



LYMPHOMA UPDATES: CLINICAL PRACTICE APPLICATIONS

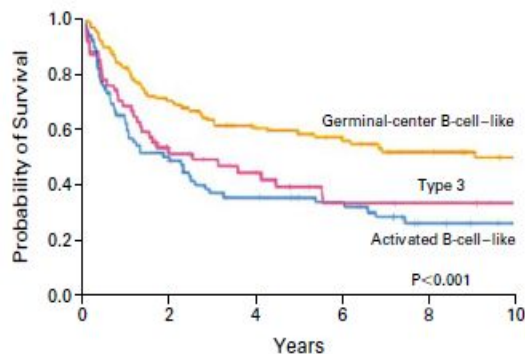
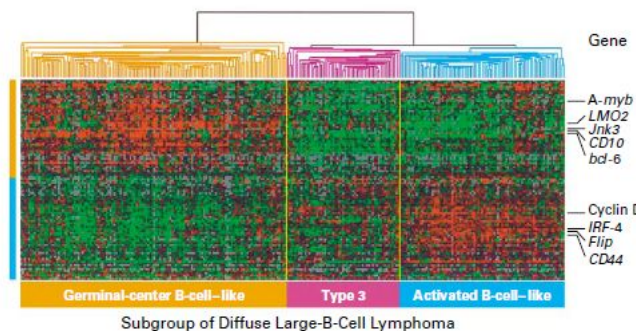
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DISCLOSURES

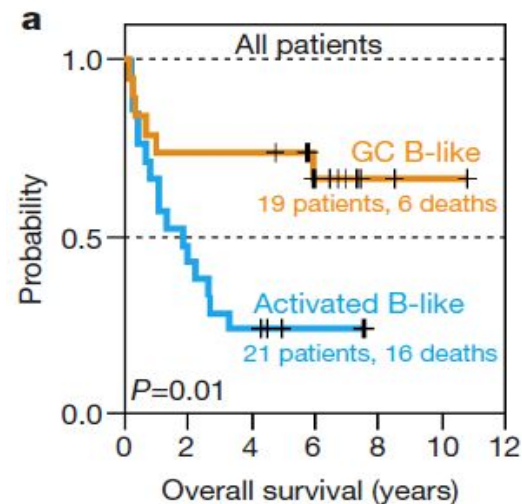
- Consulting: Kite/Gilead, Novartis, BMS, GenMab, Genentech, AstraZeneca, Autolus, Allogene
- Research support: Genmab, Janssen
- Independent review committee: Atara/Pierre Fabre

- Diagnostics: Is Hans algorithm still useful?
- CNS prophylaxis in LBCL: Does it still matter?
- Bridging therapy prior to CAR-T: To Bite or Not to Bite?

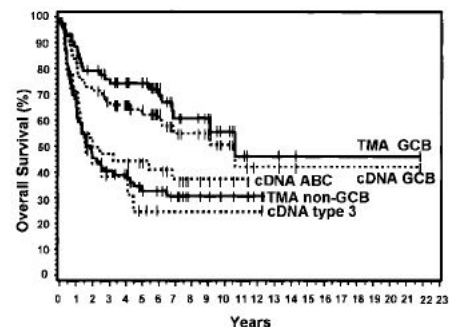
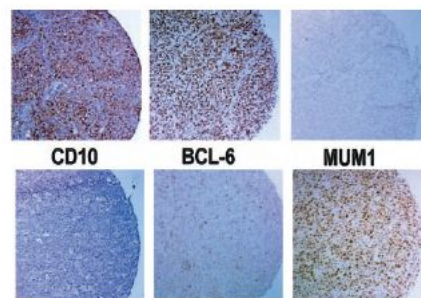
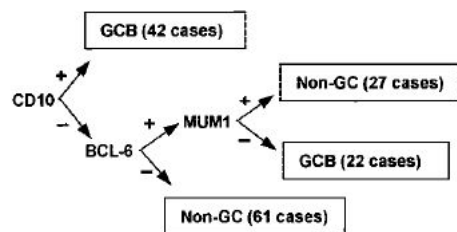
The Importance Of COO In DLBCL: GEP vs IHC



No. AT RISK						
Germinal-center B-cell-like	115	81	60	46	32	19
Type 3	52	24	18	10	8	5
Activated B-cell-like	73	35	23	19	8	5



