HAART before lymphoma n=100	p
CNS involvement (out of the 131 from the series)	1/31 (3.2%)	25/100 (25%)	0.008
PCL (out of the 131 from the series)	*1/31 (3.2%)	13/100 (13%)	0.108
Leptomeningeal spread secondary to systemic NHL (out of the 117 with systemic NHL)	0/30 (0%)	12/87 (14%)	0.023

2016

CNS$^{B:}$ 2-5% DLBCL

CNS$^{B:}$ 25-30% BL

CNS^{R} in adequately treated patients :2, 3,5%

Existing DB of 1546 pts/9 trials
2/3 pts in cART era; 53% on cART at chemo

Age, years (median, range)	39 (18-74)
Sex, male n (%)	710 (81%)
Enrolment period	
Pre-cART (1990-95) n (%)	279 (31%)
cART era (1996-2010) n(%)	607 (69%)
CD4 count, × 10^9 cells/l (median; range)	0.398 (0-15.84)
Median viral load (copies/ml; range)	27,000 (0-6,080,000)
Prior history of AIDS, n (%)	232 (28%)
Concurrent cART therapy with chemotherapy	449 (53%)
Histology, n (%)	
Diffuse large B-cell lymphoma	570 (64%)
Burkitt/Burkitt-like lymphoma	285 (32%)
Other lymphomas	31 (3%)
Age-adjusted IPI, n (%)[1]	
Low (score=0)	95 (12%)
Intermediate (score 1-2)	488 (63%)
High (score=3)	187 (24%)

2016

CNS involvement at baseline, n (%)	111 (13%)
Type of IT CNS therapy; n (%)	
CNS treatment 2nd to CNS^{B}	111 (13%)
Single drug IT chemoprophylaxis	628 (71%)
Triple drug IT chemoprophylaxis	141 (16%)
No IT CNS chemoprophylaxis	6 (7%)
Systemic chemotherapy, n(%)	
CHOP	325 (36%)
Infusional regimens[2]	134 (15%)
Dose intense regimens[3]	261 (29%)
Less intense[4]	166 (19%)
Rituximab use; n(%)	76 (31%)

44/837patients CNSR (5.26%), → 13% of all relapses (44/293).

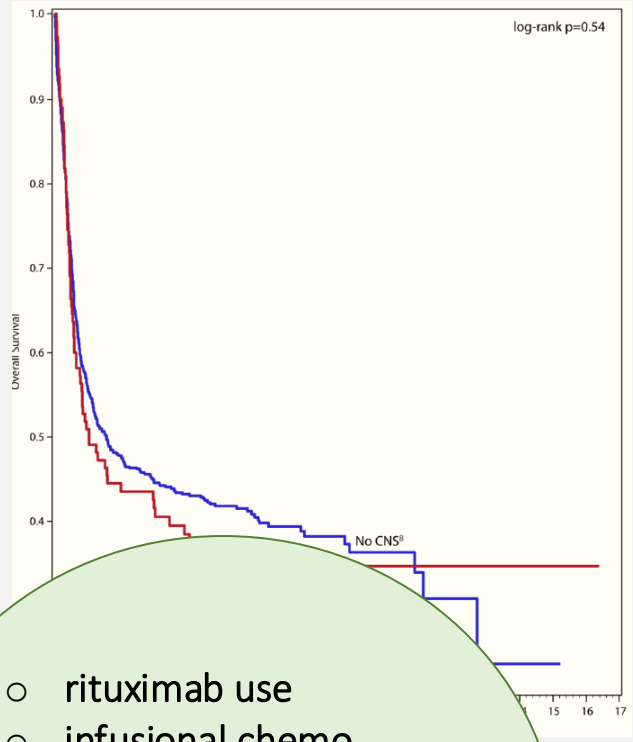
Decrease in the frequency of meningeal involvement in AIDS-related systemic lymphoma in patients receiving HAART Navarro JT; Haematologica
Central nervous system involvement in AIDS-related lymphomas Barta SK, BJH 2026

LYMPHOMA AND PLWH: CENTRAL NERVOUS SYSTEM INVOLVEMENT

Central nervous system involvement in AIDS-related lymphomas Barta SK, BJH 2026

2016

	Hazard Ratio	95% CI	*P*
Age	0.99	0.95 - 1.03	0.72
Gender (Male)	1.10	0.40 – 3.00	0.85
Enrolment Date			0.50
1990-1995	Reference		
1996-2010	0.48	0.06 - 4.11	
CD4 count	1.00	1.00 - 1.00	0.5
Viral load	1.00	1.00 - 1.00	0.09
AIDS history	1.40	0.45 - 4.39	0.56
Concurrent cART Therapy	1.90	0.23 15.97	0.56
Histology			0.07
Diffuse large B-cell lymphoma	Reference		
Burkitt/Burkitt-like lymphoma	2.45	1.14 - 5.31	
Other lymphomas	1.25	0.15 - 10.59	
Age-adjusted IPI			0.77
Low	Reference		
Intermediate	0.96	0.32 - 2.90	
High	0.61	0.12 - 3.03	
CNS[B]	3.68	1.49 – 9.10	0.005
No	Reference		
Yes	3.67	1.49 - 9.10	
Treatment[1]			0.71
CHOP	Reference		
Infusional[1]	0.00		
Dose intense[1]	1.15	0.47- 2.80	
Less intense[1]	1.72	0.70 - 4.24	
Rituximab	0.26	0.05 - 1.42	0.12
CR with initial treatment	0.14	0.07 – 0.32	<0.0001



No association with cART use with CNS relapse

no difference in CNSB in the pre-cART and cART era (13% each)

- rituximab use
- infusional chemo
- concurrent cART
- lower aaIPI scores

were independently associated with increased OS for all patients on multivariate analysis

FACTORS ASSOCIATED TO SURVIVAL: THE MUSTHAL GROUP EXPERIENCE

96 PTS (DG 1996-2023) Median age:49

Sierologie
- HIV-Ab positivo: 96 (100%)
- HBsAg positivo: 9 (9%, 95% CI 5-17%)
- HCV Ab positivo: 33 (34%, 95% CI 26-44%)

Status viro-immunologico alla diagnosi di HIV
- Conta CD4+ (media, /ul): 126 (range 3-463)
- Conta CD8+ (media, /ul): 690 (range 40-2938)
- Rapporto CD4/CD8 (media): 0.22 (range 0-1.8)
- HIV-RNA (log10): 5.09 (range 1.59-7)

Status viro-immunologico alla diagnosi di linfoma
- Conta CD4+ (media, /ul): 280 (range 4-1237)
- Conta CD8+ (media, /ul): 945 (range 40-3779)
- Rapporto CD4/CD8 (media): 0.42 (range 0-1.8)
- HIV-RNA (log10): 3.36 (range 1.59-7.04)

cART alla diagnosi di linfoma*
- Sì: 63 (66%, 95% CI 56-74%)
- No: 33 (34%, 95% CI 26-44%)

*almeno 6 mesi prima della diagnosi di linfoma

Istotipo*
- DLBCL: 82 (85%, 95% CI 77-91%)
- HGBL: 14 (15%, 95% CI 9-23%)
  - HGBL con traslocazione di MYC e BCL2: 4
  - HGBL con traslocazione di MYC e BCL2 e BCL6*: 1
  - HGBL, non altrimenti specificato (NOS): 9

Stadio
- I: 4 (4%, 95% CI 2-10%)
- II: 5 (6%, 95% CI 2-12%)
- III: 18 (19%, 95% CI 12-28%)
- **IV: 68 (71%, 95% CI 61-79%)**
- Non disponibile: 1

Siti interessati alla diagnosi
- Malattia nodale: 20 (20%, 95% CI 14-30%)
- **1 sito extranodale: 38 (40%,** 95% CI 30-50%)
- **≥ 2 siti extranodali: 38 (40%,** 95% CI 30-50%)
- **SNC: 8 (8%, 95% CI 4-16%)**
- Renale/surrenale: 6 (6%, 95% CI 3-13%)

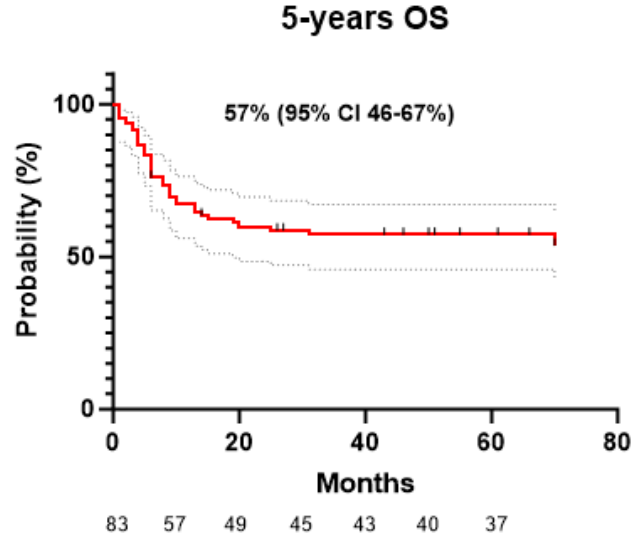
Eastern cooperative oncologic group (ECOG) performance status (PS)
- 0-1: 60 (62%, 95% CI 52-73%)
- ≥ 2: 35 (36%, 95% CI 28-46%)
- Non disponibile: 1

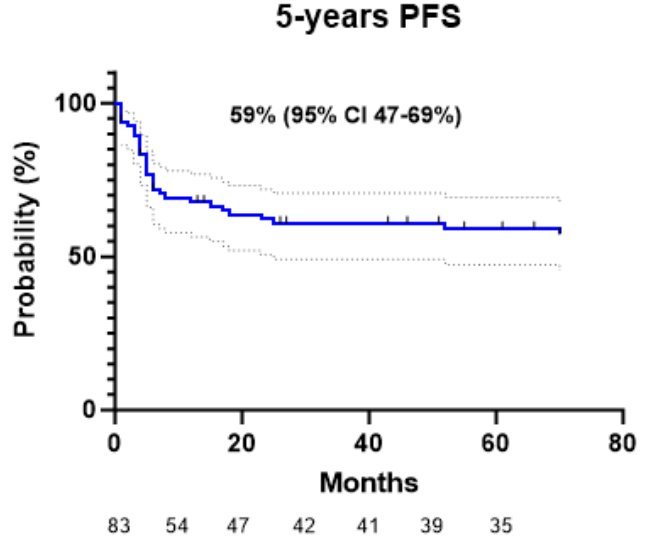
International Prognostic Index (IPI)
- Basso (0-1): 14 (15%, 95% CI 9-23%)
- **Intermedio (2-3): 58 (60%, 95% CI 50-69%)**
- **Alto (4-5): 23 (24%, 95% CI 17-33%)**
- Non disponibile: 1 (1%, 95% CI 2-6%)

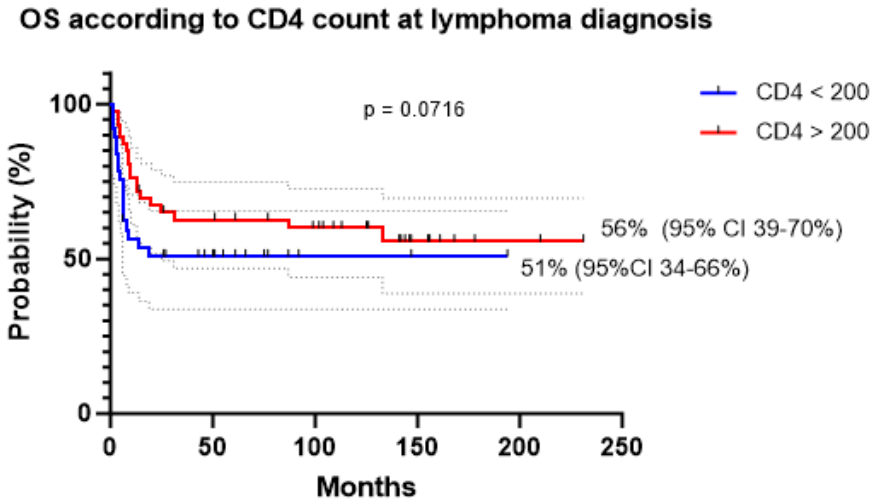
Central nervous system (CNS)-IPI
- Basso (0-1): 13 (14%, 95% CI 8-22%)
- **Intermedio (2-3): 57 (59%, 95% CI 49-68%)**
- **Alto (4-6): 25 (26%, 95% CI 18-36%)**
- Not available: 1 (1%, 95% CI 2-6%)

Unpublished data

FACTORS ASSOCIATED TO SURVIVAL: THE MUSTHAL GROUP EXPERIENCE







Impact on OS → HIV related variables

- CD4+ nadir, HR: 1.004 (0.9827 - 1.028) (p= 0.7268)
- CD8+ abs al nadir, HR: 1 (0.9982 - 1.003) (p= 0.7107)
- HIV-RNA log10 zenith, HR: 1.772 (0.8316 - 7.707) (p= 0.2512)
- CD4+ abs diagnosis, HR: 0.9913 (0.9651 - 1.003) (p= 0.2622)
- CD8+ abs diagnosis, HR: 1.001 (0.9981 - 1.003) (p= 0.4712)
- HIV-RNA log10 diagnosis, HR: 0.7787 (0.3609 - 1.645) (p= 0.4987)
- cART at diagnosis, HR: 0.3742 (0.03852 - 3.649) (p= 0.3523)

- 8 pazienti (8%, 95% CI 4-16%) recidivati/progrediti nel SNC:
  - 5/25 con **CNS-IPI HR (20%**, 95% CI 9-39%)
  - 3/57 con **CNS-IPI IR (5%**, 95% CI 2-14%)
  - 0/13 con **CNS-IPI LR (0%**, 95% CI 0-23%)
- Chemioterapia IT: 51 pazienti (53%, 95% CI 43-63%)→ **36 profilassi**
- HD-MTX EV: 13 pazienti (14%, 95% CI 8-22%) → **3 profilassi**
- Non differenze significative nell'incidenza di ricaduta/progressione SNC stratificando per profilassi

LYMPHOMA AND PLWH: DLBCL –QUESTIONS NEVER TO BE ASKED AGAIN-

HiV and Lymphoma: from Epidemiology to Clinical Management. Re A. Mediterranean Journal of Hematology and Infectious Diseases, 2016
Diffuse Large B-Cell Lymphoma in the HIV Setting, Huguet M, Cancers 2023

- Should rituximab **be** included within the regimen in CD20-positive HIV NHL?

