



Multidisciplinary Approaches to Cancer Symposium

Hematologic Tumor Board

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Disclosures

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- *Consultant for Abbvie, ADC Therapeutics, Fate Therapeutics, Genmab, Iowa Oncology Society & Regeneron; and On the Speaker's Bureau for Beigene, Genmab, & Peerview.*
- *Consultant for Kite; Previously served on the Speakers Bureau for Janssen*

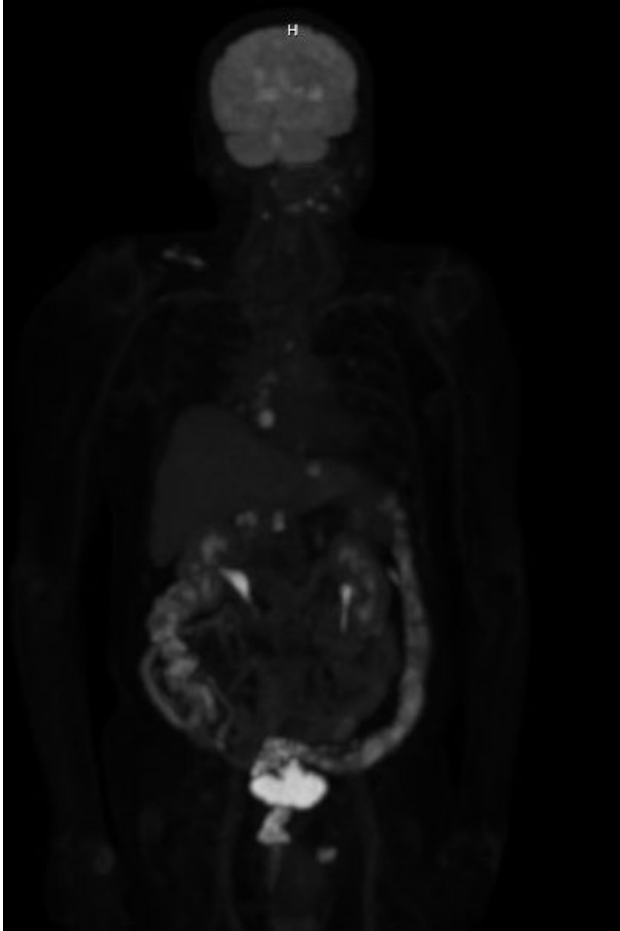
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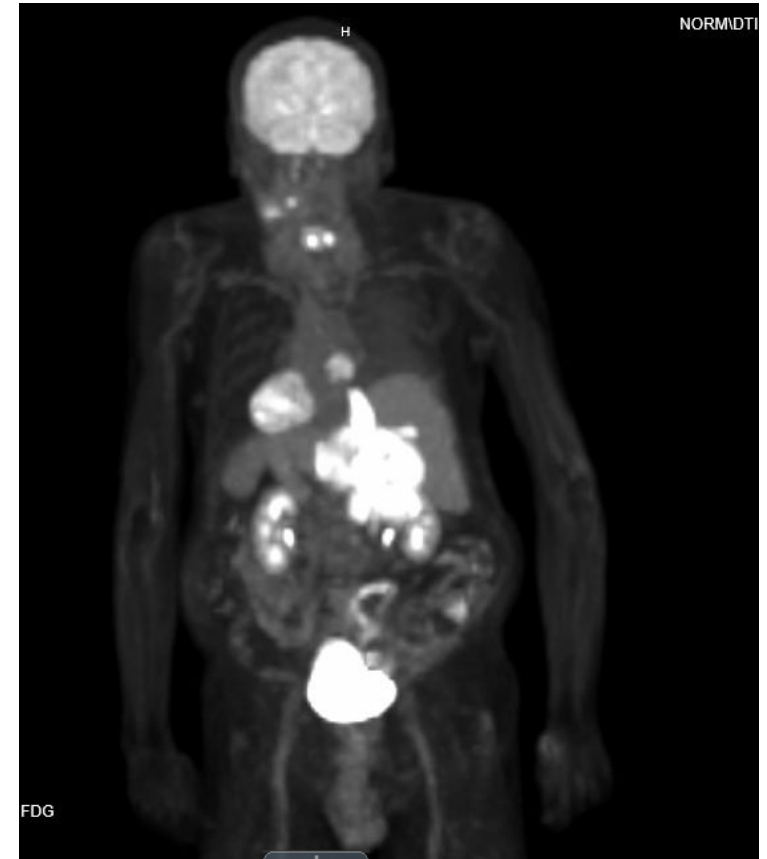
85 year old with lymphoma



Healthy retired engineer, with oral malignancy and new cutaneous lesion over the right clavicle – biopsy cutaneous follicular lymphoma . Multiple osseous lesions – 3-4 , SUV 3-4 , BMBX neg, observation – asymptomatic.



In 3 months - Focus on oral malignancy therapy
Progression to new lesions – but asymptomatic



Transformed DLBCL in elderly

Biopsy of retrocrural. Retroperitoneal mass - Transformed double hit DLBCL- biopsy from PET Avid SUV 16 lesion

Oral malignancy in remission

ECOG PS:1, LDH – 400 , patient interested in therapy

How do we approach therapy in this elderly DLBCL ?



Starting DLBCL Therapy in Older Adults: The Essentials



01

Diagnosis and workup

- Biopsy: COO, MYC/BCL2 FISH, EBV
- PET-CT, echo/MUGA, HBV serologies
- IPI, NCCN-IPI, CNS-IPI



02

Defining fitness

- G8 screen → CGA or FIL simplified GA
- Classify fit, unfit, or frail
- No dose reduction on age alone



03

Frontline regimen

- Fit, IPI 2–5: Pola-R-CHP
- Fit, low risk: R-CHOP ×4–6
- >80 or unfit: R-mini-CHOP
- Cardiac disease: R-GCVP



04

Response and relapse

- End-of-treatment PET-CT (Deauville)
- Refractory or <12 mo: CAR-T (liso-cel)
- Late: salvage → ASCT
- Non-cellular: Glofit-GemOx, Pola-BR



05

Supportive care

- Steroid pre-phase; G-CSF for age ≥65
- HBV, PJP, VZV prophylaxis; vaccines
- Goals-of-care talk before cycle 1

Frontline Trials for the Elderly DLBCL

Trial	Design	Population	Regimen	Efficacy	Safety / caveats
POLARIX <i>Tilly, NEJM 2022</i>	Phase 3 RCT N = 879	Age 18–80, IPI 2–5; fit	Pola-R-CHP ×6 vs R-CHOP ×6 (+ R ×2)	2-yr PFS 76.7% vs 70.2% HR 0.73	Grade ≥3 AEs similar to R-CHOP
LYSA R-mini-CHOP <i>Peyrade, Lancet Oncol 2011</i>	Phase 2 N = 150	Age >80 Median age 83	R-mini-CHOP ×6	CR/CRu ~63% 2-yr OS 59%, 2-yr PFS 47%	Treatment-related deaths ~8%
FIL_ReRi (R2) <i>Gini, Blood 2023</i>	Phase 2 N = 68	Age ≥70, frail by sGA Median age 83	Rituximab + lenalidomide ×6, then len maintenance	ORR 51%, CR 28% 2-yr PFS ~38%	Primary ORR endpoint not met; chemo-free benchmark
Mosunetuzumab (GO40554) <i>Olszewski, Blood Neoplasia 2026</i>	Phase 1/2 N = 54	Age ≥80, or ≥60 and unfit 76% aged ≥80	Mosunetuzumab IV, fixed duration (8 cycles if CR)	Best CR 43% Median PFS 6.6 mo; CRs durable	CRS grade 1–2 only; infections notable
Pola-R2 <i>ASH 2024 (abstract)</i>	Phase 2 N = 21	Age ≥70, unfit/frail by CGA Median age 79.5	Pola + rituximab + lenalidomide ×8	EOT CR 100% (8/8 evaluable)	Preliminary; median follow-up 6 mo