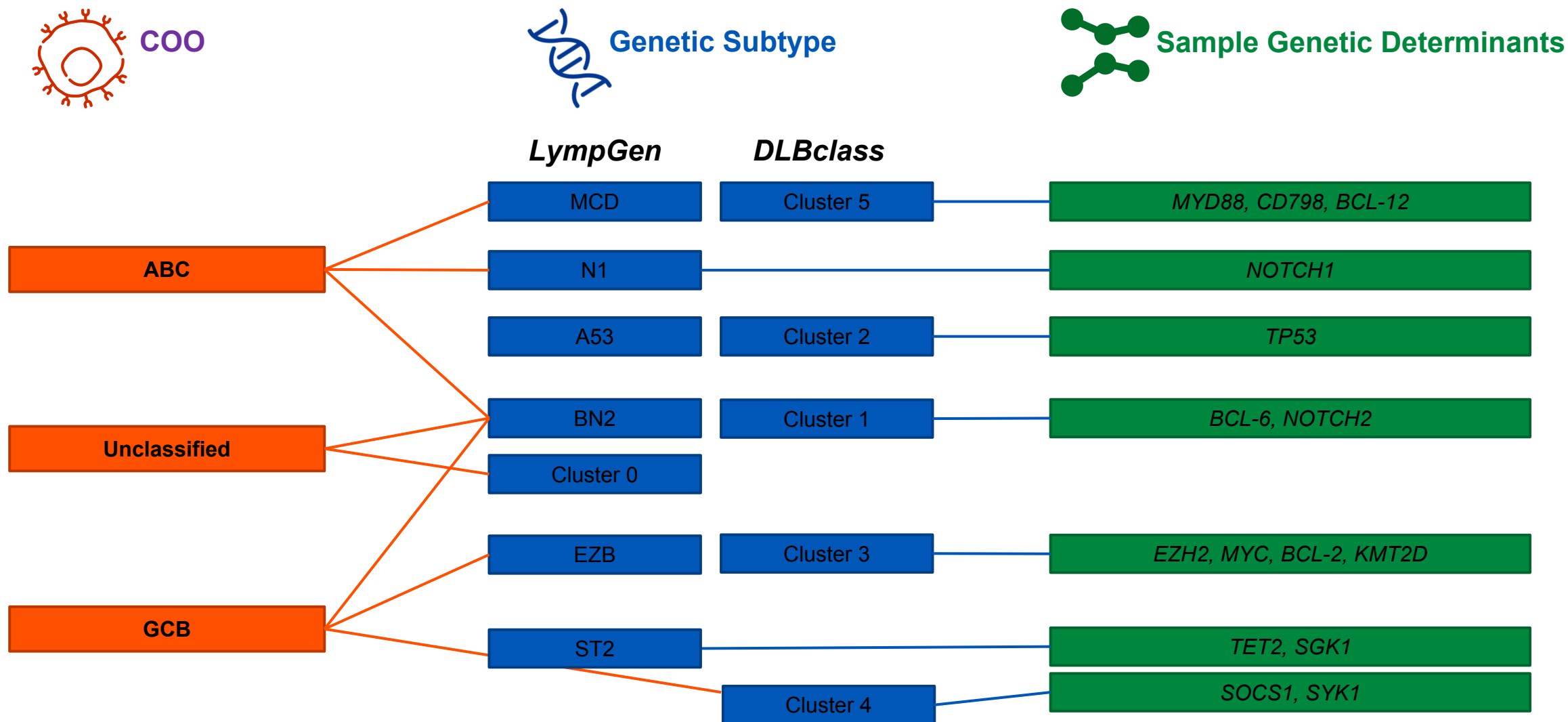
GEP



IHC

Concordance between IHC and GEP was reported 70-80%

THE SPECTRUM OF DLBCL SUBTYPES AND IMPORTANCE OF COO^{1,2}



1. Danilov A et al. *The Oncologist*. 2022;27:57-66. 2. Alig SF et al. *Histopathology*. 2025;86:94-105.

HANS IHC RELIABLY IDENTIFIES COO IN DLBCL-NOS AND IS COMPARABLE TO GENE EXPRESSION PROFILING¹

ENHANSEMENT Meta-Analysis · 19 Studies · 2,247 DLBCL-NOS Tumors

Hans IHC accuracy

90%

95% CrI: 87%-93%

GEP accuracy

95%

95% CrI: 93%-96%

Accuracy gap (Hans–GEP)