	2003	2005	2008	2013	2004	2005	2010	2010
	CHOP/R-CHOP/DR-COP				CDE/R-CDE		R-EPOCH/SC-EPOCH-RR	
	Boué et al., 2003 [74]	Kaplan et al., 2005 [73]	Ribera et al., 2008, 2012 [75,76]	Levine et al., 2013 [78]	Sparano et al., 2004 [67]	Spina et al., 2005 [71]	Sparano et al., 2010 [64]	Dunleavy et al., 2010 [41]
No. of patients	61	150	81	40	98	74	106	33
Study design	Phase II R-CHOP	Phase III CHOP vs. R-CHOP	Phase II R-CHOP	Phase II DR-COP	Phase II CDE	Pooled results from 3 phase II trials R-CDE	Phase II R-EPOCH vs. EPOCH-R	Phase II SC-EPOCH-RR
DLBCL histology, N (%)	44 (72)	120 (80)	81 (100)	39 (98)	76 (78)	53 (72)	79 (75)	33 (100)
$CD4^+$ µL, median	172	133	158	114	160	161	181 vs. 194	208
aa-IPI $\geq$ 2, N (%)	29 (48)	70 (47)	55 (67)	11 (27)	62 (67)	42 (57)	70 (66)	25 (76)
Outcome, %								
CR * rate	77	47 vs. 58	69	47	45	70	73 vs. 55	91
PFS *	69 (2-year)	9.5 vs. 11.3 months	-	52 (2-year)	36 (2-year)	59 (2-year)	66 vs. 63 (2-year)	84 (5-year)
OS *	75 (2-year)	28 vs. 35 months	56 (3-year)	62 (2-year)	43 (2-year)	64 (2-year)	70 vs. 67 (2-year)	68 (5-year)
Infectious deaths (%)	2	2 vs. 14	7	0	Unknown	7	10 vs. 7	0

LYMPHOMA AND PLWH: DLBCL –QUESTIONS NEVER TO BE ASKED AGAIN-

HiV and Lymphoma: from Epidemiology to Clinical Management. Re A. Mediterranean Journal of Hematology and Infectious Diseases, 2016
Diffuse Large B-Cell Lymphoma in the HIV Setting, Huguet M, Cancers 2023

- Should rituximab **be** included within the regimen in CD20-positive HIV NHL?

	2005	2008	2013	2004	2005	2010	2010
	CHOP/R-CHOP/DR-COP			CDE/R-CDE		R-EPOCH/SC-EPOCH-RR	
	Boué et al., 2003 [74]	Kaplan et al., 2005 [73]	Ribera et al., 2008, 2012 [75,76]	Levine et al., 2013 [78]	Sparano et al., 2004 [67]	Spina et al., 2005 [71]	Sparano et al., 2010 [64]	Dunleavy et al., 2010 [41]
No. of patients	61	150	81	40	98	74	106	33
Study design	Phase II R-CHOP	Phase III CHOP vs. R-CHOP	Phase II R-CHOP	Phase II DR-COP	Phase II CDE	Pooled results from 3 phase II trials R-CDE	Phase II R-EPOCH vs. EPOCH-R	Phase II SC-EPOCH-RR
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Outcome, %								
CR * rate	77	47 vs. 58	69	47	45	70	73 vs. 55	
PFS *	69 (2-year)	9.5 vs. 11.3 months	-	52 (2-year)	36 (2-year)	59 (2-year)	66 vs. 63 (2-ye	
OS *	75 (2-year)	28 vs. 35 months	56 (3-year)	62 (2-year)	43 (2-year)	64 (2-year)	70 vs. 67 (	
Infectious deaths (%)	2	2 vs. 14	7	0	Unknown	7	1	

Infusional regimens

- Should antiretroviral therapy be suspended during chemotherapy?

NO!
By pooled analysis of 1546 pts.
Blood, 2013

YES!
There is need to <u>maximize opportunistic infection prophylaxis</u> in patients with CD4 count <50/mL, according to current guidelines on HIV management.

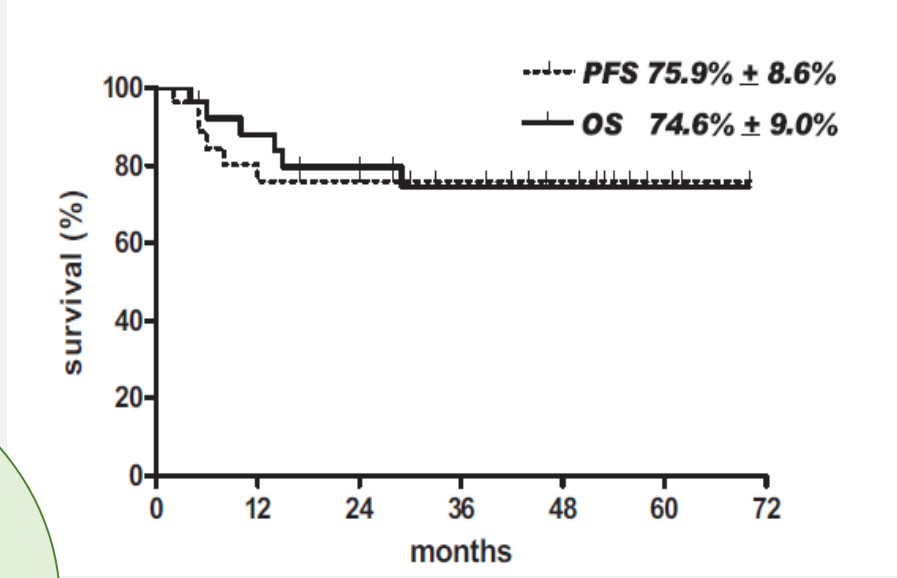
LYMPHOMA AND PLWH: DLBCL –QUESTIONS NEVER TO BE ASKED AGAIN-

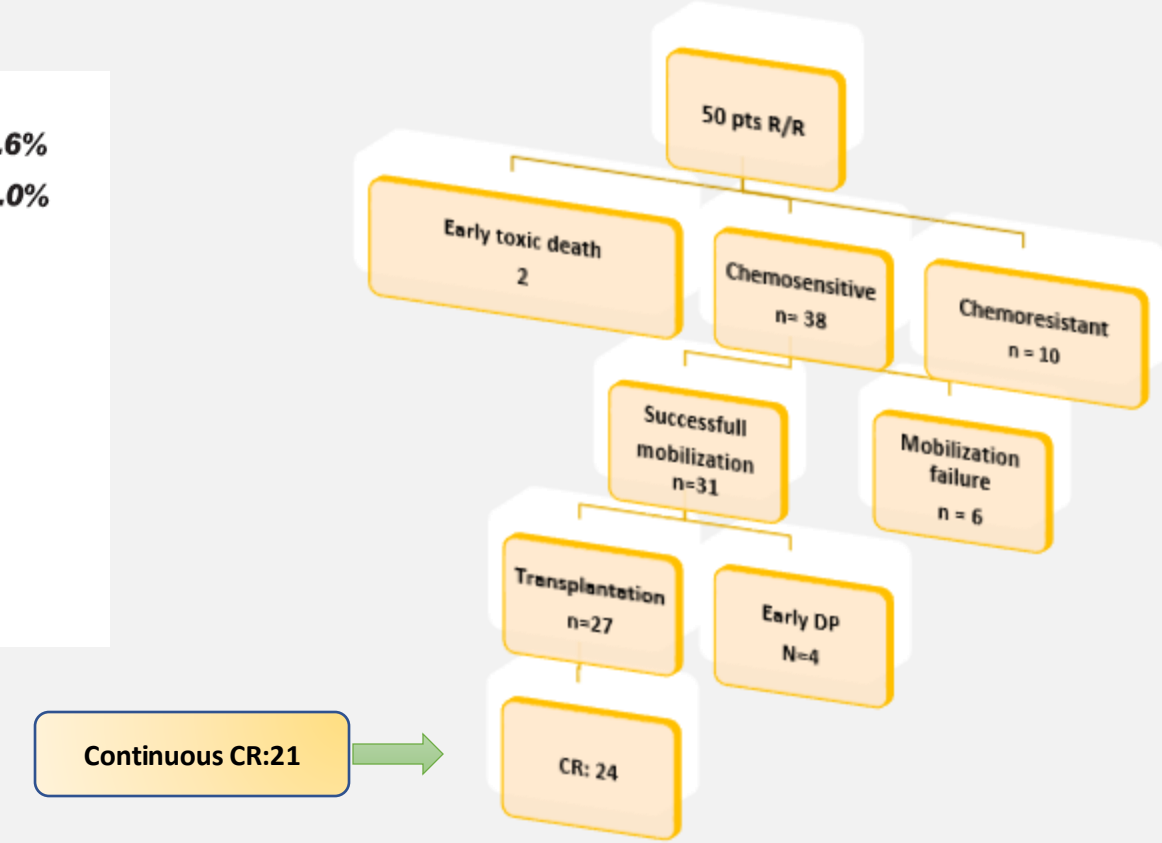
HiV and Lymphoma: from Epidemiology to Clinical Management. Re A. Mediterranean Journal of Hematology and Infectious Diseases, 2016
Diffuse Large B-Cell Lymphoma in the HIV Setting, Huguet M, Cancers 2023

- Is the approach with intensive chemotherapy and peripheral stem cell rescue feasible?

YES!

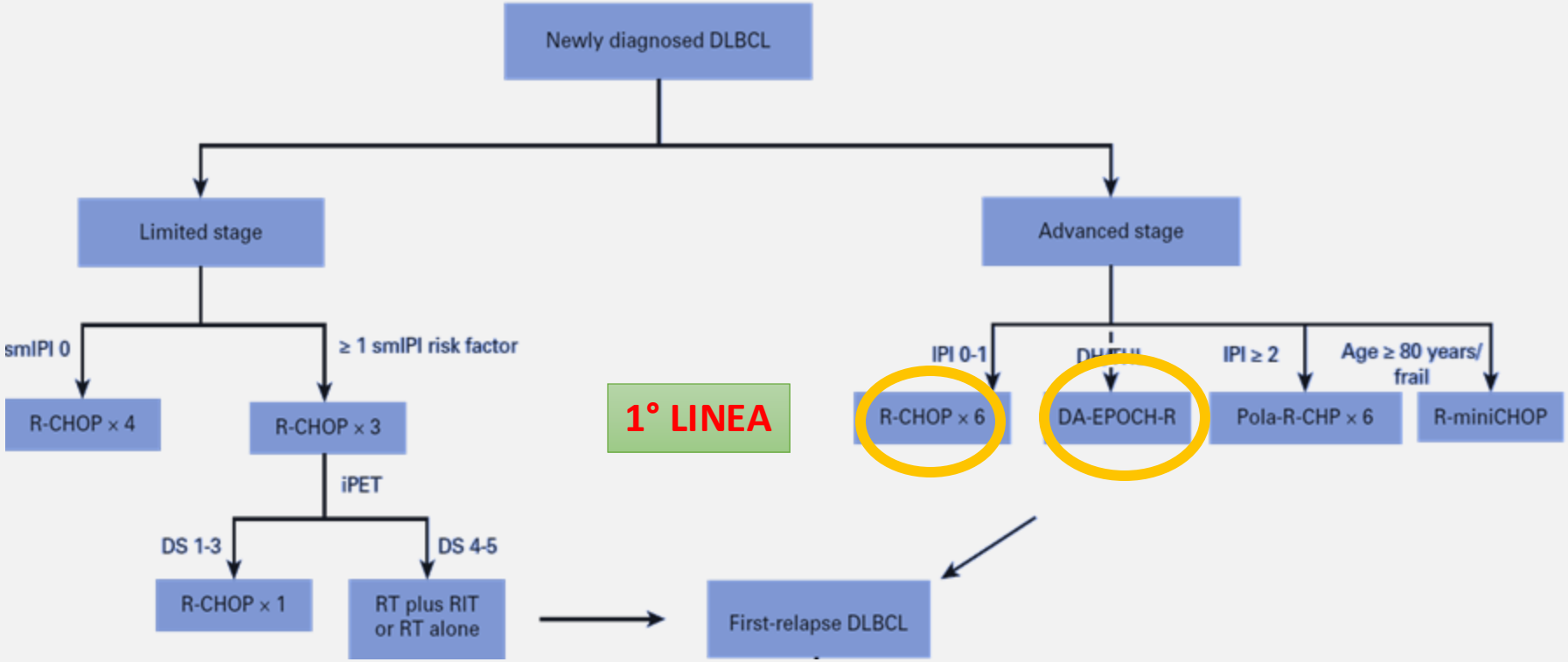
HIV infection should not preclude lymphoma patients from undergoing HDC-ASCT, according to the same eligibility criteria adopted for the general population





High-dose therapy and autologous peripheral blood stem cell transplantation as salvage treatment for AIDS-related lymphoma: long-term results of the Italian Cooperative Group on AIDS and Tumors (GICAT) study with analysis of prognostic factors; Re.A et al; Blood 2009

LYMPHOMA IN GENERAL POPULATION: DLBCL -THERAPY

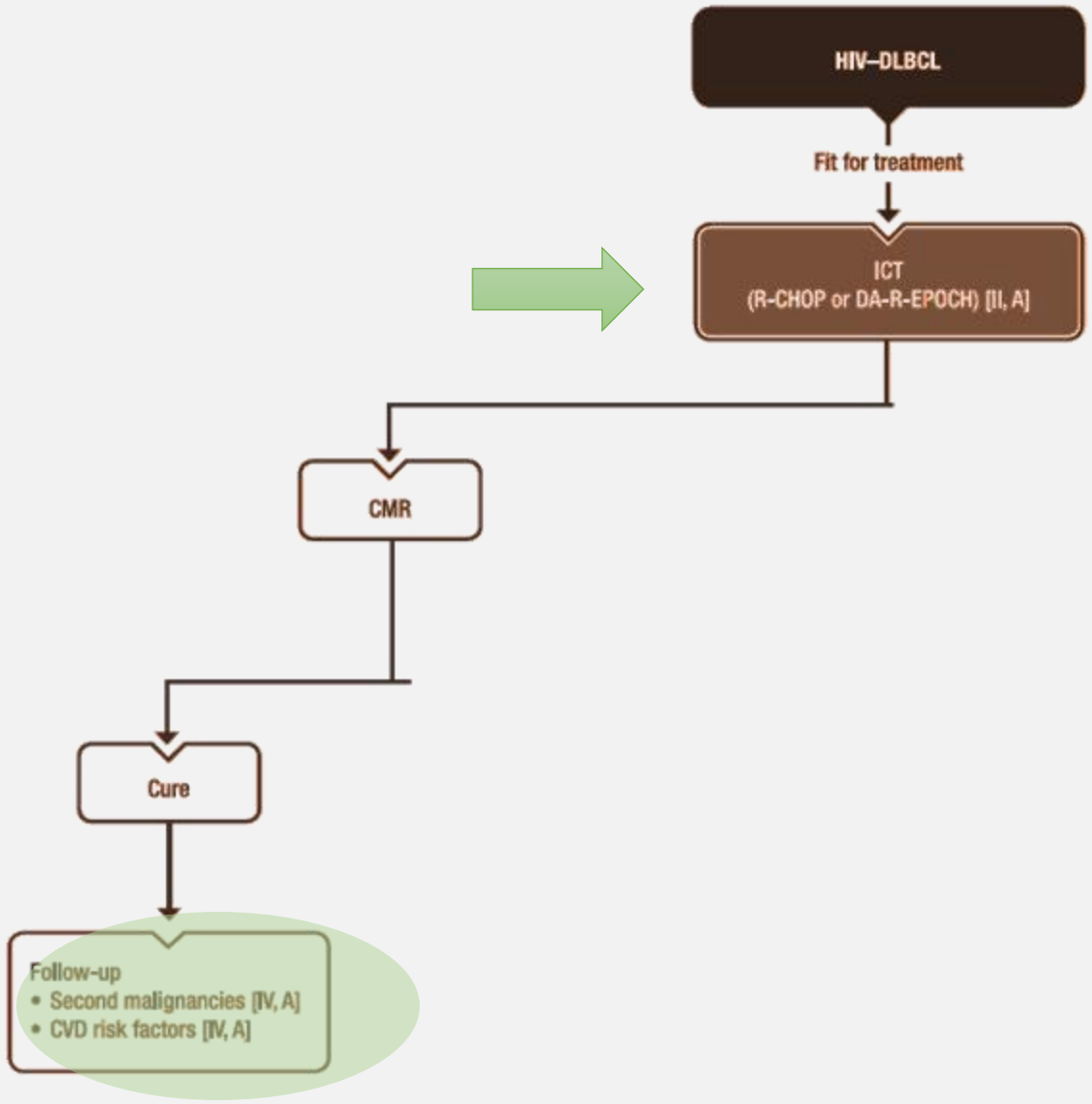


1° LINEA

Loretta J. Nastoupil,JC O 2022

First-line therapy			
IPI 0	IPI 1-2	IPI 3-5	Old/ Frail
4 x R-CHOP + 2 x R	6 x R-CHOP	6 x Pola-R-CHP	R-miniCHOP