● Fit: full-intensity chemoimmunotherapy

● Unfit / >80: attenuated chemoimmunotherapy

● Frail / unfit: chemo-free

Cross-trial comparisons are not valid: populations, fitness definitions, and endpoints differ. CGA, comprehensive geriatric assessment; EOT, end of treatment; sGA, simplified geriatric assessment.



Supportive Care Is What Makes Curative Intent Deliverable



Goals of care

Discuss what matters most before cycle 1; document advance directives; involve palliative care early, not only at relapse



Infection prevention

HBV prophylaxis if HBsAg+ or anti-HBc+; consider PJP and VZV prophylaxis; vaccinate (influenza, COVID-19, pneumococcal, recombinant zoster)



Myelotoxicity

Primary G-CSF prophylaxis for age ≥ 65 ; steroid pre-phase; early dose-delay rules agreed with the patient



TLS and organ protection

Hydration and allopurinol; rasburicase for high tumor burden or renal impairment; track cumulative anthracycline and LVEF



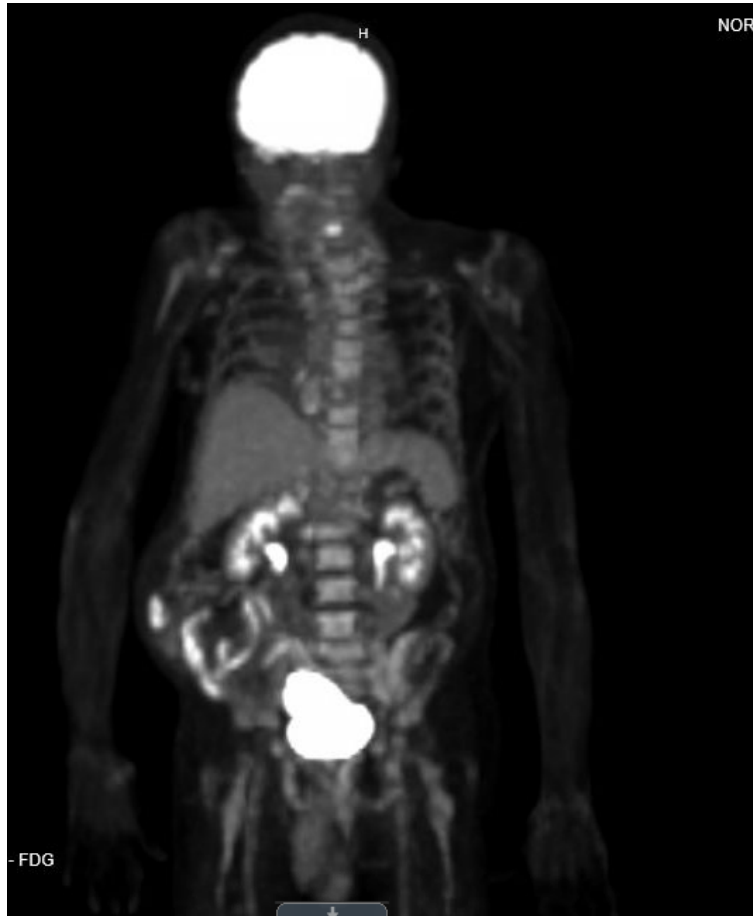
Geriatric interventions

Deprescribe and review polypharmacy; falls, nutrition, cognition and delirium screening; PT/OT



Caregiver and logistics

Transport, caregiver availability, and proximity to the center, which is especially relevant for CAR-T



Completed 6 cycles of
RCHP + polatuzumab
, interim PET – CR,
however, end of
treatment PET –
recurrent disease,
biopsy proven CD 19,
20 presence with
DLBCL



Next line of
therapy options ?



Relapse Timing Sets the Path



End of treatment

- PET-CT: Deauville 1–3 = complete metabolic response
- Biopsy PET-positive residual disease before calling it refractory
- No routine surveillance imaging in asymptomatic CR



Early relapse or refractory

- Primary refractory or relapse <12 months: 2L CAR-T
- Axi-cel (ZUMA-7) or liso-cel (TRANSFORM)
- Transplant-ineligible: liso-cel (PILOT)



Late relapse or CAR-T not an option

- Late relapse, ASCT-eligible: salvage → ASCT if CR
- Glofitamab-GemOx (STARGLO), Pola-BR, tafasitamab-lenalidomide
- 3L+: bispecifics (glofitamab, epcoritamab), loncastuximab

Re-biopsy at relapse: confirm histology, exclude transformation or a second process, and document CD19 status before CD19-directed therapy.



Relapsed DLBCL in Older Patients: Choosing Treatment Intent

DLBCL is an aggressive lymphoid malignancy that can be cured with full-intensity frontline chemoimmunotherapy



Older patients are at increased risk of relapse, as they may not be eligible for full-intensity frontline treatment



Assess eligibility for the available therapeutic options



Geriatric assessment



Patient preference



Side-effect profiles



NON-CURATIVE INTENT

Novel therapies

Options

- CD3×CD20 bispecific antibodies
- Bispecific + chemotherapy
- Polatuzumab vedotin + BR
- Tafasitamab + lenalidomide
- Loncastuximab tesirine

Key questions

- Sequencing?
- Dosing schedule?
- Side effects?