4.5%

95% CrI: 1%-8%

*Within the 10%
noninferiority
margin*

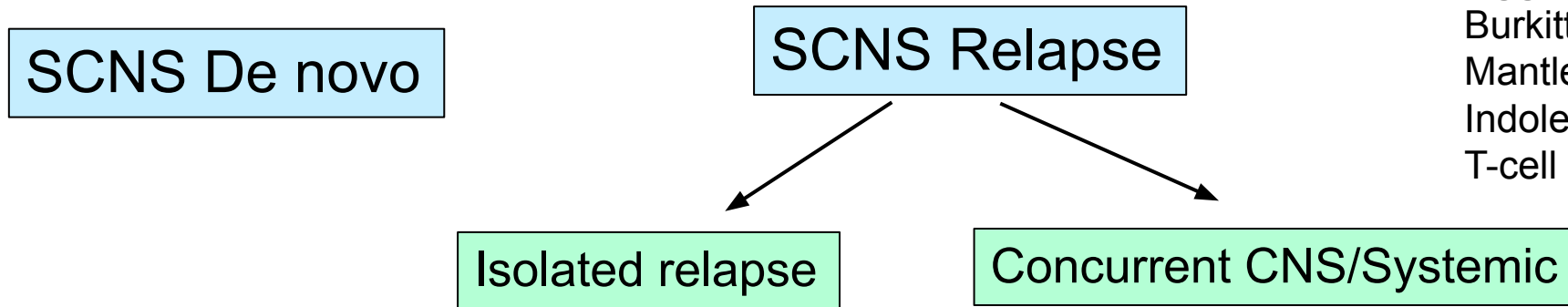
- Hans IHC = broad availability, FFPE compatibility, and fast turnaround
- Reliable method for COO classification—particularly where GEP access is limited

The Prognosis of Secondary CNS Lymphomas is Poor

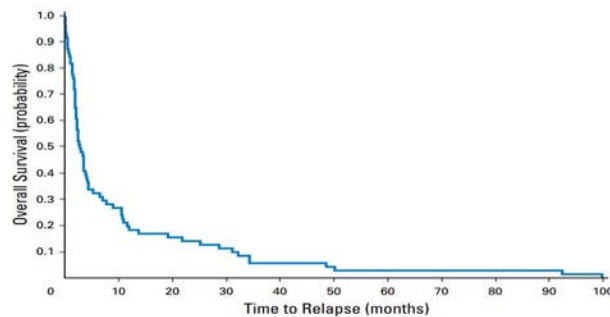
Histology

Aggressive B-cell lymphomas

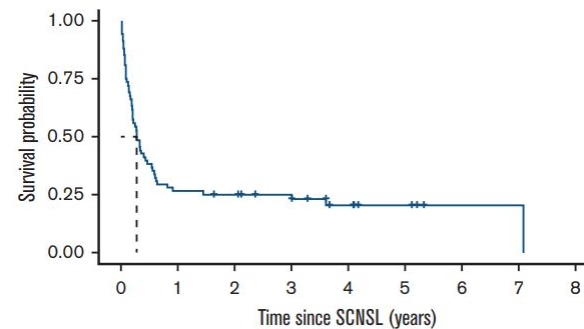
Burkitt's lymphoma
Mantle cell lymphomas
Indolent lymphomas
T-cell lymphomas



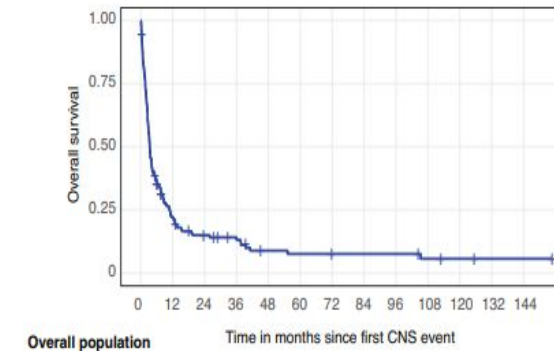
German/British Columbia



Danish/LYFO



LYSA/GLA (German)