LYMPHOMA AND PLWH : DLBCL THERAPY –first line-



Human immunodeficiency virus-associated lymphomas: EHAeESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, K. Hübel, 2024

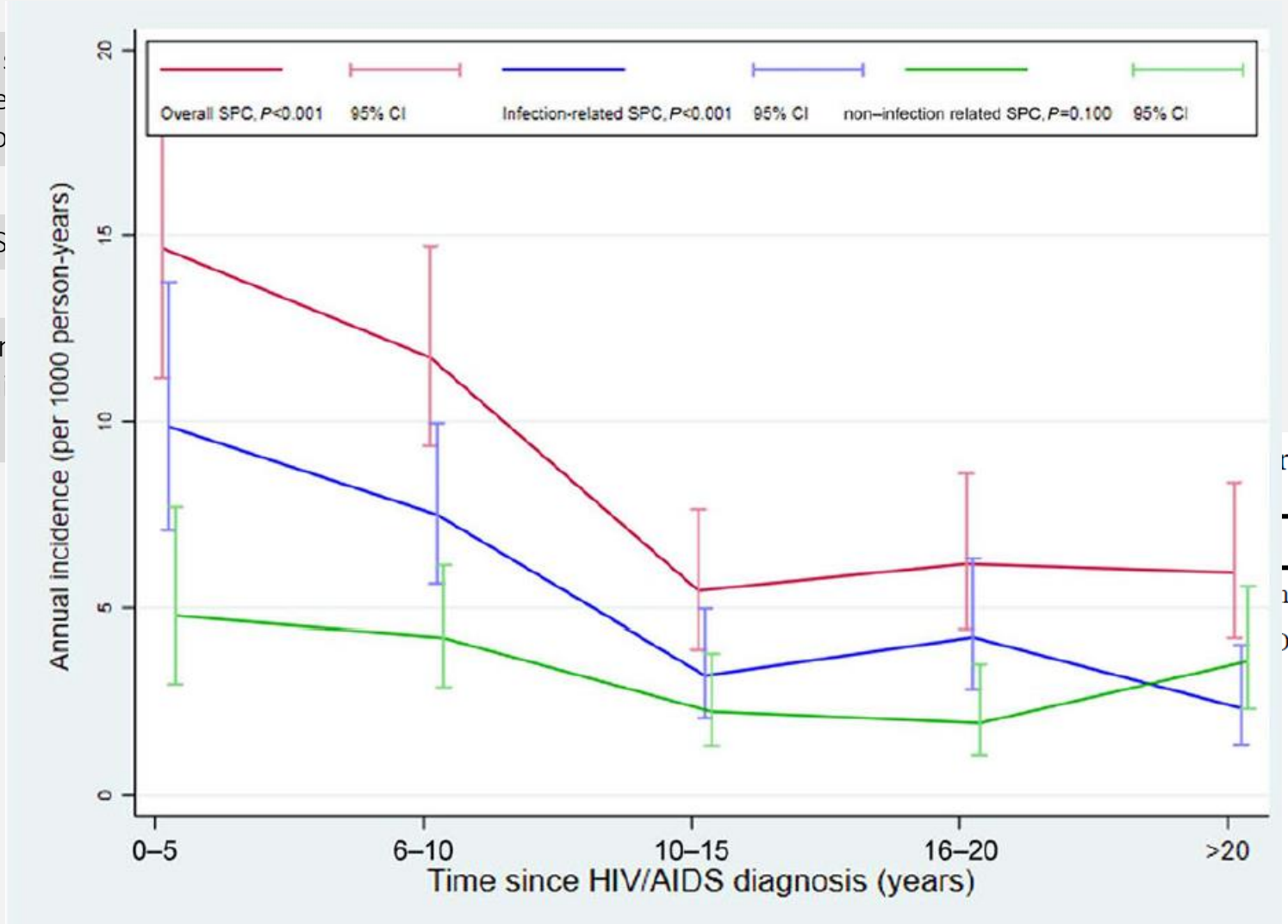
LYMPHOMA AND PLWH: risk of developing second primary cancer

Second Primary Cancers in People With HIV/AIDS: A National Data Linkage Study of Incidence and Risk Factors Di Ciaccio PR, J Acquir Immune Defic Syndr. 2023

Of 29,383 individuals were included in the person-years of follo

The most common S

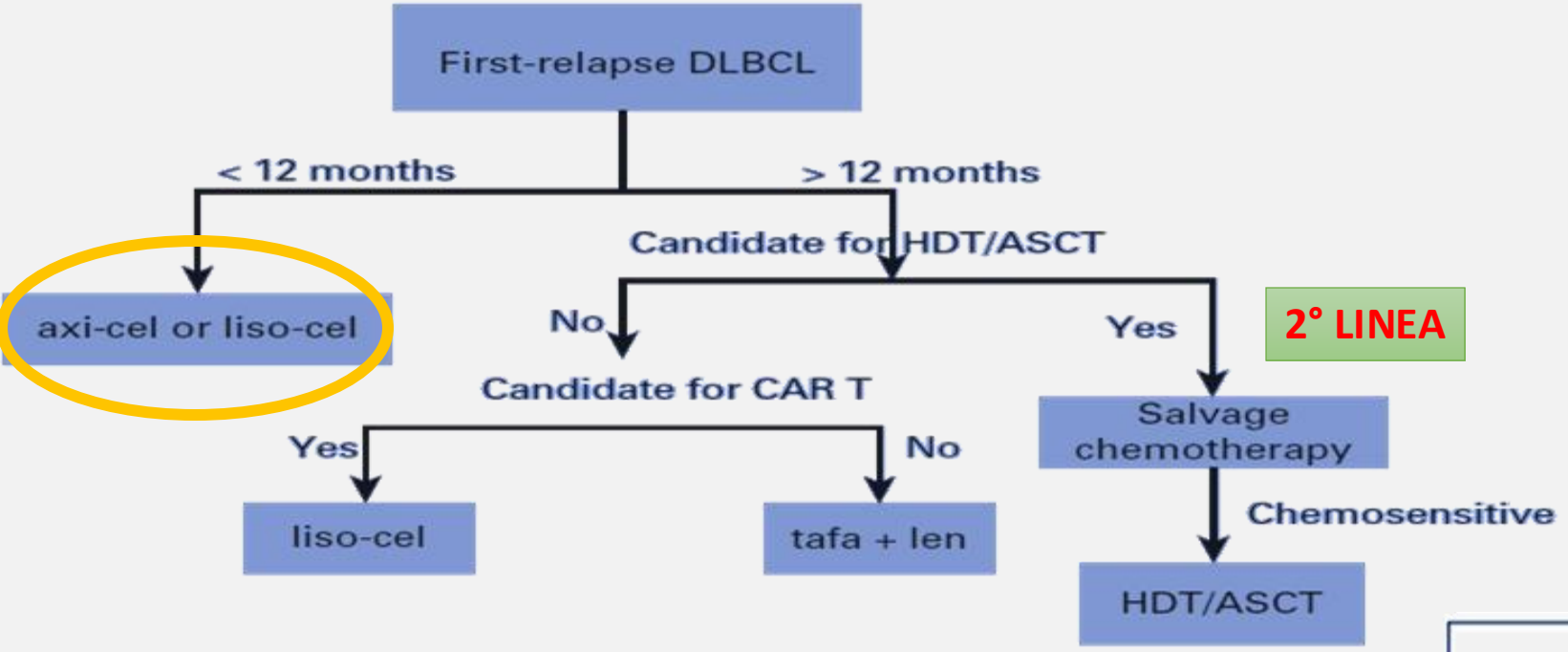
The incidence of nor 0.005) and the acqu



rs Identified in the Cohort

	Number of Second Cancers	% (Rounded)
ıa	41	18
)S	30	13	
	27	12
	25	11
	14	6
	9	4
	83	36
Total	229	100

LYMPHOMA IN GENERAL POPULATION: DLBCL –THERAPY 2° LINES

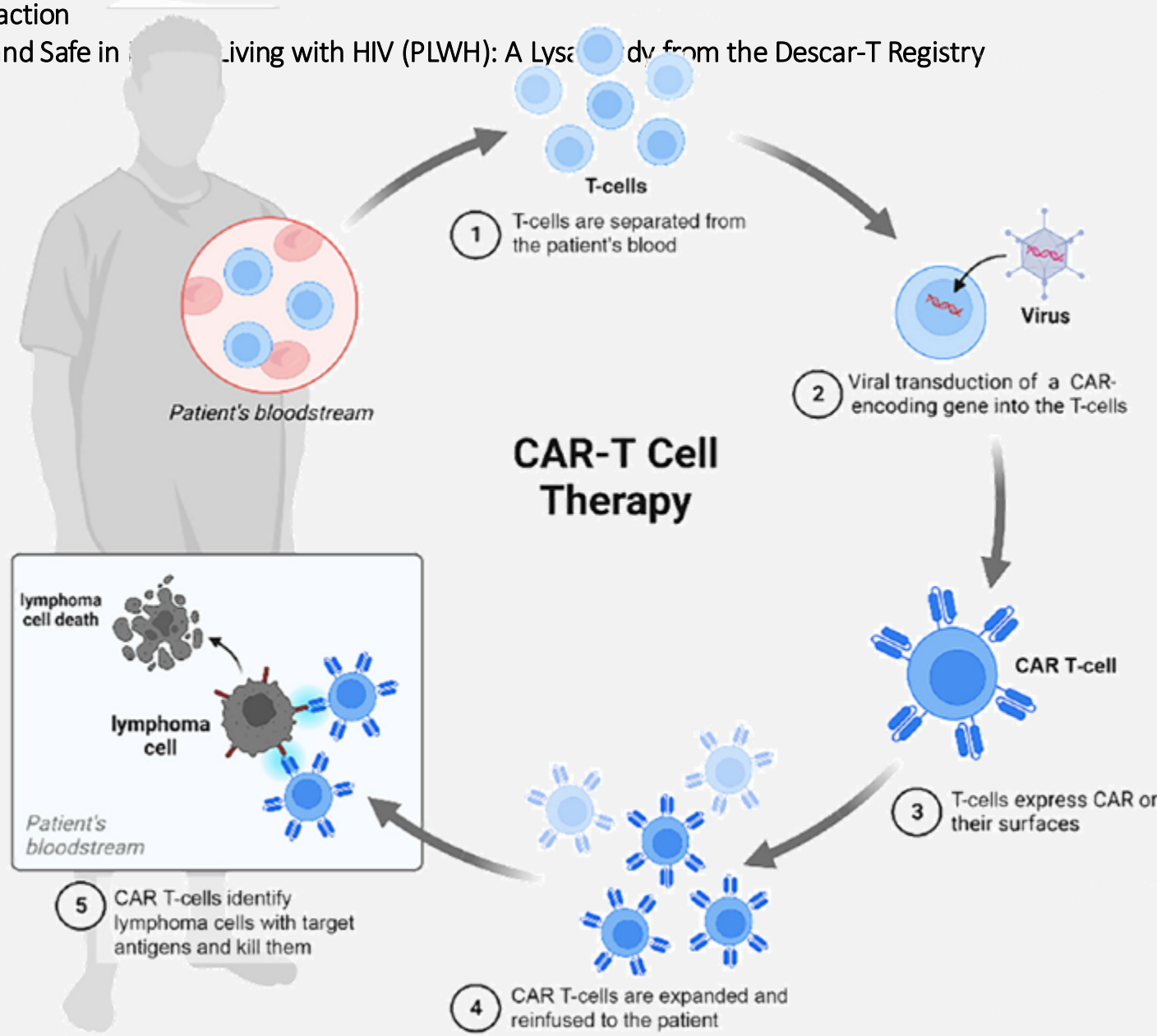


Second-line therapy		
Primary refractory/early relapse (≤12 mo.), CAR-T eligible patients	Late relapse (>12 mo.), HDCT/ASCT eligible	CAR-T and HDCT/ASCT ineligible patients
CAR-T cell therapy (Axicabtagene ciloleucel, Lisocabtagene maraleucel)	Platin-based salvage immunochemotherapy followed by HDCT/ASCT	Pola-BR Tafasitamab/ Lenalidomide R-GemOx

LYMPHOMA AND PLWH: DLBCL –THERAPY 2° LINES

Enabling CAR T-cell therapies for HIV-positive lymphoma patients – A call for action

CAR T-Cells Treatment for Relapsed/Refractory B-Cell Lymphoma Is Effective and Safe in Living with HIV (PLWH): A Lysa dy from the Descar-T Registry



LYMPHOMA AND PLWH: DLBCL –THERAPY 2° LINES

Enabling CAR T-cell therapies for HIV-positive lymphoma patients – A call for action

CAR T-Cells Treatment for Relapsed/Refractory B-Cell Lymphoma Is Effective and Safe in [redacted]iving with HIV (PLWH): A Lysa[redacted]dy from the Descar-T Registry

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)

reinfused to the patient

LYMPHOMA AND PLWH: DLBCL –THERAPY 2° LINES

Enabling CAR T-cell therapies for HIV-positive lymphoma patients – A call for action
CAR T-Cells Treatment for Relapsed/Refractory B-Cell Lymphoma Is Effective and Safe in People Living with HIV (PLWH): A Lysa Study from the Descar-T Registry
ASH2024 Clerrico m.

Histological subtypes : diffuse large B-cell lymphoma (n=20, 84%),
follicular lymphoma (n=2, 8%),
transformed follicular lymphoma (n=1, 4%)
grey zone lymphoma (n=1, 4%).

17% prior ABMT

Median time from HIV diagnosis to CAR T was 136 months
(range 11-342) and HIV viral load at lymphodepletion was undetectable in all available cases (11/24 patients).

At time of CAR T infusion, 4 patients (17%) had ECOG PS 2, 15 (63%) elevated LDH, and 10 (42%) elevated ferritin.