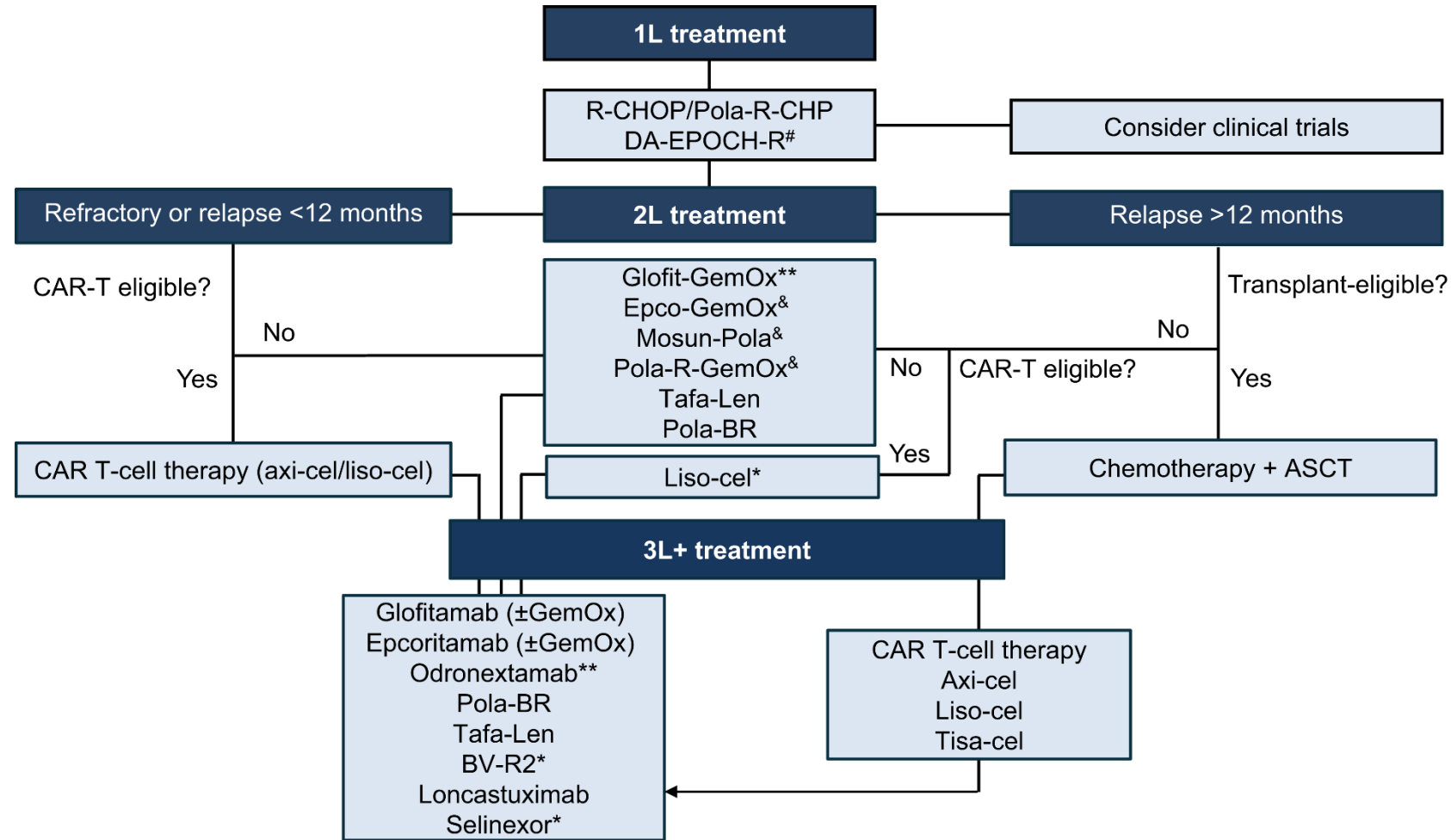
CURATIVE INTENT

CAR-T or autologous transplant

Key questions

- Timing of relapse?
- Medical comorbidities?
- Which CAR-T product?
- Bridging therapy?
- Side-effect management?
- Social support?

Selecting the best treatment approach and optimizing sequencing strategies in large B-cell lymphoma



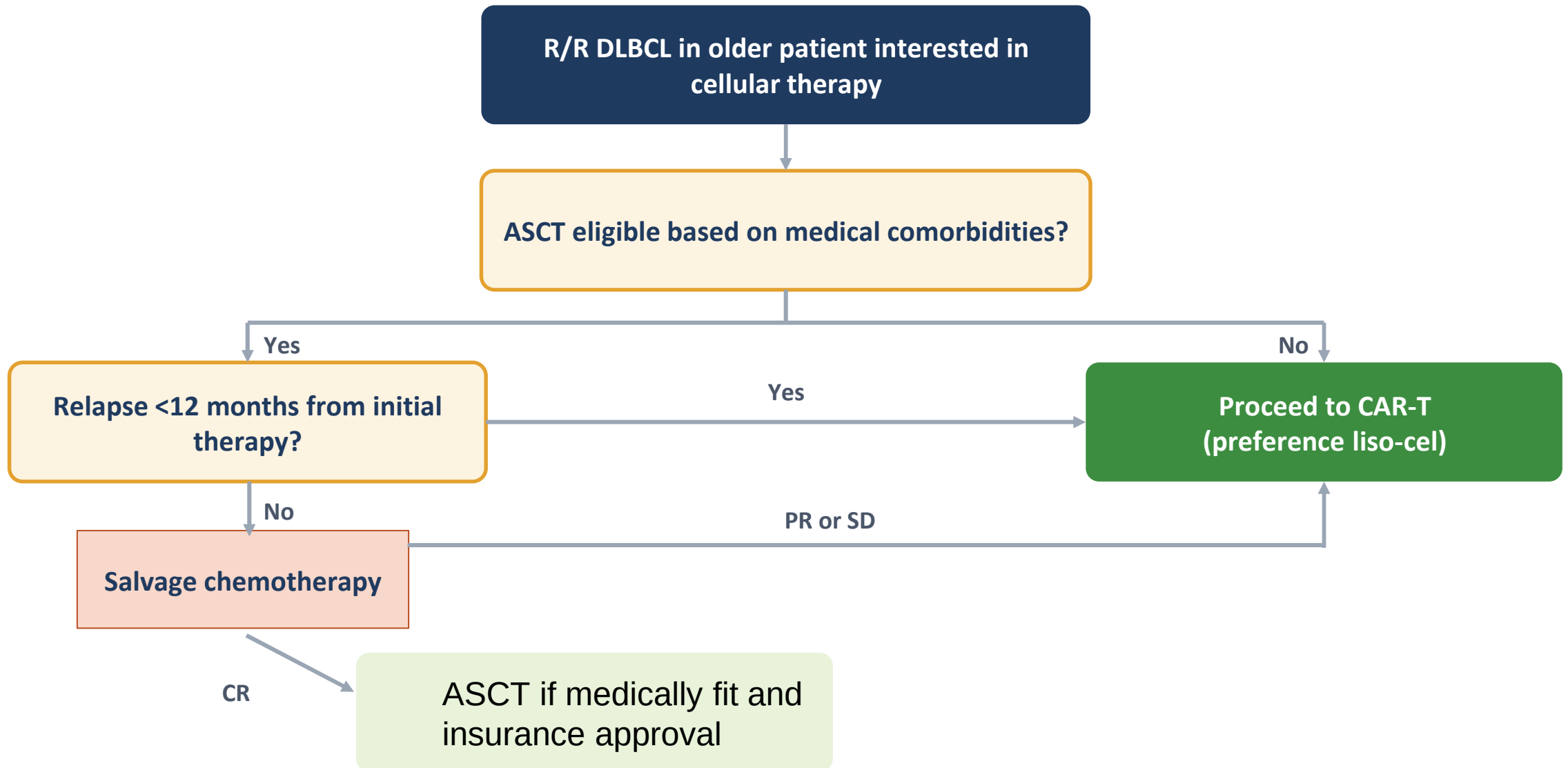
Gloria Iacoboni, Franck Morschhauser, Selecting the best treatment approach and optimizing sequencing strategies in large B-cell lymphoma, Hematology Am Soc Hematol Educ Program, 2025, Figure 1.