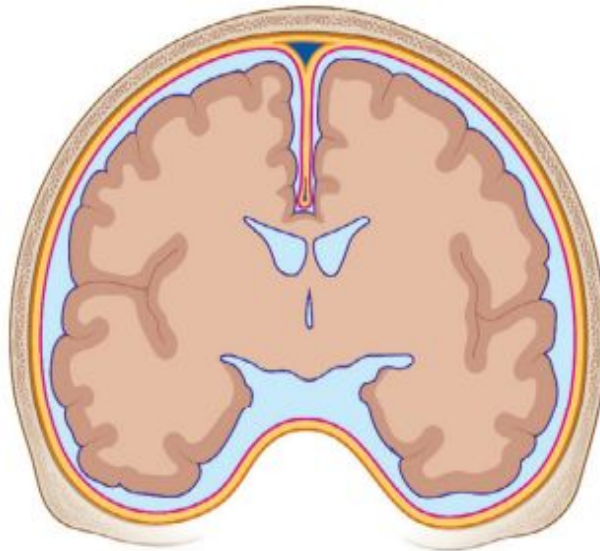
Schmitz N et Al. J Clin Oncol 2016, Tolley et al. Blood Adv 2025, Frontzek et al. Leukemia 2024

DOES CNS PROPHYLAXIS WORK? NO



Bobillo et al (N=585)
HR-EN, DHL
CNS-IPI ≥ 4

	Relapse risk	
{	None	7.5% (HR .76[0.35-.1,5])
	IT-MTX	5.5%
	HD-MTX	5%
	Relapse reduction at 1-y but not a 5-y	



CNS-directed prophylaxis

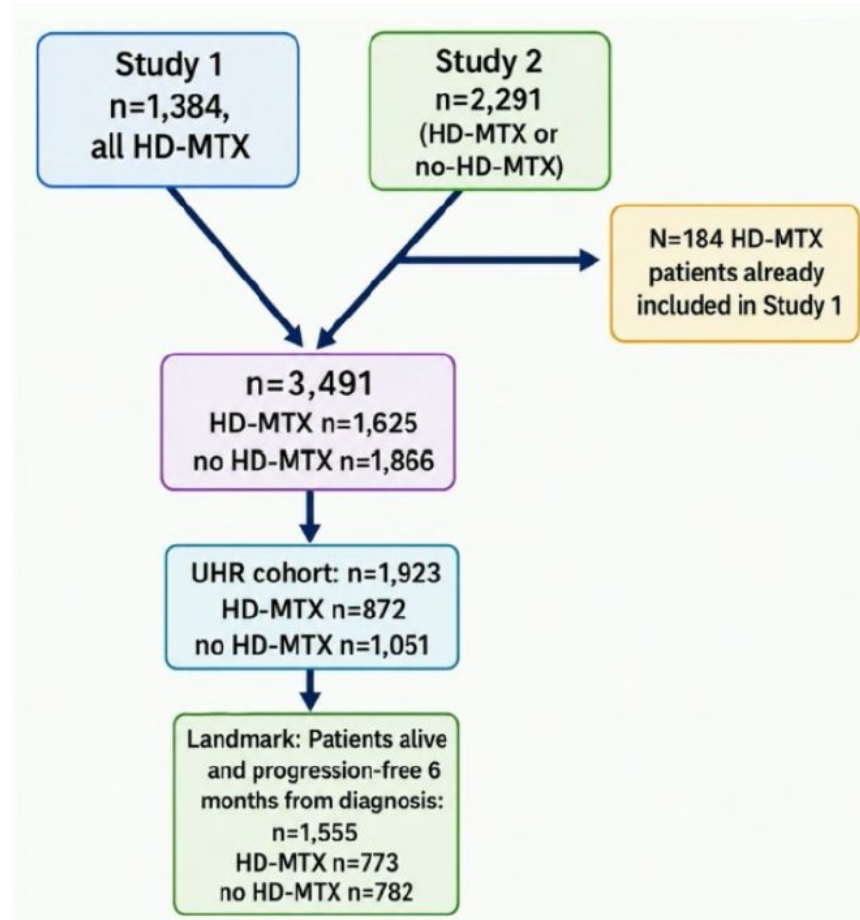
Puckrin et al (N= 906)
CNS-IPI ≥ 4 , DHL,HR-EN
>1 EN, PS> 1, LDH