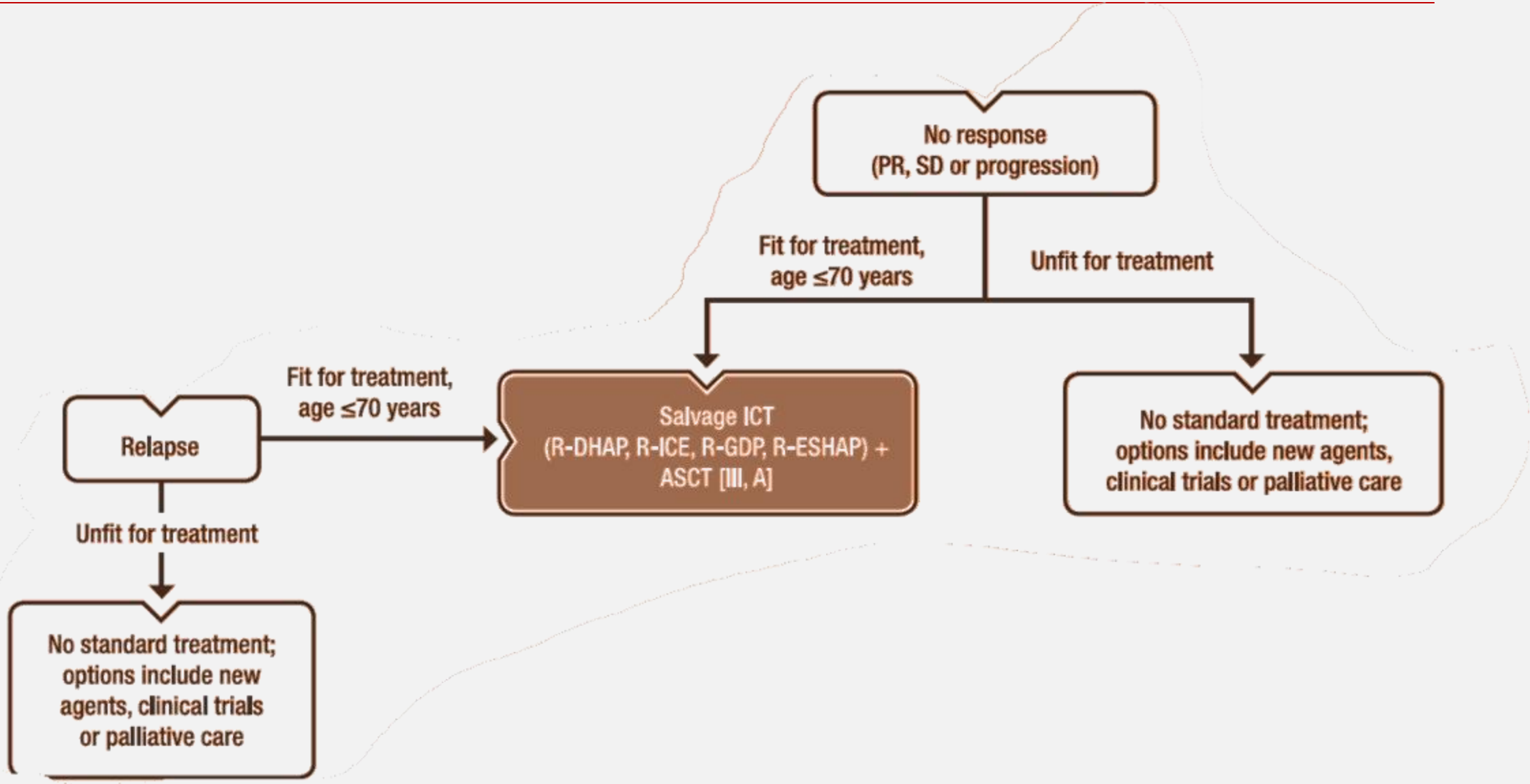
CRS : 21 patients (88%)
ICANS: 33%

Overall Response Rate (ORR) among PLWH at 90 days (M3) from axi-cel infusion was 50%, with 42% Response Rate (CRR).

With a median follow-up of 10.5 months (95% CI, 6-16), PFS and OS at 12 months were 40% (95% CI, 1 (95% CI, 28-75) respectively.

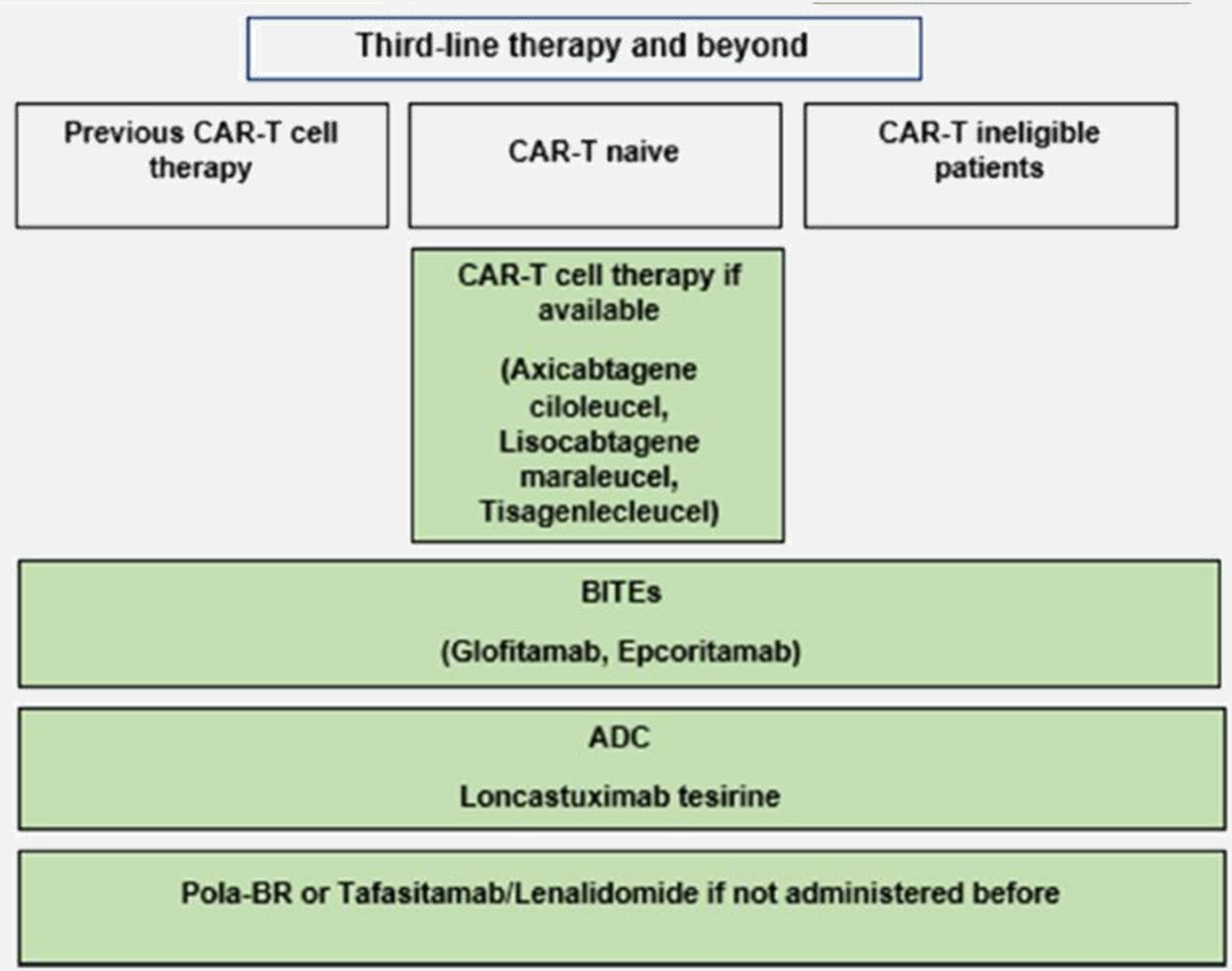
Ten deaths were reported:
8 patients
died of disease
progression, 1 of
Pseudomonas infection,
and 1 of progressive
multifocal
leukoencephalopathy not
directly
related to CAR T-cells.

LYMPHOMA AND PLWH: DLBCL –THERAPY 2° LINES

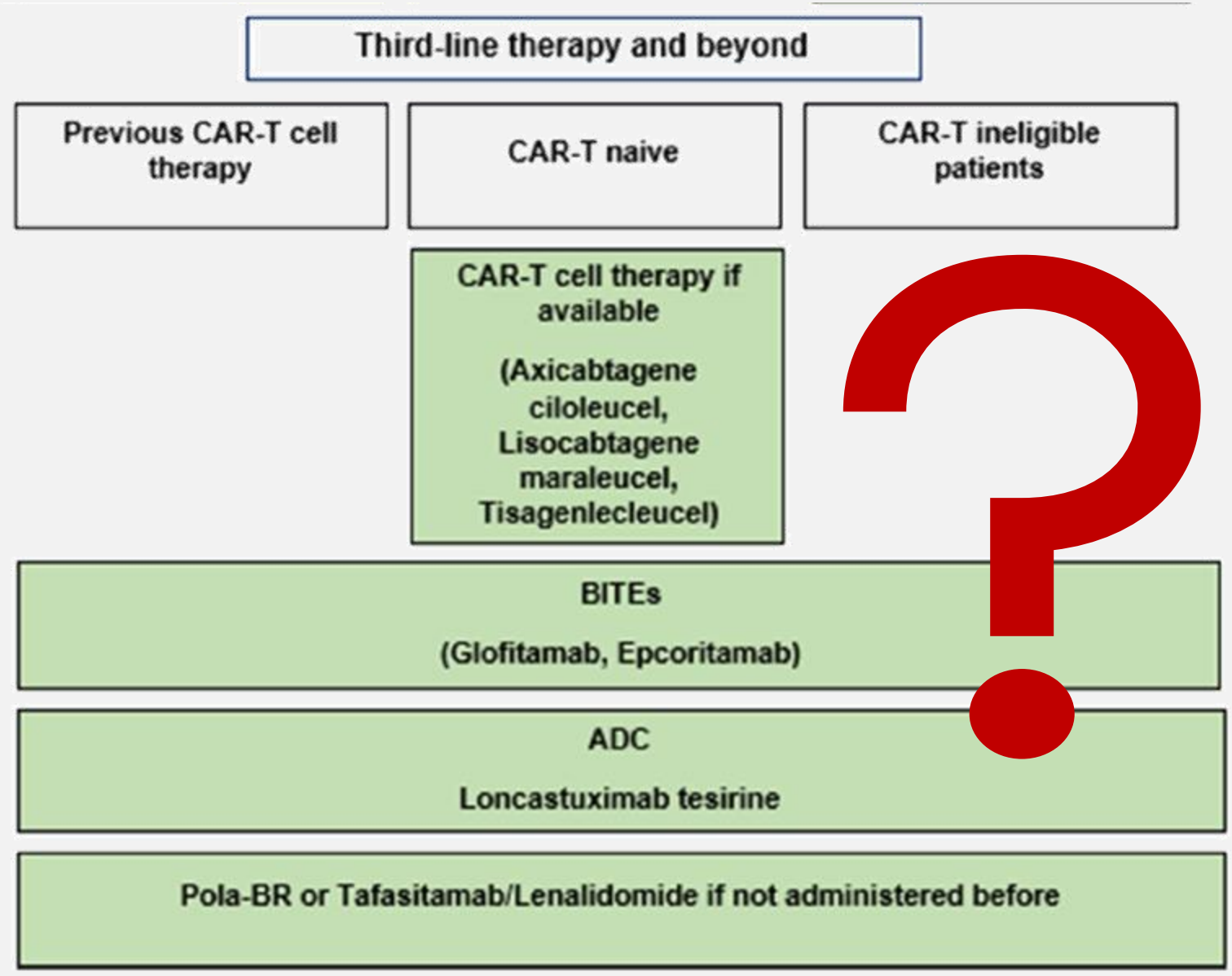


Human immunodeficiency virus-associated lymphomas: EHAeESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, K. Hübel, 2024

LYMPHOMA IN GENERAL POPULATION: DLBCL –THERAPY 3° LINES



LYMPHOMA AND PLWH: DLBCL –THERAPY 3° LINES



LYMPHOMA AND PLWH: DLBCL –THERAPY 3° LINES: EPICO TRIAL

International single-arm phase 2 trial addressing feasibility and efficacy of epcoritamab in PLWH with relapsed/refractory large B-cell lymphoma

Inclusion criteria:

- Adult (≥ 18 yo) HIV+ pts with CD20+ ***RR LBCL***
- ECOG PS score of 0-2
- **Prior lines ≥ 2 (anti-CD20)**
- CD4 >50 cell/mcL
- Failed or not eligible for HDT-ASCT

15 centers:

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

Primary endpoint: ORR

P0 : ORR 35%
P1 : ORR 60% (GCT3013-01 LBCL expansion cohort)

Sample size: 27 patients with RR HIV+ DLBCL

Two-step Simon minimax model:
First step: 16 pts →if 7 responses observed →*Second step*

Treatment active if 13 responses observed

Courtesy of Prof Ferreri

LYMPHOMA AND PLWH: BURKITT LYMPHOMA

BL International Prognostic Index (BL-IPI) Olszewski,a. JCO 2021

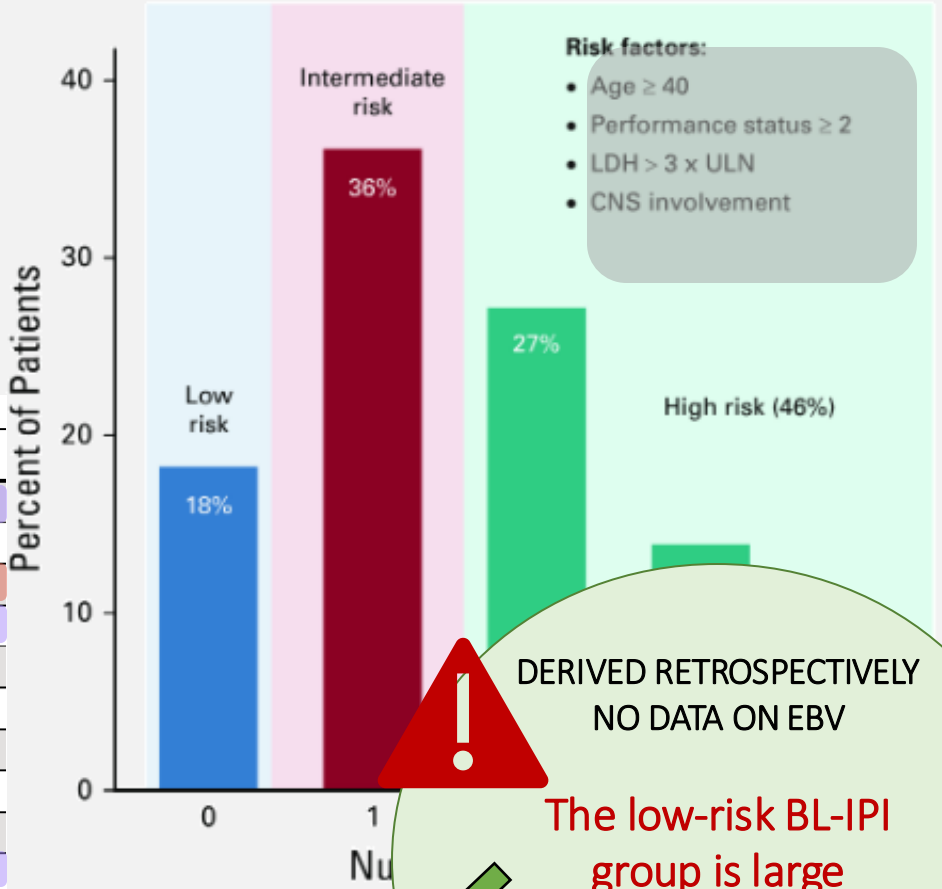
"Historical" risk factors

HR at least one of

- ECOG performance status above 1
- Ann Arbor stage III or IV
- elevated serum LDH (>ULN)
- tumour mass of 7 cm or greater