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R/R DLBCL in Older Patients: Cellular Therapy Algorithm



CAR T-Cell Safety and Efficacy in Older vs Younger Patients

Reference	Type of study	Age cutoff, y	Products	PFS or EFS (older vs younger)	OS (older vs younger)	ORR (older vs younger)	Grade ≥3 CRS (older vs younger)	Grade ≥3 ICANS (older vs younger)
Ram et al	Multicenter matched cohort analysis	<70 vs ≥70	Axi-cel and tisa-cel	Median PFS 3.6 mo vs not reached (P = .21)	Not reached in both groups (P = .79)	63% vs 78% (P = .337)	9.8% vs 7.3% (P = .29)	2.5% vs 4.9% (P = .54)
Berning et al	Multicenter retrospective analysis	<70 vs ≥70	Axi-cel and tisa-cel	Median PFS 11.1 vs 10.2 mo (P = .93)	34.4 vs 21.8 mo (P = .97)	78.3% vs 77.7% (P = .63)	7.9% vs 11.9% (P = .45)	22.2% vs 18.4% (P = .57)
Chihara et al	Medicare claims database analysis	65–69, 70–74, and ≥75	Axi-cel and tisa-cel	Median EFS 5.3 vs 12.6 vs 6.5 mo (P = .001, 70–74 vs ≥75 y; P = .01, 65–69 vs ≥75 y)*	Median OS 17.1 mo in all patients (P = .11, 65–69 vs ≥75 y; P = .67, 70–74 vs ≥75 y)	Not available	Not available	Not available
Dreger et al	Multicenter retrospective analysis	<65 vs ≥65	Axi-cel and tisa-cel	PFS at 12 mo 36% vs 26% (P = .04)*	OS at 12 mo 55% vs 51% (P = .17)	69% vs 58% (P = .043)*	10% vs 13% (P = .50)	16% vs 9% (P = .06)
Neelapu et al	Subgroup analysis of ZUMA-1	<65 vs ≥65	Axi-cel	Median PFS 13.2 vs 5.6 mo	OS at 24 mo 54% vs 49%	92% vs 81%	7% vs 12%	44% vs 28%
Jacobson et al	CIBMTR analysis	<65 vs ≥65	Axi-cel	HR 0.87 (95% CI, 0.74–1.02)	HR 1.05 (95% CI, 0.88–1.26)	OR 1.39 (95% CI, 1.05–1.83)*	OR 1.52 (95% CI, 1.00–2.31)*	OR 1.38 (95% CI, 1.04–1.82)*

 *Statistically significant.

Axi-cel, axicabtagene ciloleucel; CIBMTR, Center for International Blood and Marrow Transplant Research; CRS, cytokine release syndrome; EFS, event-free survival; HR, hazard ratio; ICANS, immune effector cell–associated neurotoxicity syndrome; OR, odds ratio; ORR, overall response rate; OS, overall survival; PFS, progression-free survival; tisa-cel, tisagenlecleucel.



SECOND-LINE CAR T-CELL THERAPY · OLDER PATIENTS- ZUMA-7 vs ALYCANTE vs PILOT

	ZUMA-7	ALYCANTE	PILOT
	Axi-cel vs SOC · phase 3 · ≥65 y subgroup, n = 109	Axi-cel · phase 2 · transplant-ineligible, n = 62	Liso-cel · phase 2 · transplant not intended, n = 61
PFS / EFS	Median EFS 21.5 vs 2.5 mo (HR 0.28)	Median PFS 11.8 mo; 12-mo PFS 49%	Median PFS 9.0 mo; 18-mo PFS 43%
ORR (CR)	88% (75%) vs 52% (33%)	Best ORR 90% (CMR 79%)	80% (54%)
OS	Median 43.5 vs 19.6 mo (HR 0.69; CI crosses 1)	Median NR; 12-mo OS 78%	Median NR; 18-mo OS 59%

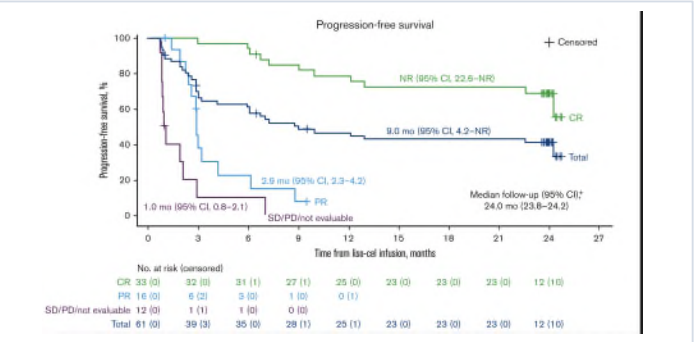
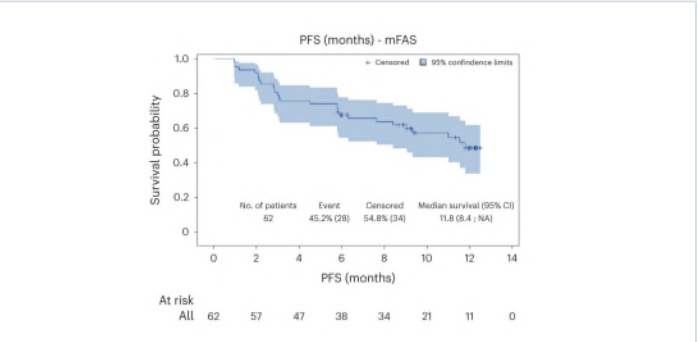
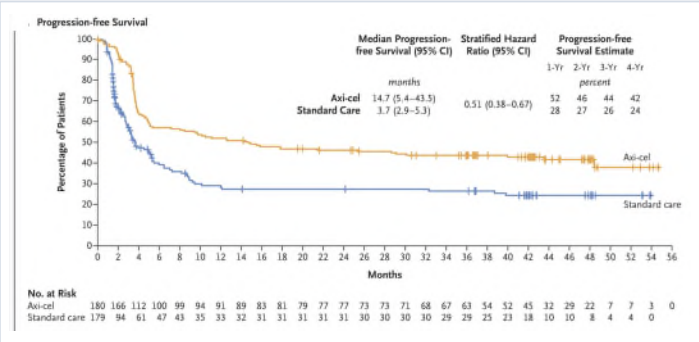
Gr ≥3 CRS / neurotox

8% / 27% (NE)