	Relapse risk	
No HD-MTX	12.2%	(p= NS)
HD-MTX	11.2.%	

Lewis et al (N= 2418)
CNS IPI ≥ 4 , HR-EN, DHL
Testicular/breast

	Relapse risk	
None	9.1%	(p= 0.43)
HD-MTX+/- IT	8.4%	

HD MTX Does Not Reduce CNS Relapse In Ultra High Risk Disease: International Study of 1923 pts

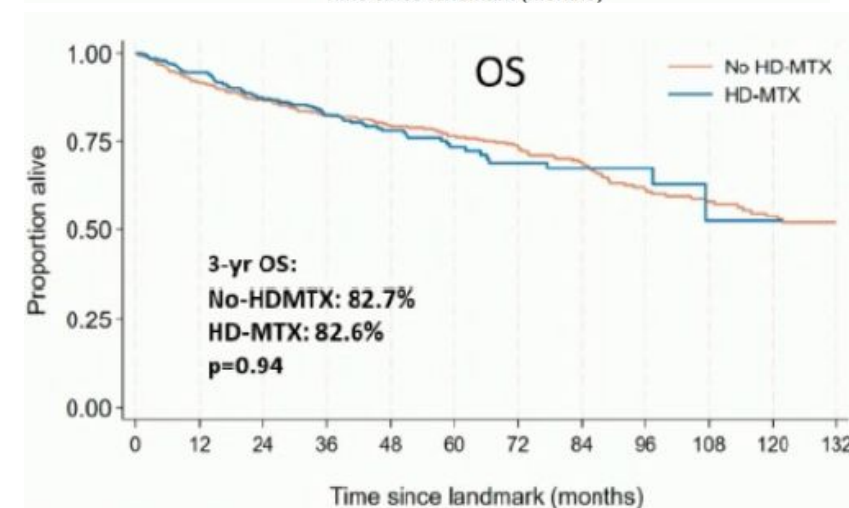
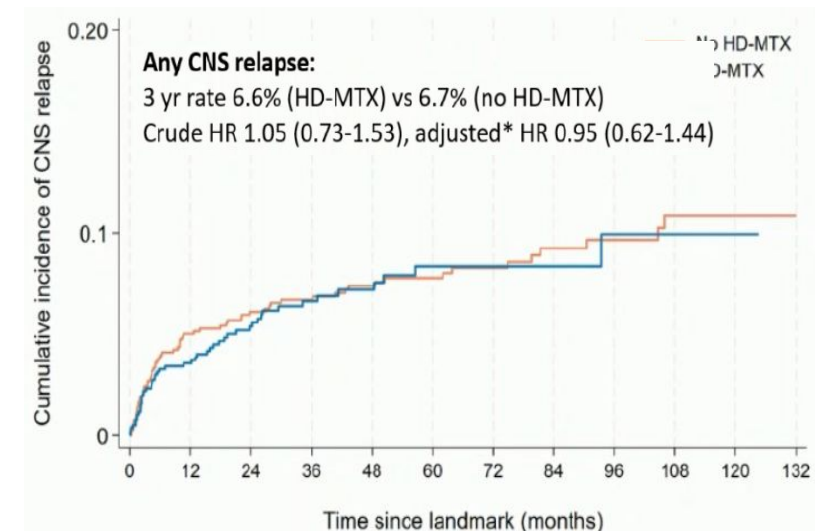
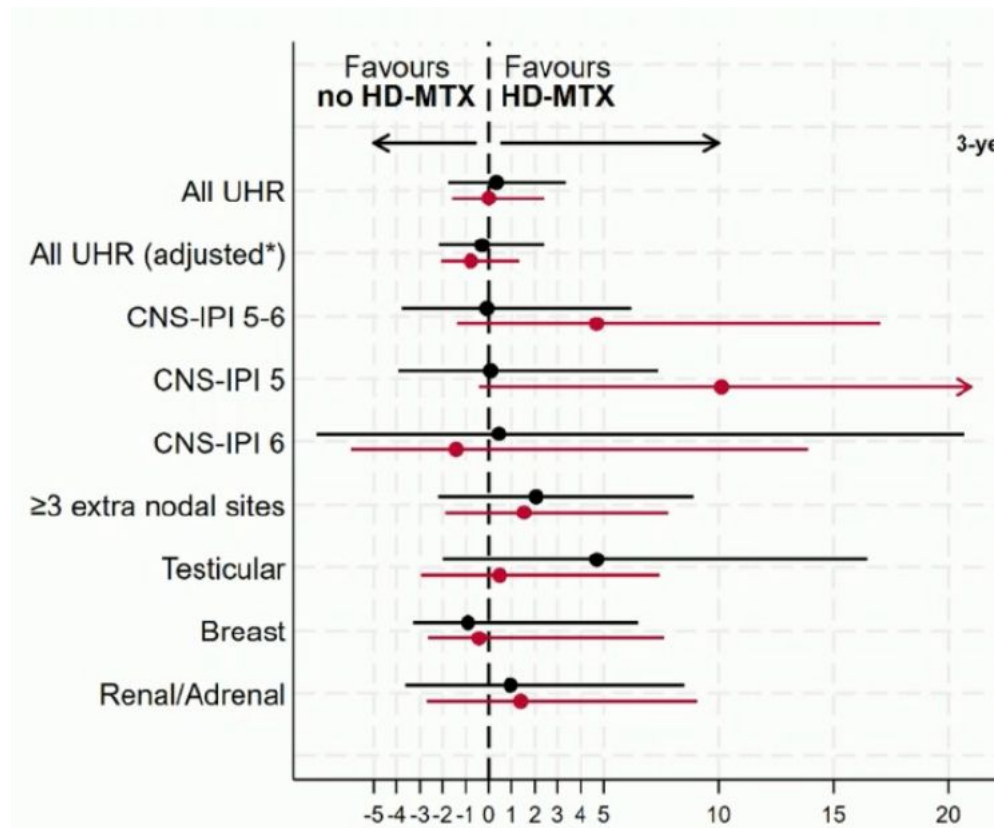