	Univariable			Multivariable		
Variable	HR	95% CI	*P*	HR	95% CI	*P*
Age ≥ 40	1.79	1.34 to 2.38	< .001	1.53	1.14 to 2.05	.005
Female	1.05	0.78 to 1.41	.74			
HIV-positive	1.15	0.85 to 1.56	.36			
PS ECOG ≥ 2	2.22	1.69 to 2.92	< .001	1.62	1.20 to 2.17	.001
No *MYC* rearrangement	0.82	0.53 to 1.29	.39			
Stage 3 or 4	2.35	1.57 to 3.53	< .001			
B symptoms	1.23	0.95 to 1.59	.12			
> 1 extranodal site	1.24	0.95 to 1.60	.11			
Marrow involvement	1.64	1.27 to 2.13	< .001			
CNS involvement	2.02	1.52 to 2.69	< .001	1.61	1.20 to 2.16	.002
LDH > 3 × ULN	2.12	1.62 to 2.77	< .001	1.71	1.29 to 2.27	< .001
Hemoglobin < 11.5 g/dL	1.63	1.25 to 2.12	< .001			
Albumin < 3.5 g/dL	1.55	1.19 to 2.03	.001			

BL International Prognostic Index (BL-IPI)



DERIVED RETROSPECTIVELY
NO DATA ON EBV

The low-risk BL-IPI group is large enough to consider de-escalated treatment strategies

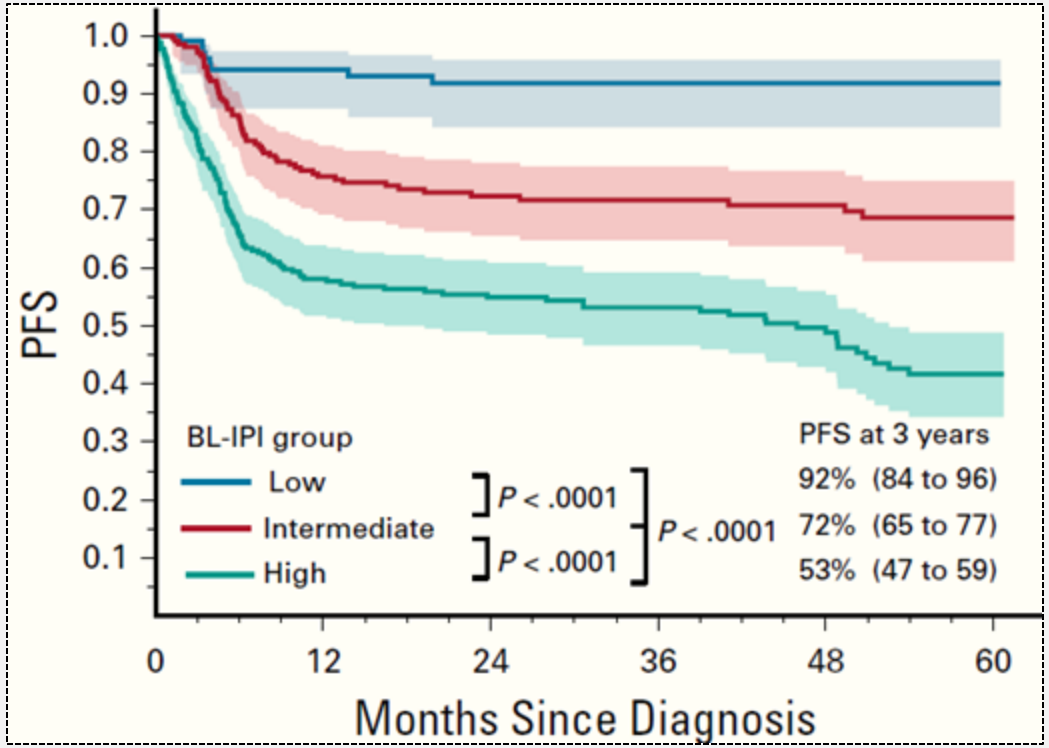
BL

LYMPHOMA AND PLWH: BURKITT LYMPHOMA

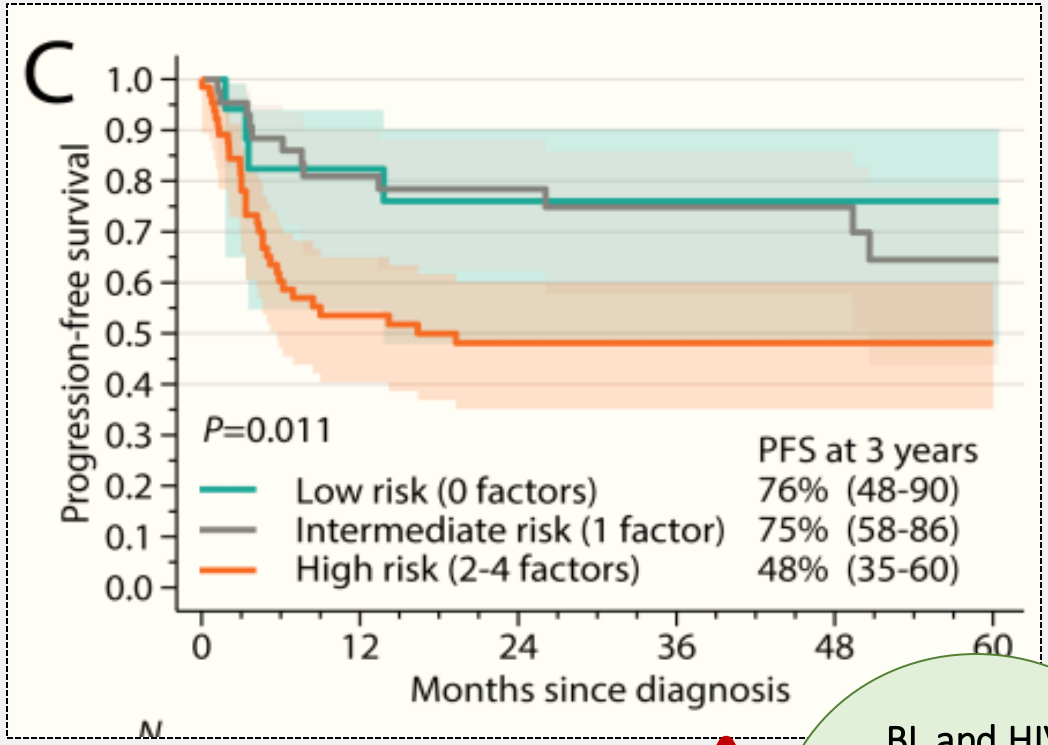
BL International Prognostic Index (BL-IPI) Olszewski,a. JCO 2021

BL International Prognostic Index (BL-IPI)

HIV NEG

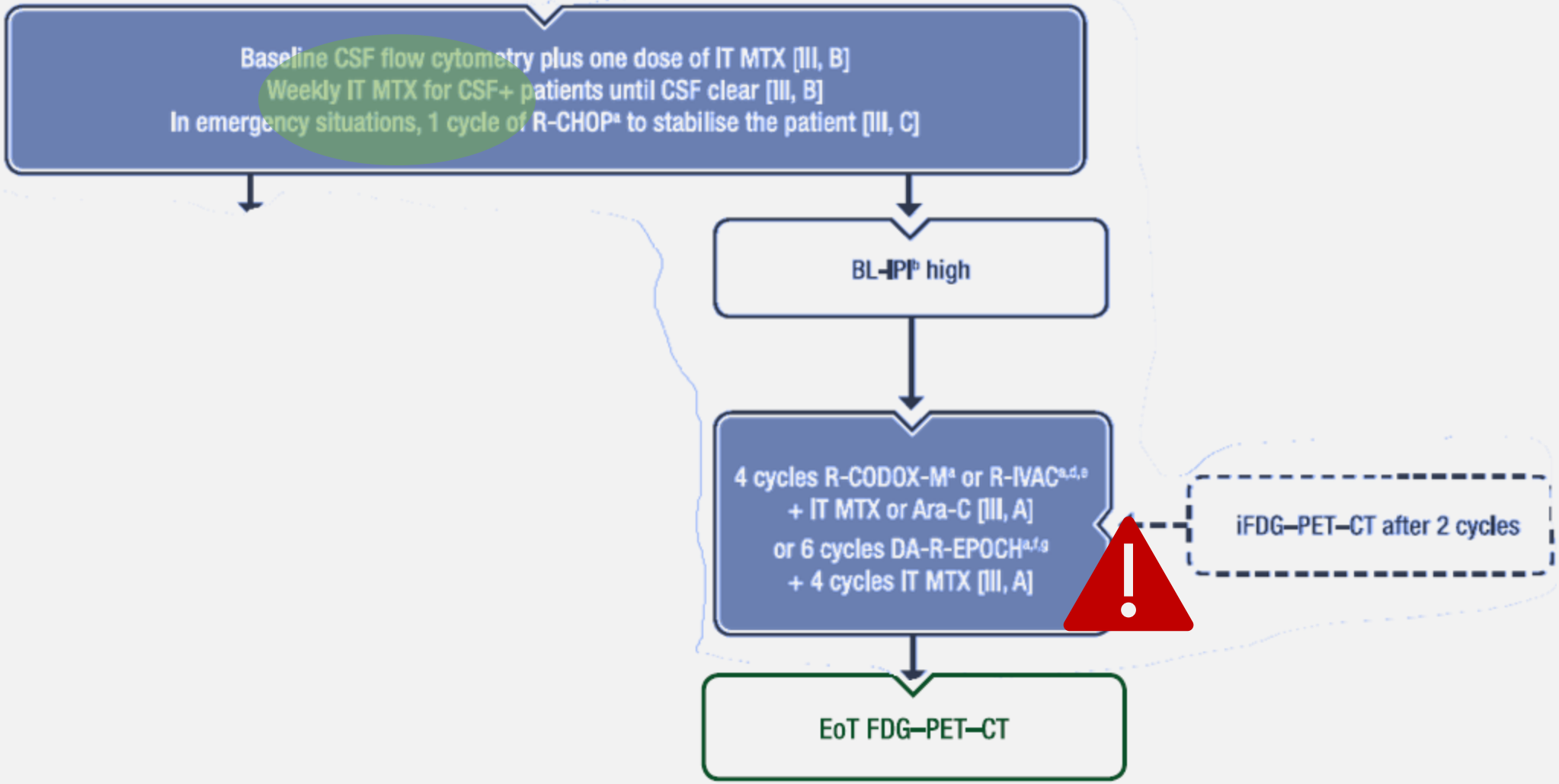


HIV POS



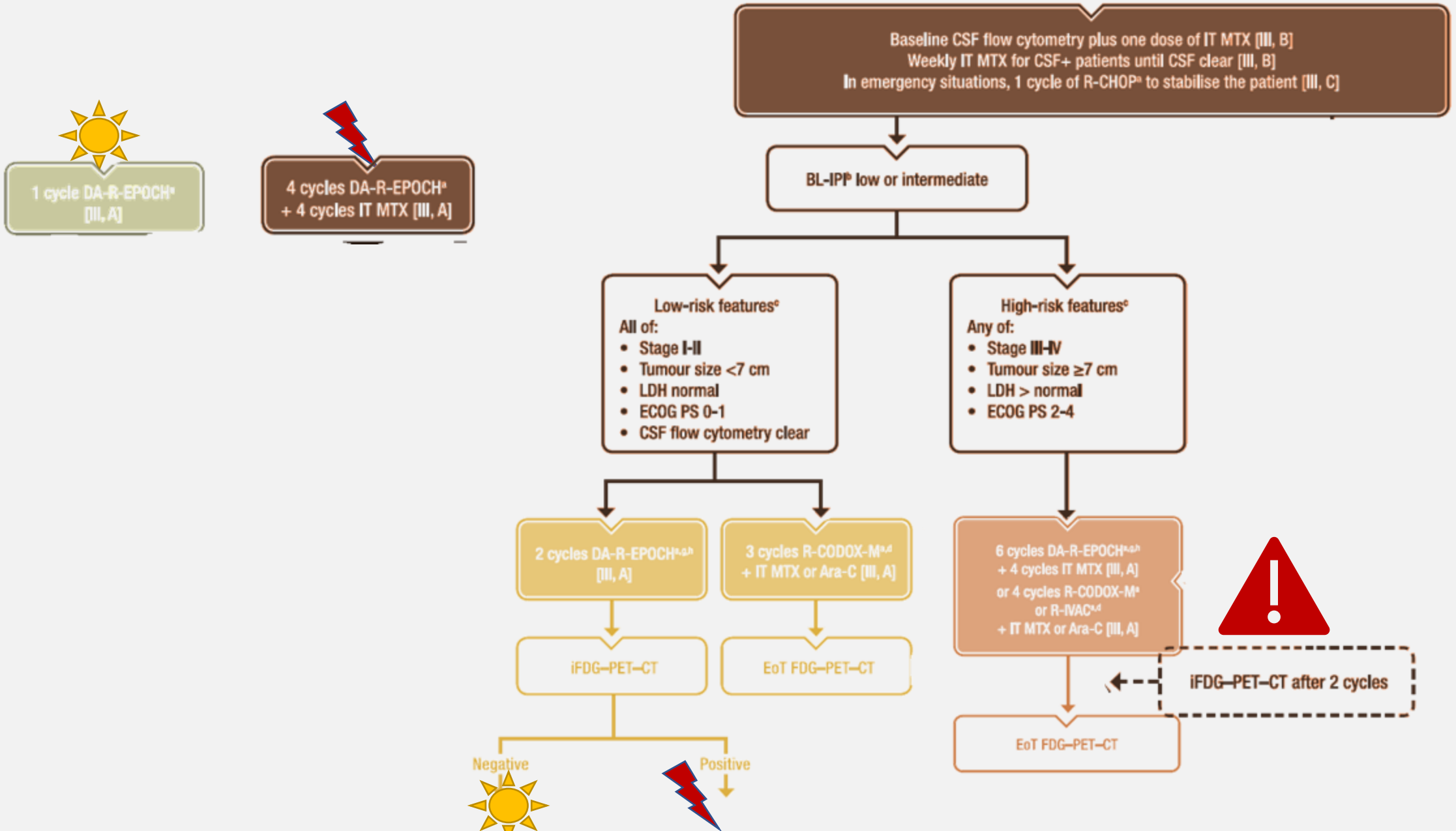
BL and HIV about 20% of CNS involvement at diagnosis

LYMPHOMA AND PLWH: BURKITT LYMPHOMA



Human immunodeficiency virus-associated lymphomas: EHAeESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, K. Hübel, 2024