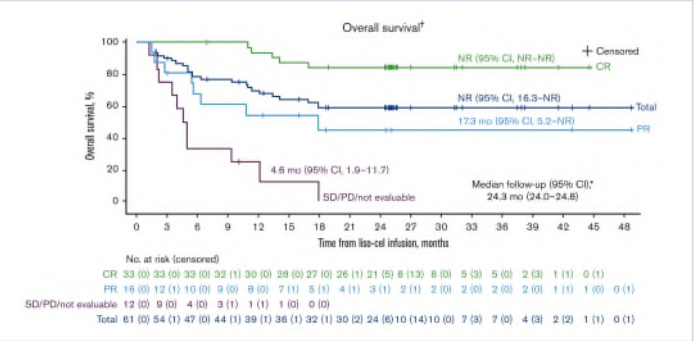
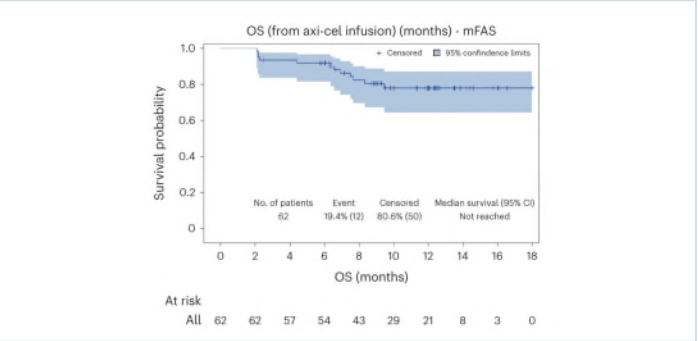
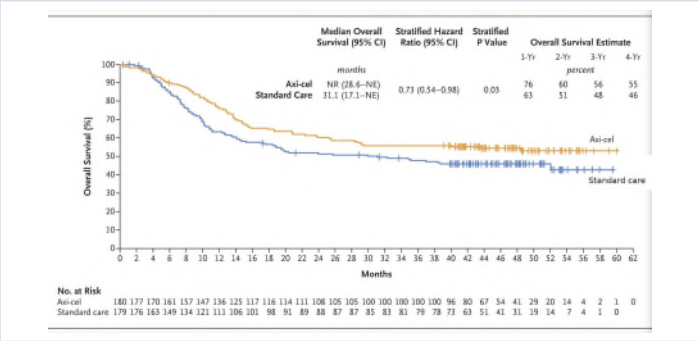
8% / 15% (ICANS)

2% / 5% (NE)

PFS
ZUMA-7: ITT, all ages. PILOT: by best response.



OS
ZUMA-7: ITT, all ages. PILOT: by best response.



Curves: ZUMA-7 ITT population, all ages (Westin, NEJM 2023); ALYCANTE (Houot, Nat Med 2023); PILOT final analysis (Sehgal, Blood Adv 2025). ZUMA-7 table values are from the ≥65 y subgroup (Westin, Clin Cancer Res 2023; ASH 2023). NE and ICANS grading differ; cross-trial comparison is not valid.



Managing CAR T-Cell Toxicities in Older Adults



BEFORE INFUSION

Pre-infusion optimization

- Geriatric assessment, echo, cognition
- Renal-adjust fludarabine; deprescribe
- Consider liso-cel if frail



DAYS 0–14

CRS

- ASTCT grading; early tocilizumab
- Watch for AF, hypotension, fluid overload
- Dexamethasone if tocilizumab fails



DAYS 0–14

ICANS

- ICE score at least twice daily
- Seizure prophylaxis; dex for grade ≥ 2
- Avoid benzodiazepines, anticholinergics



DAYS 0–90+

Infections

- Acyclovir, PJP prophylaxis, HBV plan
- Mold-active azole if neutropenia or steroids
- IVIG for low IgG with infections



DAYS 14–90

Cytopenias (ICAHT)

- Predict risk with CAR-HEMATOTOX
- G-CSF for prolonged neutropenia
- TPO-RA or stem cell boost if refractory



BEYOND DAY 30

Function and late effects

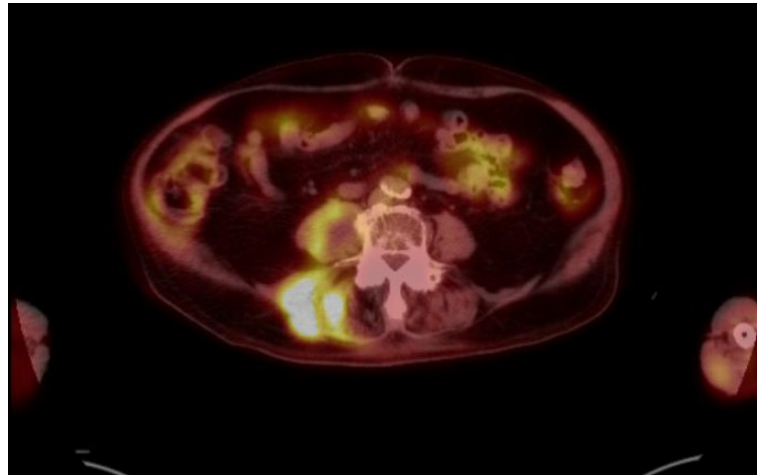
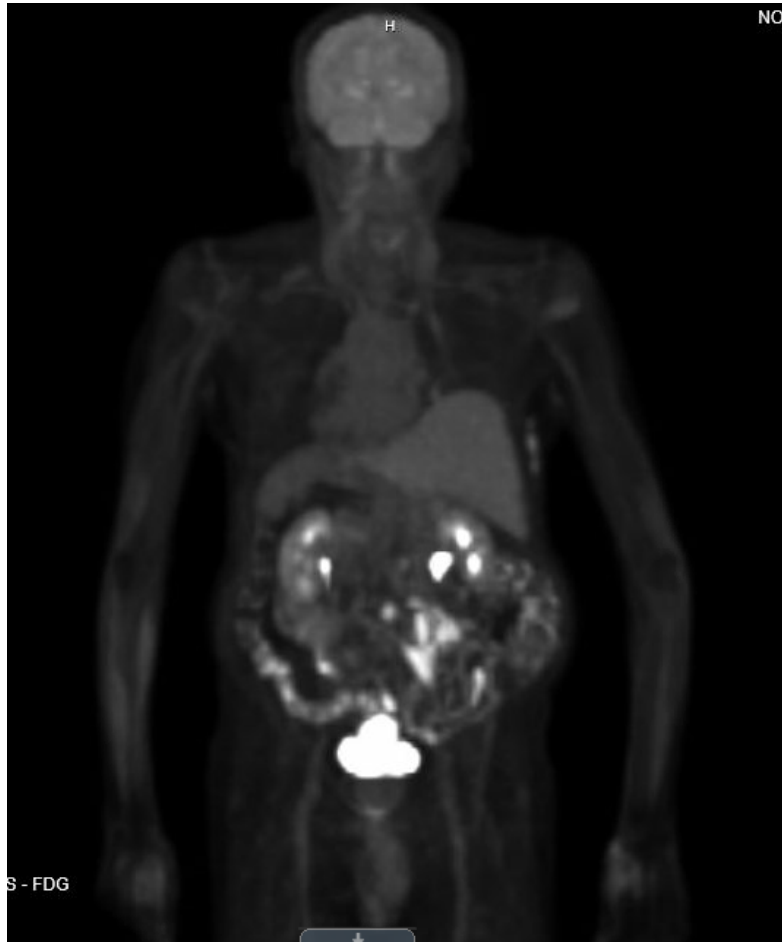
- Early PT/OT, fall prevention, nutrition
- Watch for IEC-HS, late infections, SPMs
- Caregiver plan; driving guidance

Principle: toxicity risk tracks physiologic reserve, not age alone. Intervene early, keep steroids short, protect function.