Definition of ultra high risk

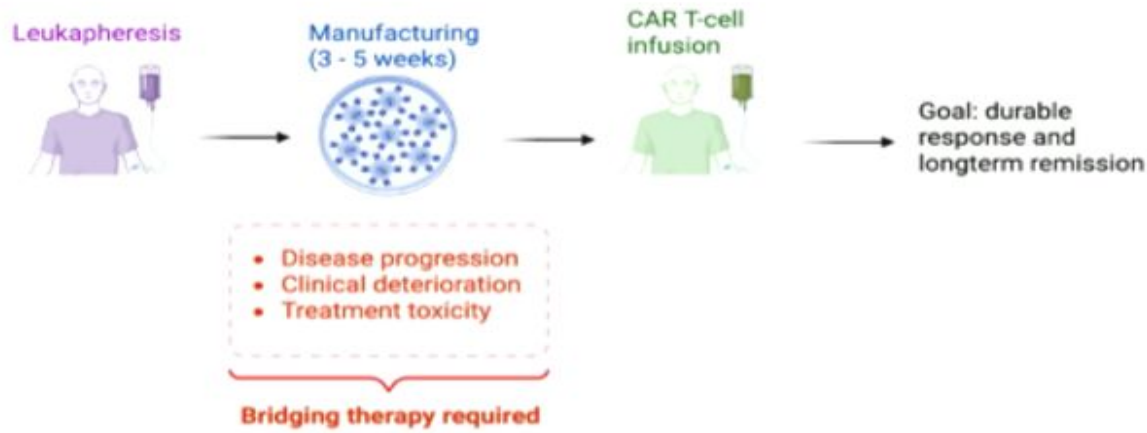
- CNS-IPI 5-6
- ≥ 3 extranodal sites
- Testicular, adrenal, breast involvement

Landmark analysis: 6 months progression free or relapse free

HD-MTX as CNS Prophylaxis For UHR LBCL: No CNS relapse benefit, No OS benefit



Analysis Of Bridging Therapy Pre-CART: BiAbs vs Conventional Therapy



German multicenter analysis of bridging therapy pre CART

BisCAR (n=67): Glofi, EpcO, Glofi-GemOx
ConCAR (n= 45): conventional BT or no BT (Pola-BR 29%, GDP-R, R-DHAP)

BisCAR:

- 52% glofitamab
- 36% Glo-GemOx
- 12% epcoritamab

Median washout time:
24 days

ConCAR:

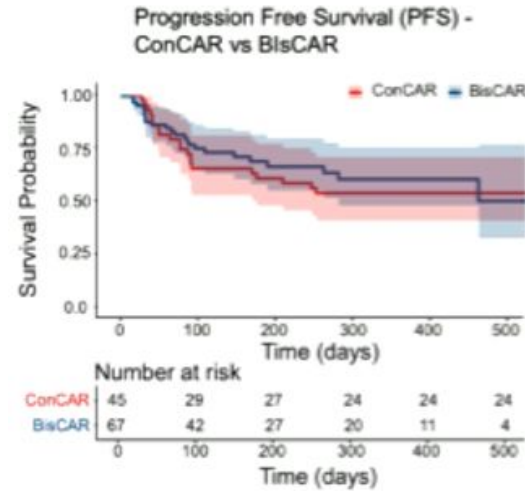
- 29% Pola-BR
- 20% None
- 18% R-GDP
- 13% Tafasitamab/Lenalidomide
- 9% GemOx
- 2% Ibrutinib
- 2% Ibrutinib, Venetoclax
- 2% Pola-R-ICE and R-DHAP
- 2% R-DHAP
- 2% R-ICE

BiAbs As Bridging Therapy (BT) Prior To CART

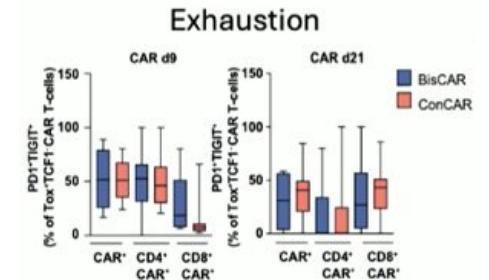
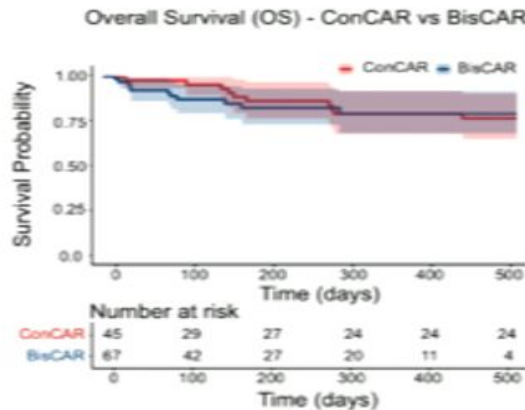
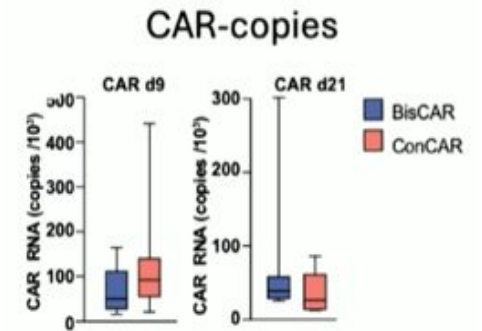
BiAbs as BT did not increase CRS or ICANS

		CRS		ICANS	
		Gr. 1-2	Gr. 3-4	Gr. 1-2	Gr. 3-4
BisCAR	Total (n=67)	47 (70%)	1 (2%)	15 (22%)	3 (4%)
	Axi-cel (22)	21 (95%)	1 (5%)	10 (45%)	1 (5%)
	Liso-cel (41)	23 (56%)	0	4 (10%)	2 (5%)
	Tisa-cel (2)	2 (100%)	0	1 (50%)	0
	MBCART2019 (2)	1 (50%)	0	0	0
ConCAR	Total (n=45)	30 (67%)	3 (7%)	7 (16%)	6 (13%)
	Axi-cel (29)	24 (83%)	1 (3%)	6 (21%)	6 (21%)
	Liso-cel (16)	6 (37%)	2 (13%)	1 (6%)	0

BiAbs as BT did not affect CAR-T efficacy



BiAbs as BT did not affect CAR-T expansion Or T-cell stemness



CONCLUSIONS

- Hans algorithm may still be utilized in real practice for COO determination in DLBCL
- CNS prophylaxis with HD-MTX in high risk LBCL remains controversial
- BiAbs as bridging therapy for CAR-T does not seem to affect outcomes. Consider CD20 loss (80%) with prior BiAbs exposure