LYMPHOMA AND PLWH: BURKITT LYMPHOMA



LYMPHOMA AND PLWH: BURKITT LYMPHOMA

Outcomes of Burkitt lymphoma with central nervous system involvement: evidence from a large multicenter cohort study

Zayac A.S. Haematologica 2021

multicenter retrospective study
641 pts patients aged ≥18 BL 2009- 2018

Prevalence of baseline CNS inv: 19%

CHEMO REGIMENS:

CODOX –M/IVAC: 30%
HYPER-C-VAD/MA: 30%
R-DA-EPOCH:28%

BL RELAPSE:26%
CNS RELPASE:6%

Risk factors for central nervous system recurrence in Burkitt lymphoma

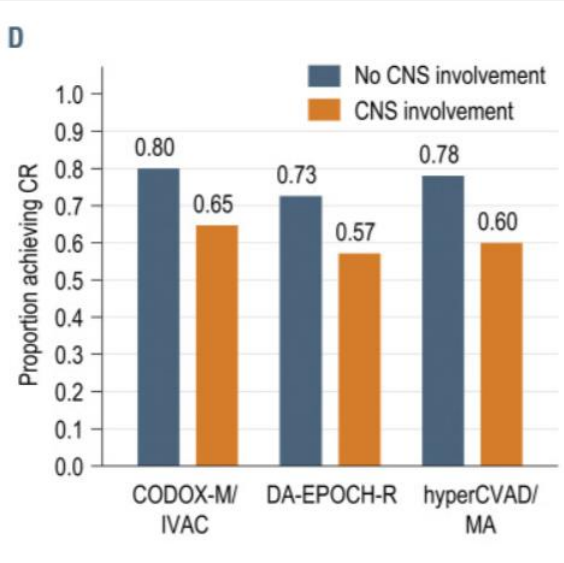
Variable	Cumulative incidence at 3 years				Univariate model		
	With		Without		SHR	95% CI	P
	%	95% CI	%	95% CI			
Age ≥40 years	6	(4-9)	7	(4-11)	0.92	(0.47-1.79)	0.80
Age ≥60 years	5	(2-11)	7	(5-9)	0.86	(0.38-1.95)	0.72
Female sex	9	(5-14)	6	(4-8)	1.57	(0.78-3.13)	0.20
HIV infection	11	(6-17)	5	(3-8)	2.04	(1.05-4.00)	0.036
Stage 4	9	(6-12)	1	(0-3)	13.47	(1.83-98.9)	0.011
B symptoms	7	(4-11)	6	(4-9)	1.25	(0.65-2.40)	0.50
ECOG PS 2-4	11	(6-17)	5	(3-7)	2.31	(1.14-4.67)	0.019
Hemoglobin <11.5 g/dL	9	(6-14)	4	(2-7)	2.54	(1.26-5.11)	0.009
Albumin <3.5 g/dL	9	(5-13)	5	(3-8)	1.84	(0.92-3.66)	0.08
LDH > ULN	7	(5-10)	6	(2-11)	1.48	(0.62-3.55)	0.38
LDH >3x ULN	10	(6-14)	4	(3-7)	2.30	(1.17-4.50)	0.016
LDH >5x ULN	10	(6-16)	5	(3-8)	2.04	(1.05-3.97)	0.036
≥2 extranodal sites	9	(6-14)	4	(2-7)	2.13	(1.09-4.16)	0.027
Involvement at diagnosis:							
CNS	18	(11-26)	4	(2-6)	5.73	(2.98-11.0)	<0.001
Bone marrow	9	(6-14)	5	(3-7)	2.14	(1.09-4.17)	0.026
Intestine	5	(2-11)	7	(5-9)	0.74	(0.29-1.88)	0.52
Liver	8	(3-16)	6	(4-9)	1.30	(0.54-3.14)	0.55
Pancreas	9	(2-24)	6	(4-9)	1.31	(0.32-5.30)	0.70
Pleura/peritoneum	5	(2-11)	7	(5-9)	0.76	(0.27-2.15)	0.60
Kidney/adrenal	4	(1-12)	7	(5-9)	0.61	(0.15-2.58)	0.51
Testis[a]	26	(6-52)	5	(3-8)	5.93	(1.74-20.2)	0.004
Uterus/ovary[a]	8	(1-31)	9	(5-15)	0.97	(0.13-7.35)	0.97
Female breast[a]	8	(1-29)	9	(5-15)	0.90	(0.11-7.22)	0.92

LYMPHOMA AND PLWH: BURKITT LYMPHOMA

Outcomes of Burkitt lymphoma with central nervous system involvement: evidence from a large multicenter cohort study

Zayac A.S. Haematologica 2021

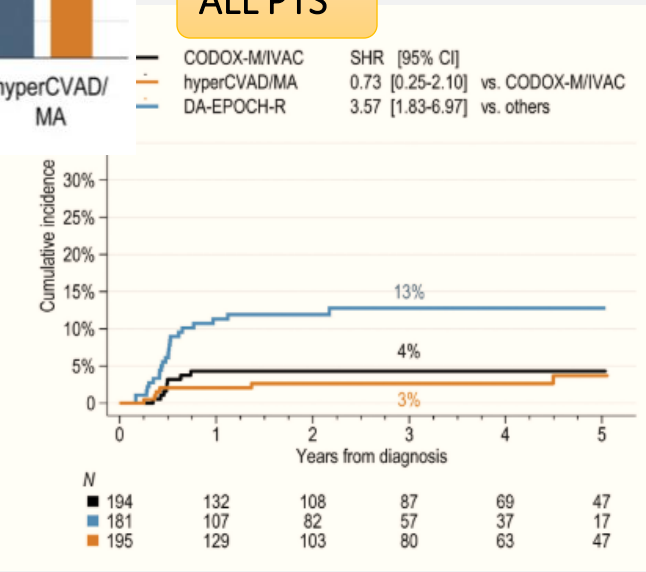
CNS recurrence: 6%



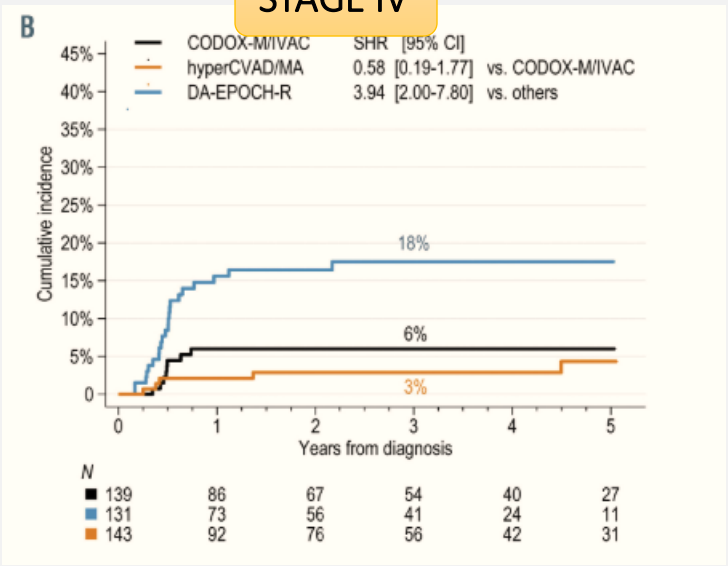
Underdiagnosis of occult leptomeningeal disease might result in suboptimal intrathecal treatment WITH DA-EPOCH!

intensive intrathecal regimen (starting with twice-weekly administration) in cases with CSF involvement

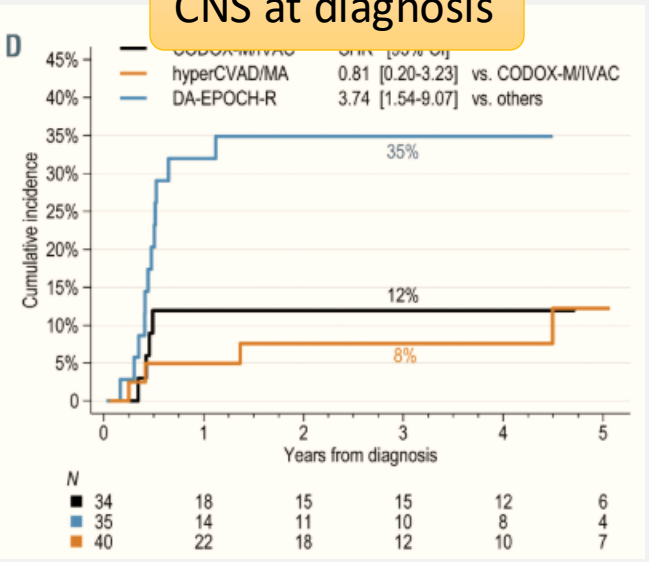
ALL PTS



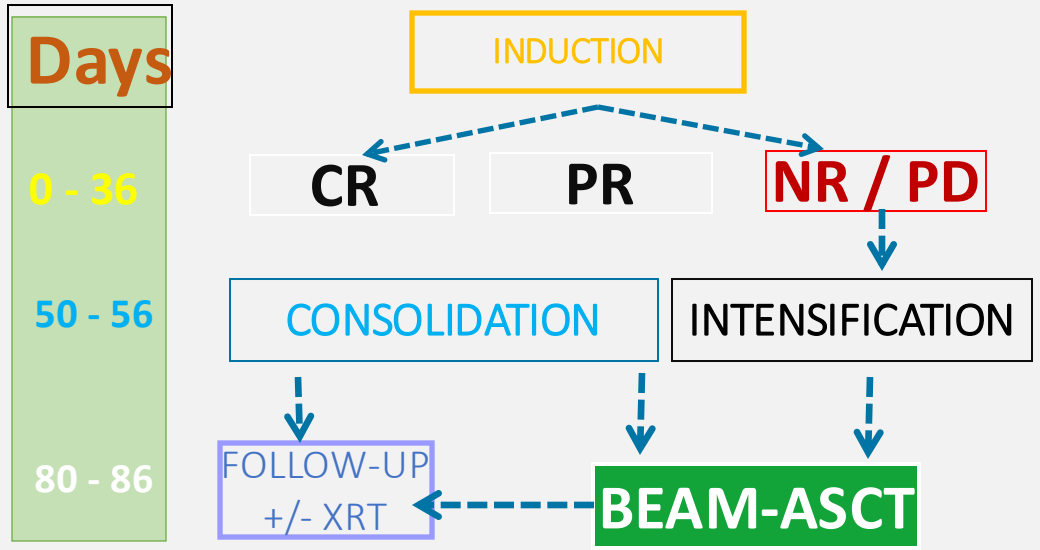
STAGE IV



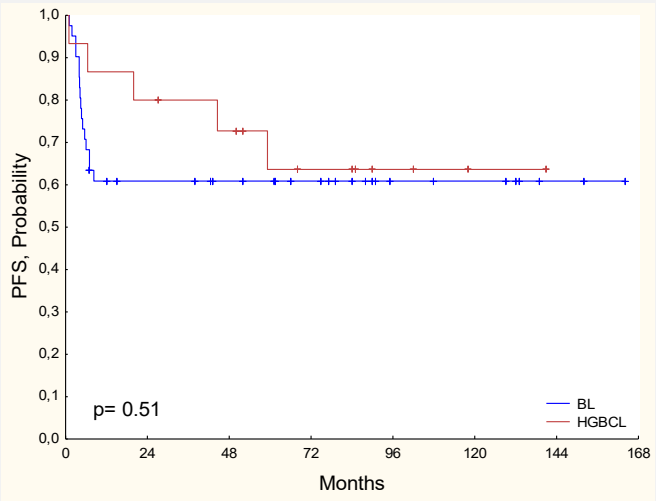
CNS at diagnosis

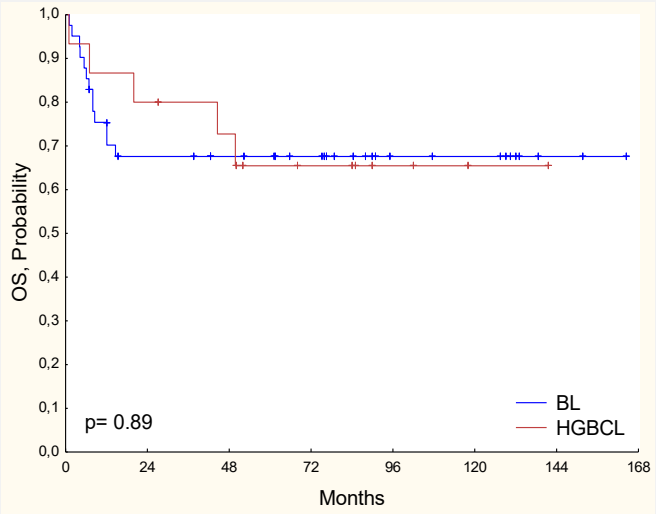


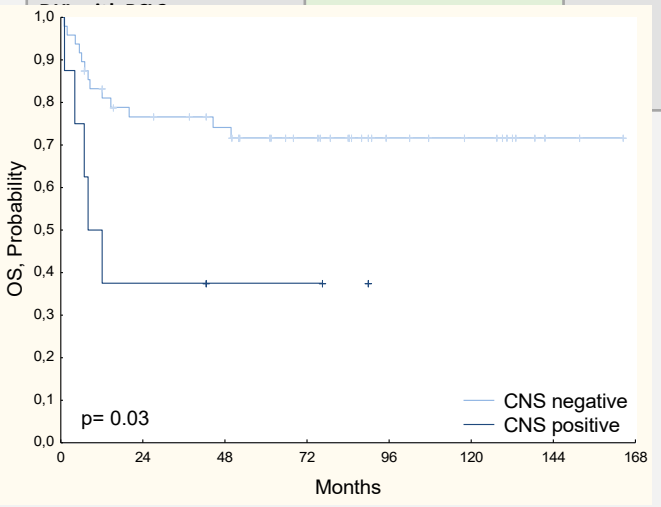
LYMPHOMA AND PLWH: BURKITT LYMPHOMA, Carmen protocol



	BL (n=41)	HGBCL (n=15)
Median age (range)	42 (27-66)	47 (26-63)
Gender - males	38 (93%)	12 (80%)
ECOG-PS >1	18 (44%)	8 (53%)
HBsAg or HBcAb positivity	10 (24%)	7 (47%)
HCV sieropositivity	5 (12%)	1 (7%)
B symptoms	16 (39%)	4 (27%)
IPI ≥2	36 (88%)	14 (93%)
High LDH serum level	36 (88%)	14 (93%)
Stage (Ann Arbor) III-IV	38 (93%)	14 (93%)
Extranodal disease	36 (88%)	15 (100%)
CNS involvement	7 (17%)	1 (7%)
Bone marrow infiltration	10 (24%)	4 (27%)
Bulky disease	18 (44%)	8 (53%)
Single Hit*	-	9 (60%)
Double Hit (DHL)**	-	1(7%) 0 1 (7%)