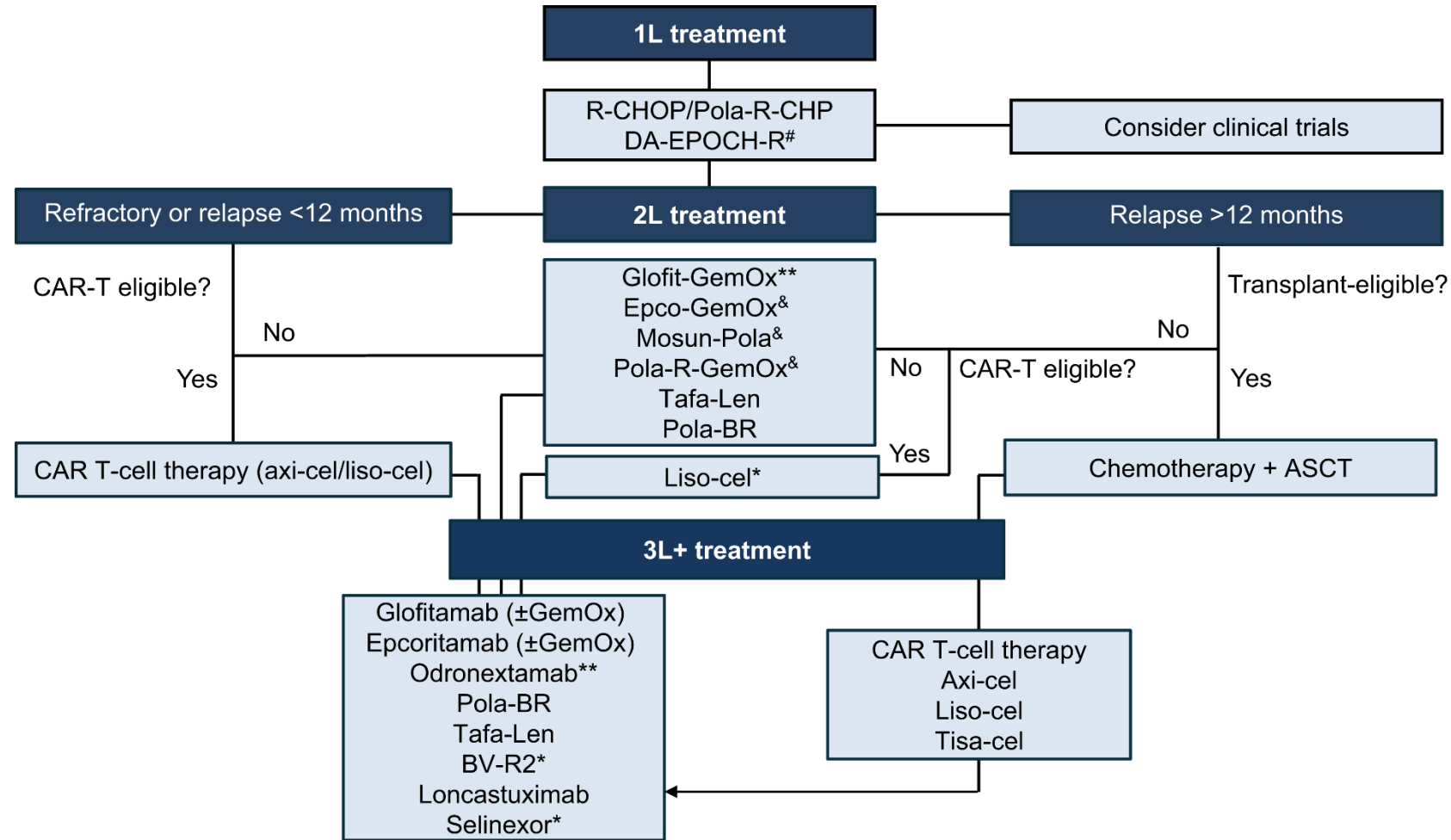
- ❖ After discussion with patient, radiation bridging and Lisocel
- ❖ Grade 2 CRS and no ICANS , discharged in 10 days
- ❖ Went into remission, CR at 30 day and 3 month PET scan.

6 months post CART recurrence



Third line options ?

Selecting the best treatment approach and optimizing sequencing strategies in large B-cell lymphoma



Gloria Iacoboni, Franck Morschhauser, Selecting the best treatment approach and optimizing sequencing strategies in large B-cell lymphoma, Hematology Am Soc Hematol Educ Program, 2025, Figure 1.



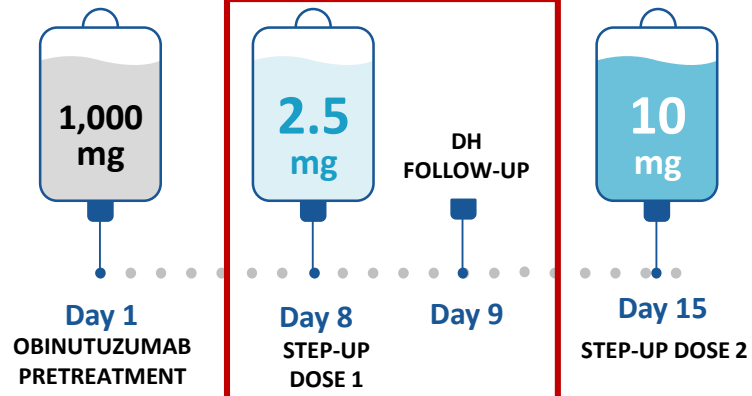
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Bispecific antibodies

Glofitamab-gxbm (Columvi™) – time-limited (12 cycles)

Cycle 1 (21 Days)



24 hour monitoring period

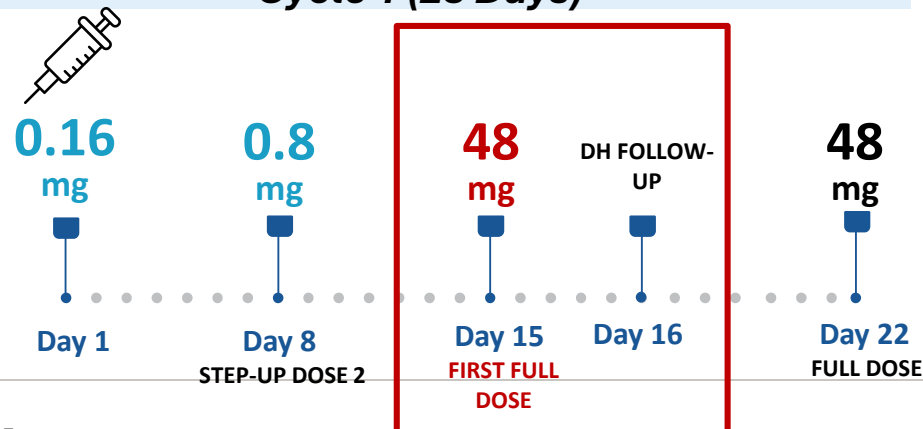
Glofitamab (NP30179, N=145): CRS and Neurologic Toxicity by Grade

Grade	CRS	Neurologic tox. / ICANS
1	52%	—
2	14%	—
3	2.8%	—
4	1.4%	—
Any grade	70%	4.8%
Grade ≥3	4.2%	2.1%

Source: COLUMVI (glofitamab-gxbm) US Prescribing Information, Genentech, Inc. (accessdata.fda.gov, label 761309s000), Study NP30179.

Epcoritamab-bysp (Epkinly™) – continuous therapy

Cycle 1 (28 Days)



24 hour monitoring period

Epcoritamab (EPCORE NHL-1, N=157): CRS and ICANS by Grade

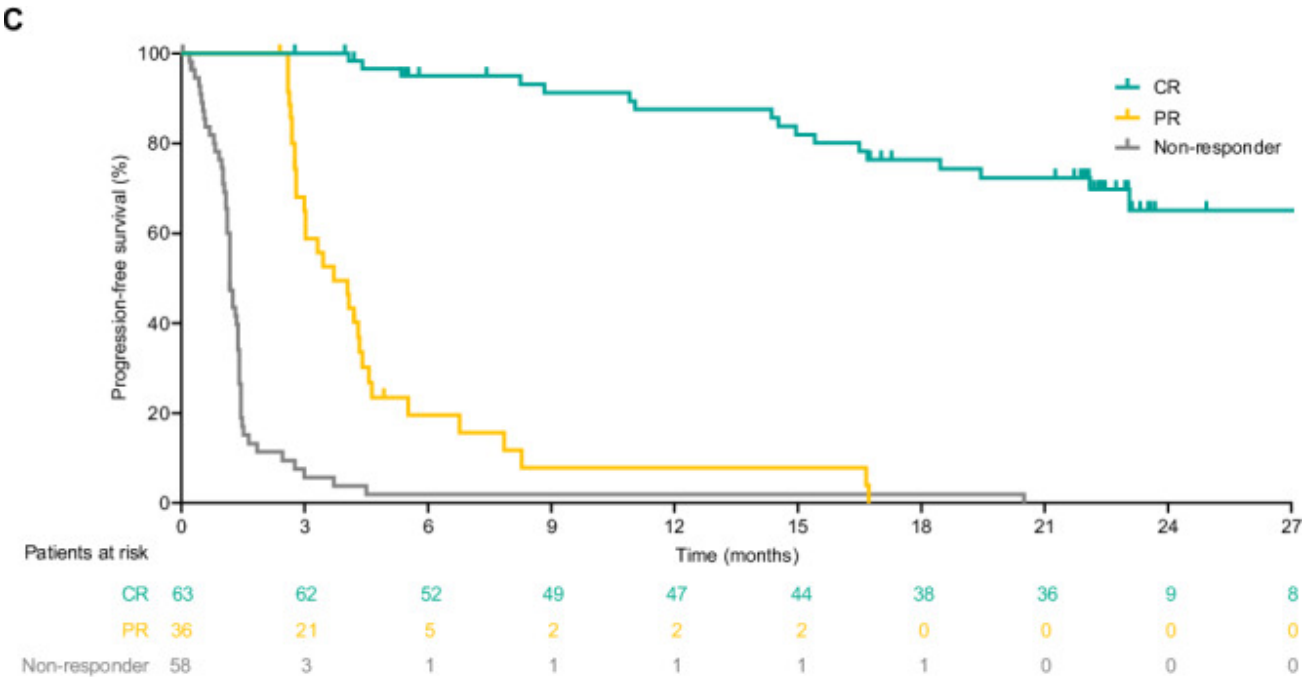
Grade	CRS	ICANS
1	37%	4.5%
2	17%	1.3%
≥3	2.5%	0.6%*
Any grade	51%	6%

*Includes 1 fatal ICANS event (0.6%). Source: EPKINLY (epcoritamab-bysp) US Prescribing Information, Genmab US/AbbVie (accessdata.fda.gov, label 761324s000), Study EPCORE NHL-1.

Bispecific Monotherapy Outcomes

Epcoritamab (EPCOR-NHL-1)

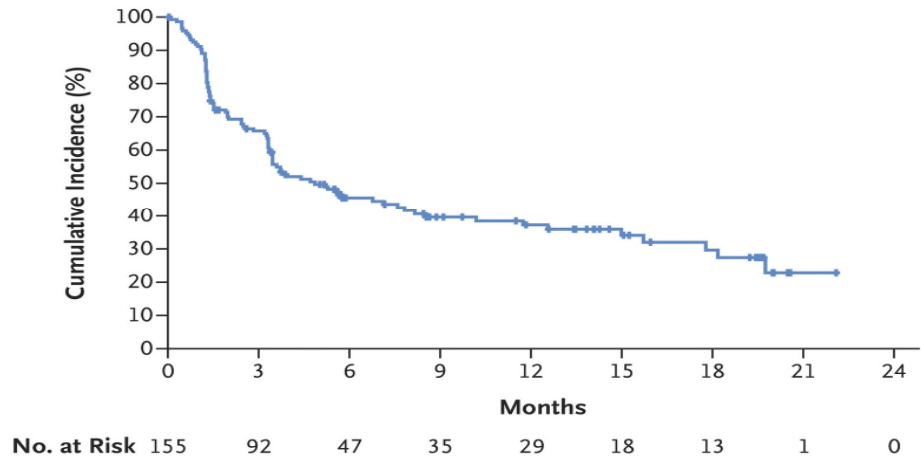
ORR 63.1% CR 40.1%
mPFS 4.4 m OS 18.5 m
PFS pts in CR: 65.1% at 24 mo



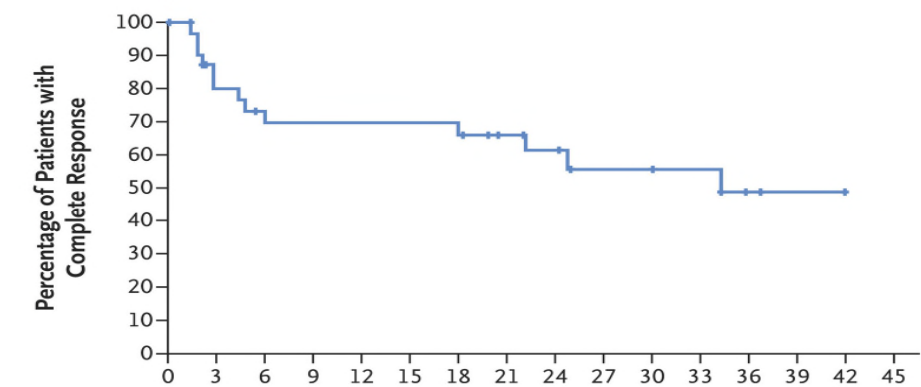
Glofitamab

ORR 52% CR 39%
PFS 37% at 12 mos; OS 50% at 12 mos
DOR 18.4 m; DOR in 79% at 12 m

B Progression-free Survival in the Main Analysis Cohort



C Duration of Complete Response among Patients with a Complete Response in the Supporting Cohort



FDA approved options, EPCOR or GLOFIT monotherapy achieves 40% CR rates, but DOR in responders is sustained



Real-World Outcomes with Bispecific Antibodies in DLBCL

REALBiTE Consortium

Epcoritamab + glofitamab, R/R LBCL (N=245, 21 US centers) • ~60% prior CAR-T • ~70% trial-ineligible

51–53%

epco 51% / glofit 53%
ORR

23–30%

epco 23% / glofit 30%
CR rate

2.6 mo

6-mo PFS 36%
Median PFS

7.8 mo

6-mo OS 60%
Median OS

Safety: treatment-related deaths from CRS/ICANS were infrequent; per-grade CRS/ICANS rates not reported in this abstract.