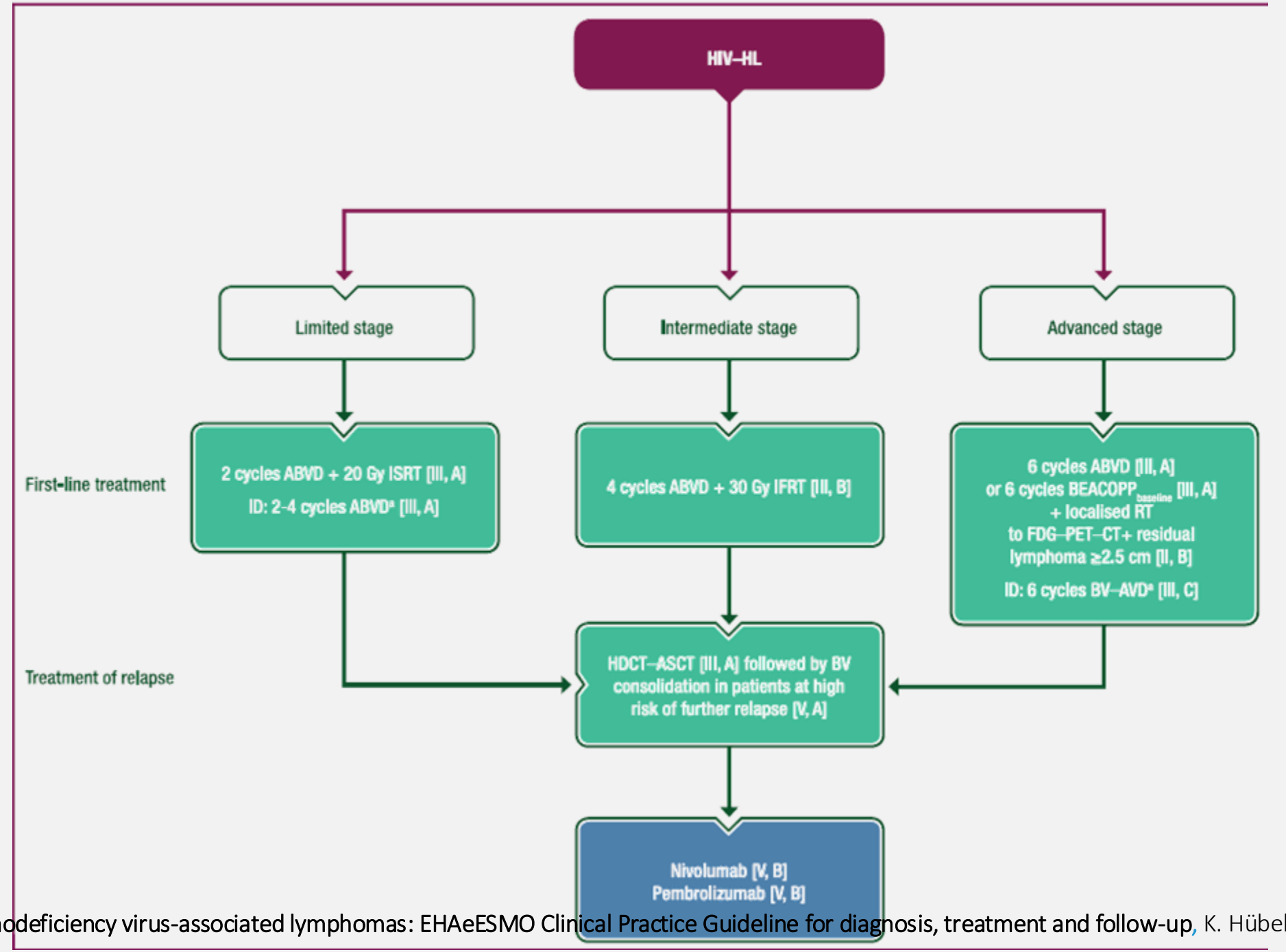






Courtesy of Prof Ferreri

HL



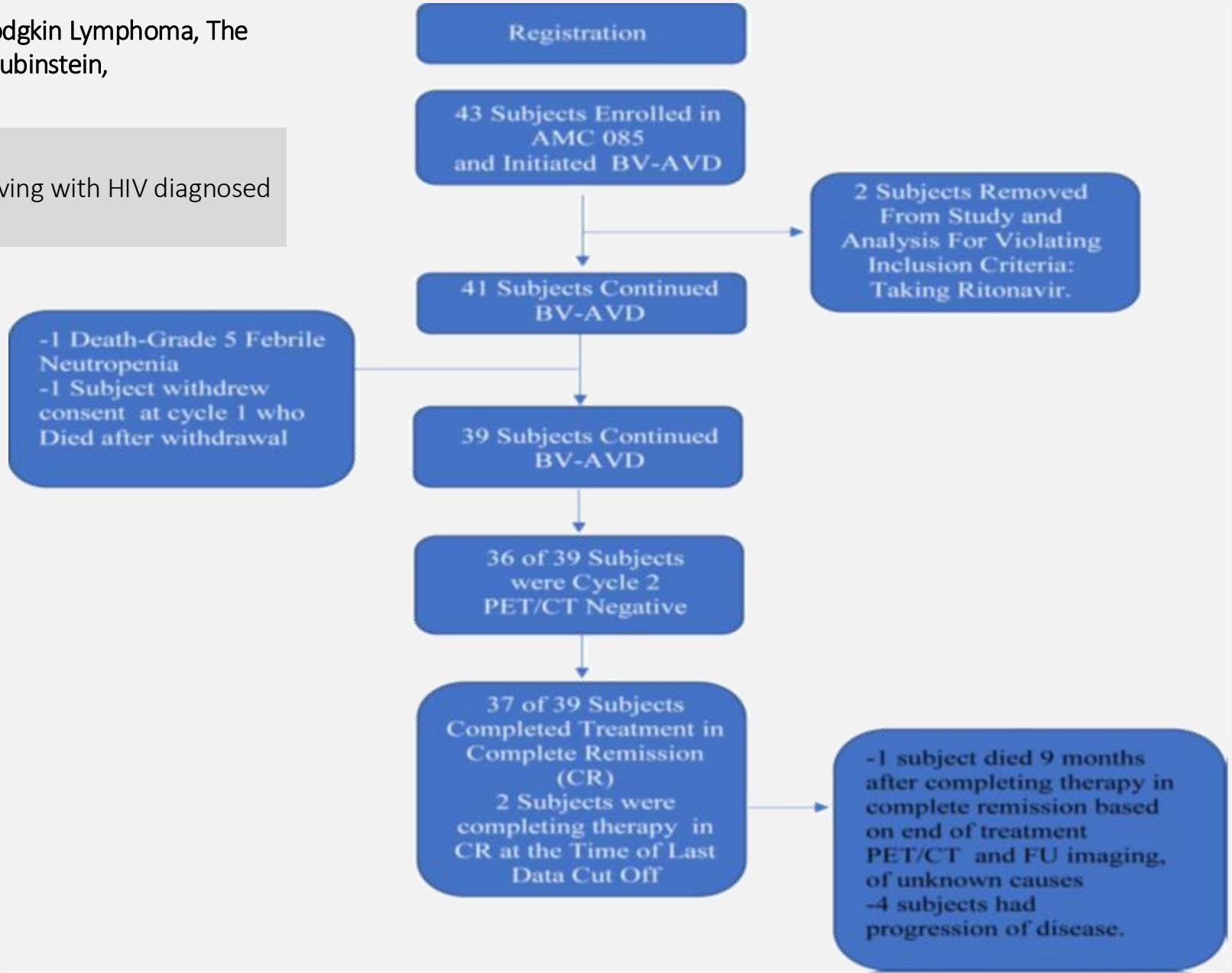
Human immunodeficiency virus-associated lymphomas: EHAeESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, K. Hübel, 2024

LYMPHOMA AND PLWH: BURNING ISSUE WITH HL : Brentuximab Vedotin

Brentuximab Vedotin with AVD for Stage II-IV HIV-Related Hodgkin Lymphoma, The Phase 2 Portion of AMC 085, a Multicenter Phase I/II Trial . Rubinstein,
Lancet hematol 2023

AIM:
to understand the activity and safety of BV-AVD in people living with HIV diagnosed with Hodgkin lymphom

Eligible patients
≥ 18 years of age,
untreated stage II-IV HIV-associated classical HL
KPS> 30%,
CD4 + T-cell count ≥ 50 cells/µl,
were required to take ART,
were not on strong CYP3A4/P-glycoprotein inhibitors



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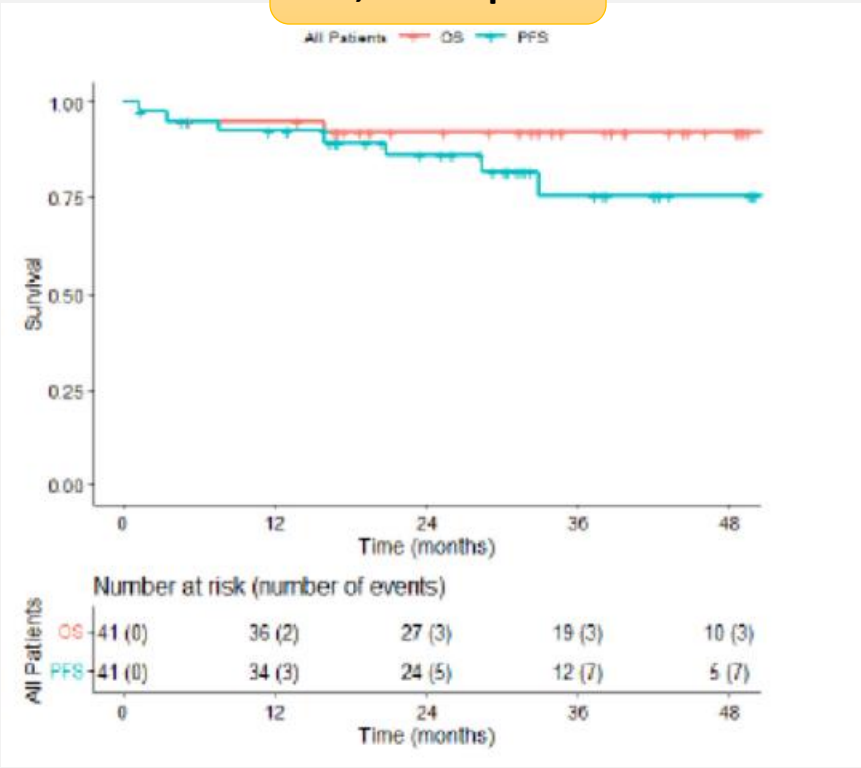
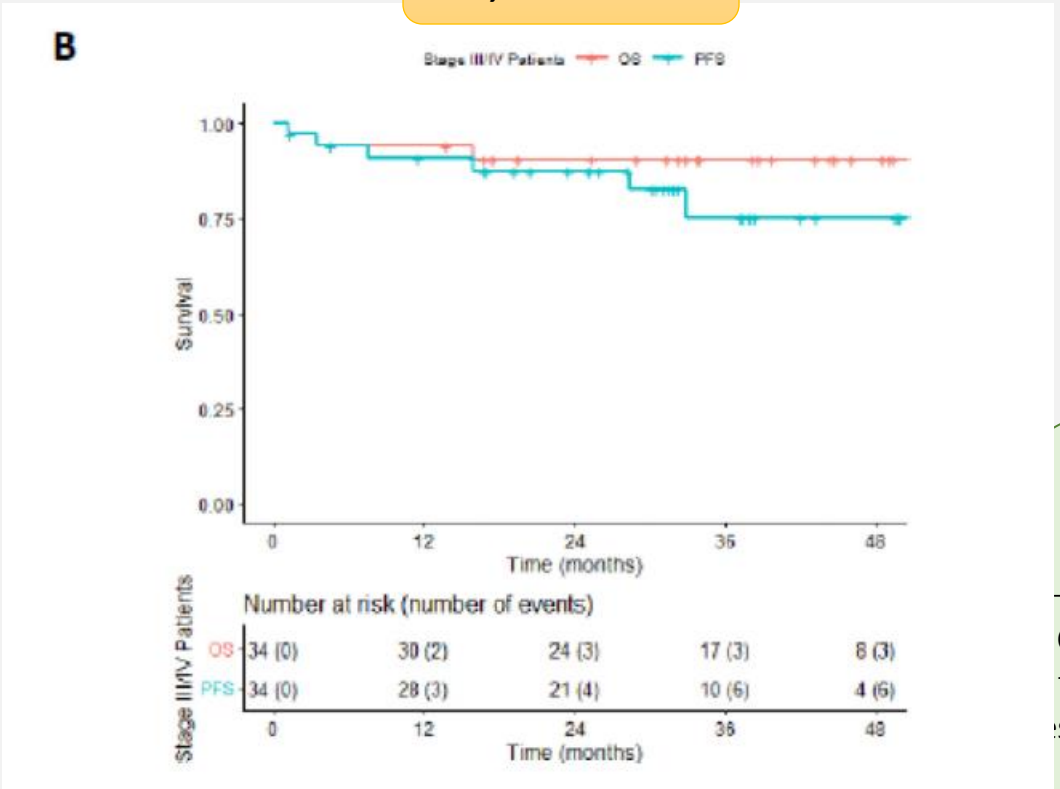
PFS, OS all pts



PFS, OS III-IV



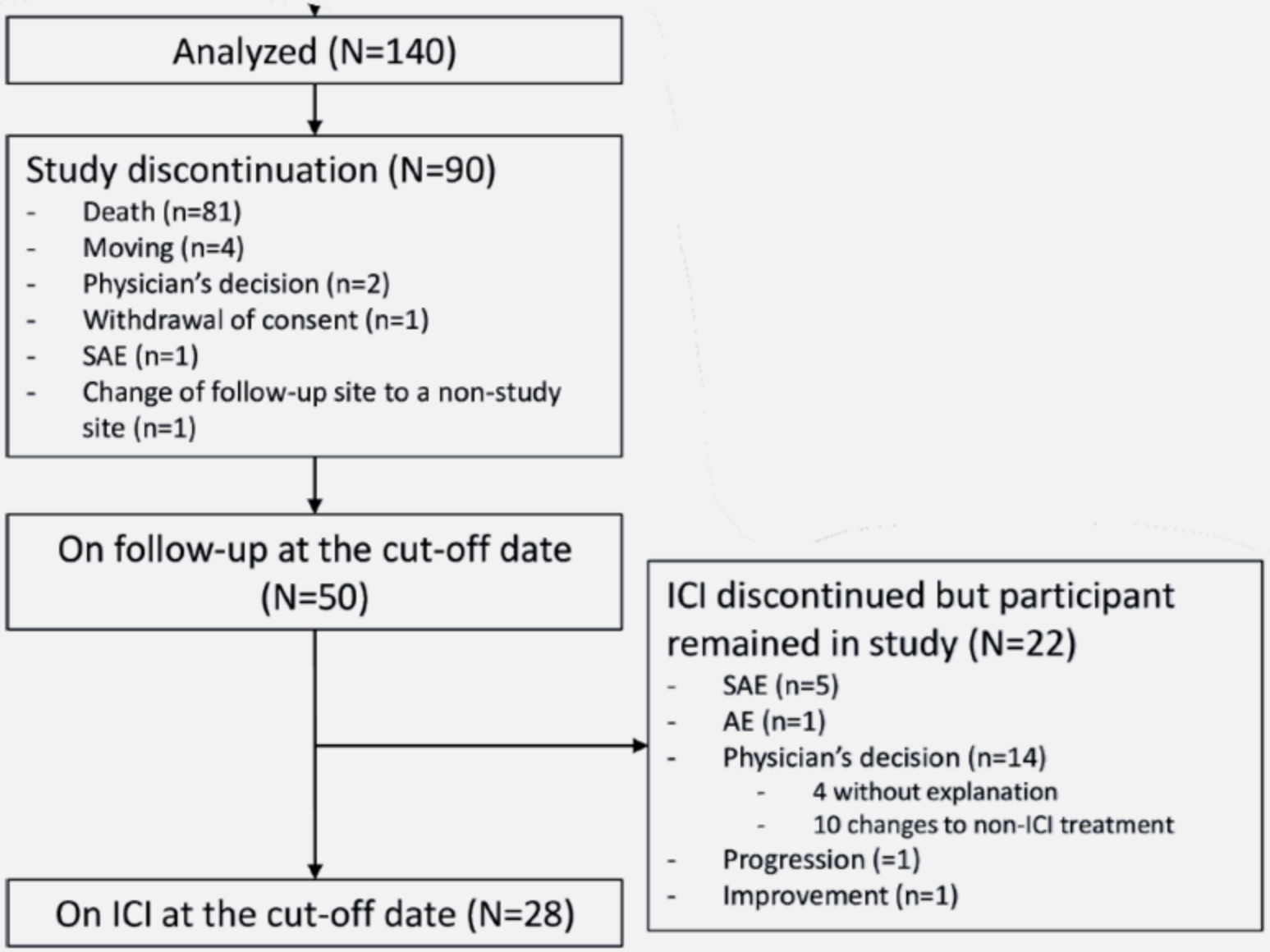
More pronounced neutropenia
-AVD induces an increase CD4 and CD8+ T-cells, in the setting of HIV and spite the concurrent use of lympho-toxic chemotherapy, AVD.

LYMPHOMA AND PLWH: BURNING ISSUE WITH HL: ICI

Safety and tolerability of immune checkpoint inhibitors in people with HIV infection and cancer: insights from the national prospective real-world OncoVIHAC ANRS CO24 cohort study. Assoumou L, *et al. J Immunother Cancer* 2024

Prospective, multicenter
WHO
participants ≥18 years of age,
with HIV infection and a
histologically proven cancer,
naïve for ICI therapy
any CD4 lymphocytes count or HIV VL.

Primary outcome: the incidence of the first occurrence of grade ≥3 irAEs during the study period



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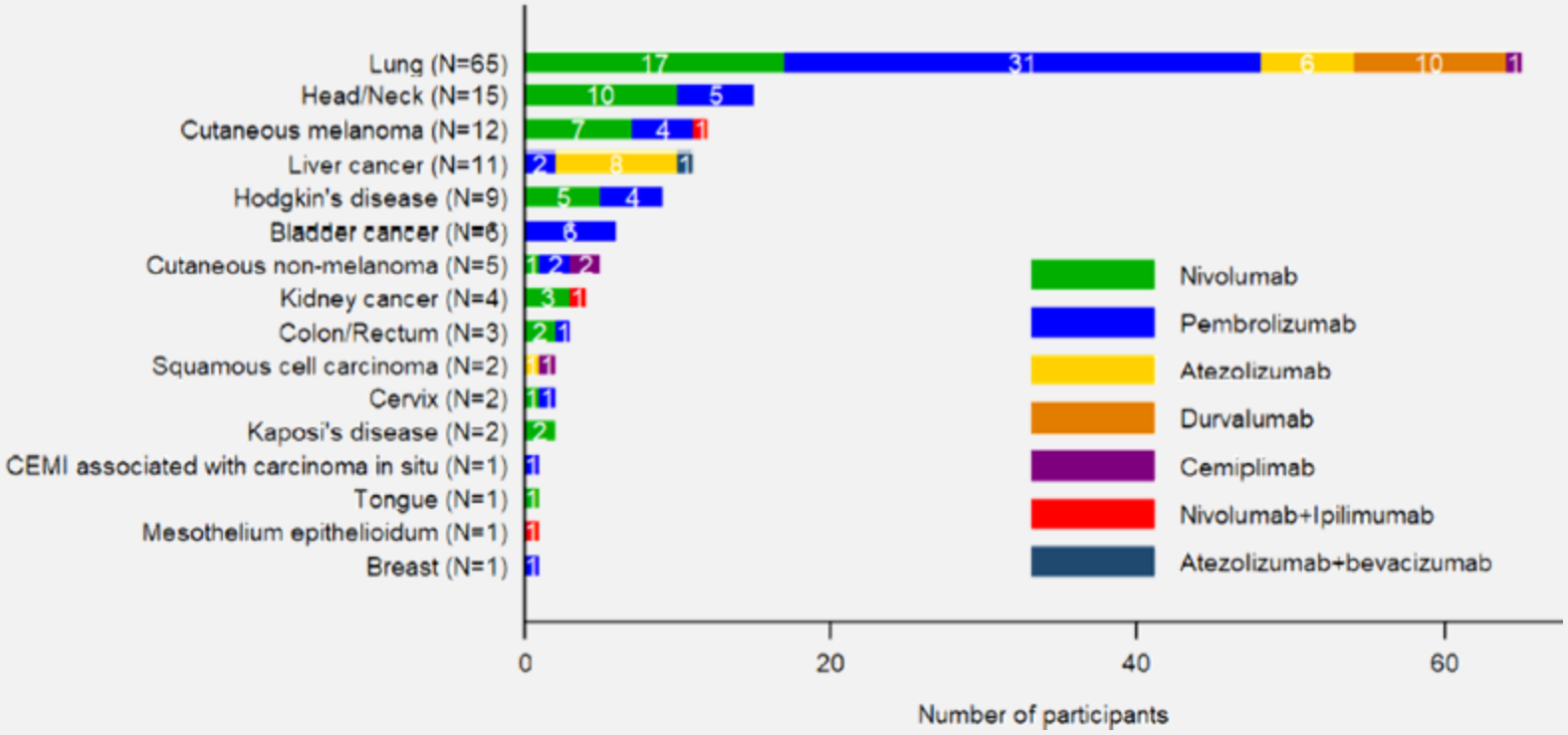

severe irAEs between 13.8% at 6 months,
15.0% at 12 months
18.7% at 18 months.

majority of events were
reversible after systemic glucocorticoid use, and then safely managed.

Lower CD4 cell count and longer duration since HIV diagnosis played a role in the incidence of serious treatment-related toxicity.

viral infections, such as CMV could play a role in remodeling the tumor's immune microenvironment, altering the host immune response and thus favoring the development of irAEs

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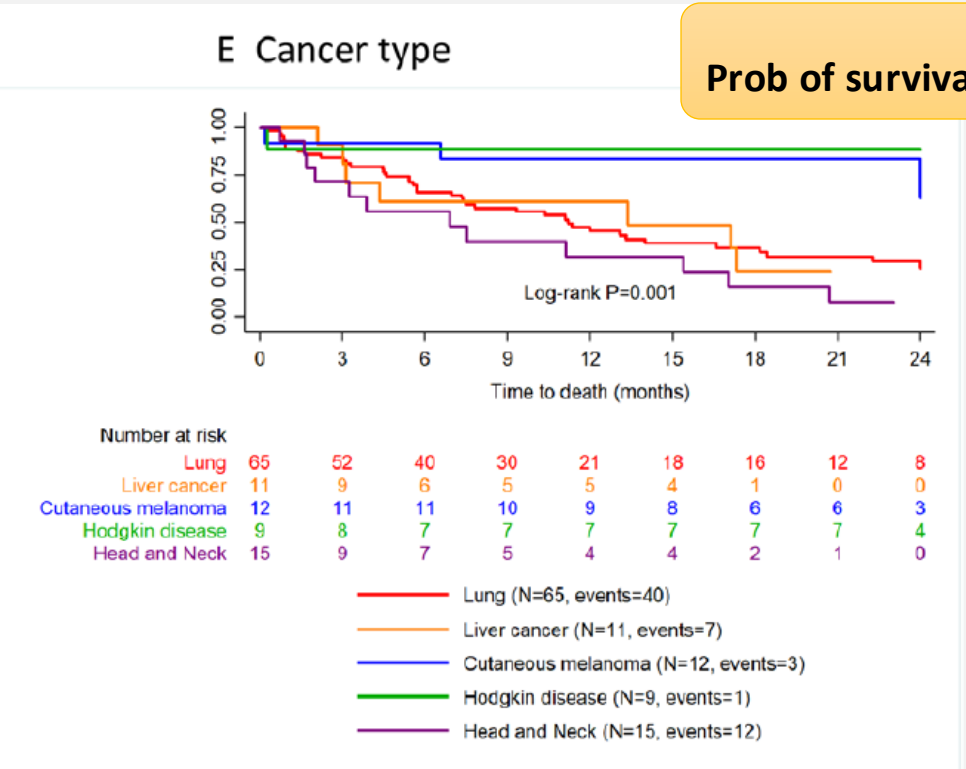

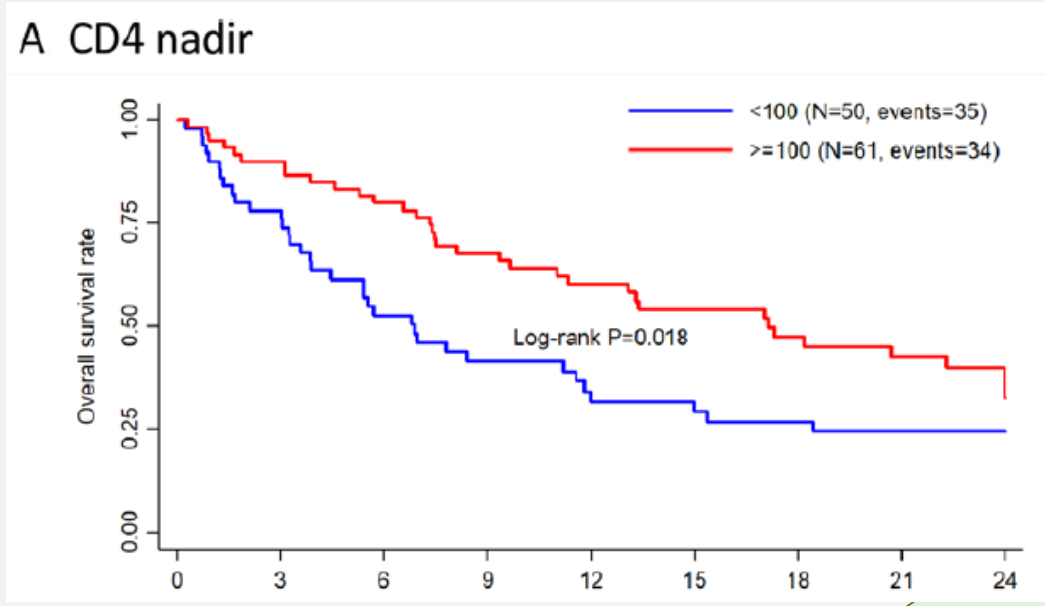

Pay attention to TB HBV/HCV !!

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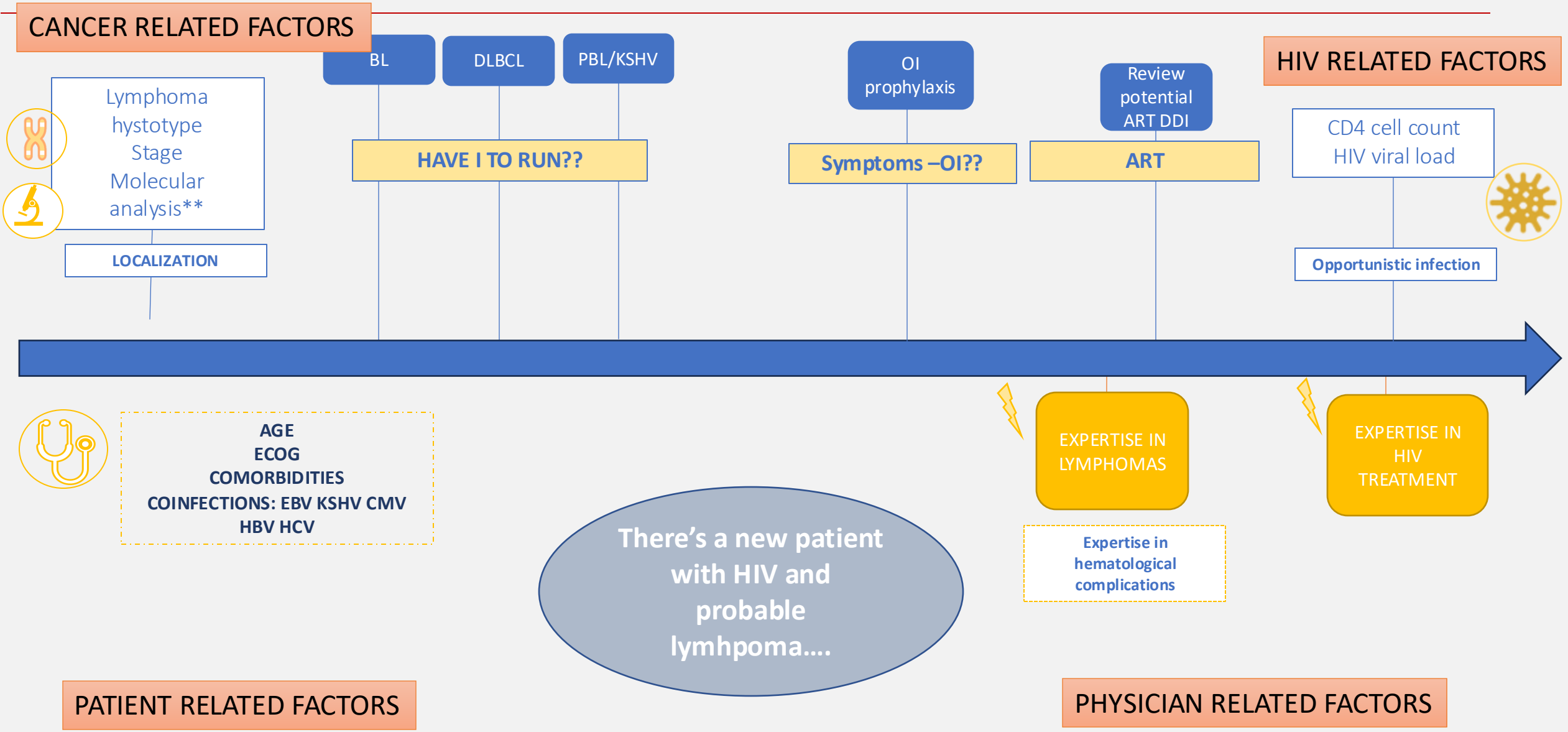
LYMPHOMA AND PLWH: «everything» THE HEMATOLOGIST NEEDS TO KNOW



STAPLES:

1) We're not alone!

2) The power of ART

3) Pay attention to CD4 but do not hesitate to cure

4) Look for clinical trialS!

5) Offer standard, full dose cancer therapy as appropriate for cancer type

6) Always check if that specific cancer therapy raise concern for OI or infections