CUBIC Consortium

Bispecific monotherapy, R/R LBCL (N=179)

~50%

R/R LBCL cohort
ORR

~32%

R/R LBCL cohort
CR rate

3.1 mo

95% CI 2.2–4.3
Median PFS

7.1 mo

95% CI 5.4–10.8
Median OS

Safety: CRS any-grade ~43–58%, grade ≥2 ~23%; ICANS any-grade ~12–15%, grade ≥2 ~4–8%.

Real-world ORR (~50–54%) and median OS (~7–8 mo) are markedly lower than pivotal-trial results. These cohorts are more heavily pretreated and higher-risk (majority prior CAR-T or trial-ineligible).

1. Brooks T, et al. Real-World Outcomes with Bispecific T-Cell Engagers (REALBiTE) for Relapsed/Refractory Large B-Cell Lymphoma: A Multi-Center, Retrospective Cohort Study. Blood. 2025;146(Suppl 1):402.

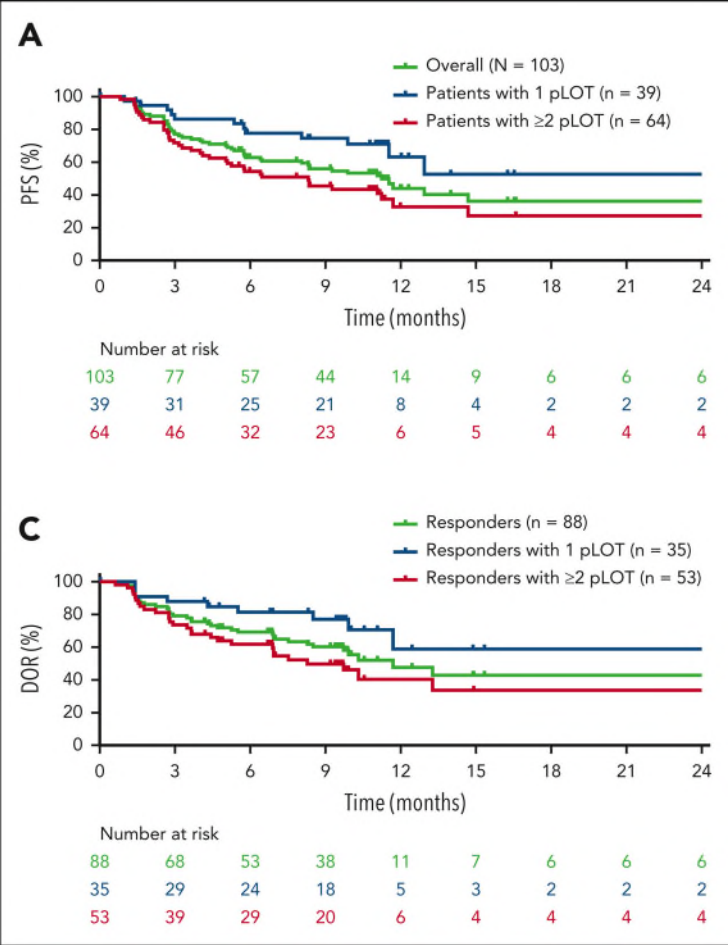
2. Xiao A, et al. Prior Bendamustine Exposure Does Not Compromise Clinical Outcomes of Bispecific Antibody Therapy in Patients with Relapsed/Refractory Non-Hodgkin Lymphoma: A CUBIC Consortium Analysis. Blood. 2025.



Epco-GemOx and Glofit-GemOx combinations

Epcoritamab + GemOx (EPCORE NHL-2)

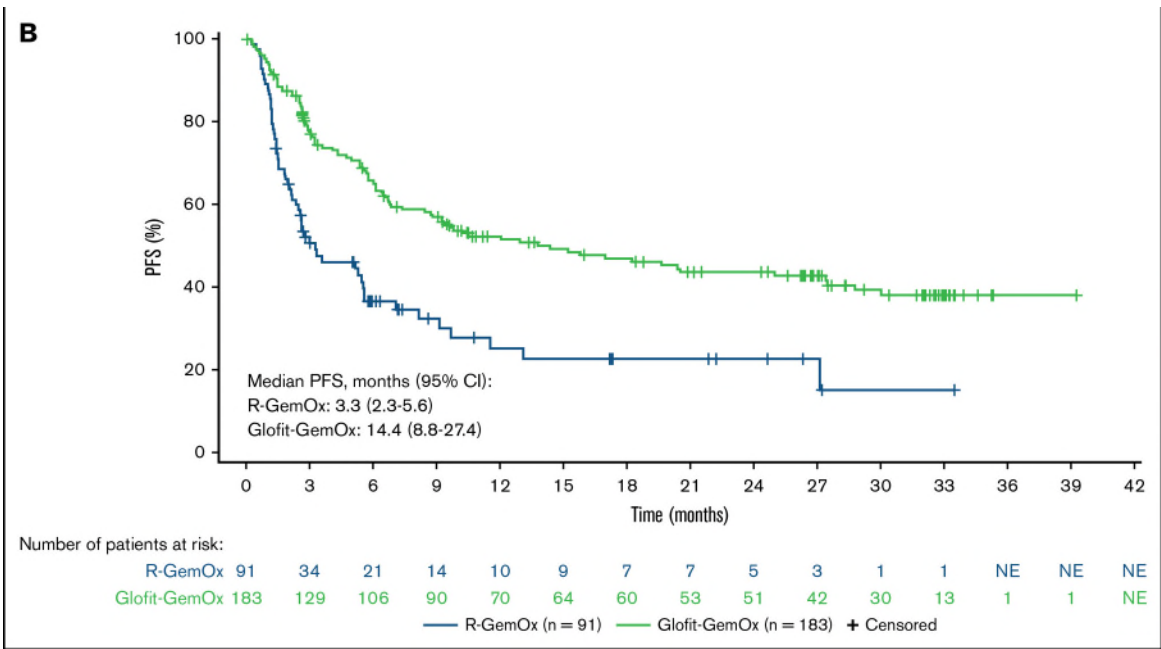
ORR 85% CR 61%
PFS at 12 m: 44%; OS at 12 mo 56.6%
mDOCR 23.6 m



Glofitamab + GemOx (STARGLO)

randomized phase III vs R-GemOx

ORR 68.3% vs 40.7%; CR 58% vs 25%
mOS 25.5 vs 12.9 mo
PFS at 12 mo: 53.2% vs 20.5%
DOR: NR vs 10.3 mo



Adding Gem-Ox to BisAb increases the CR rate to ~60%, maintains durability



SUNMO (Phase III): Mosun-Pola vs R-GemOx

70.3%

vs 40.0% (R-GemOx)
ORR (P<.0001)

51.4%

vs 24.3%
CR rate

11.5 mo

vs 3.8 mo (HR 0.41)
Median PFS

18.7 mo

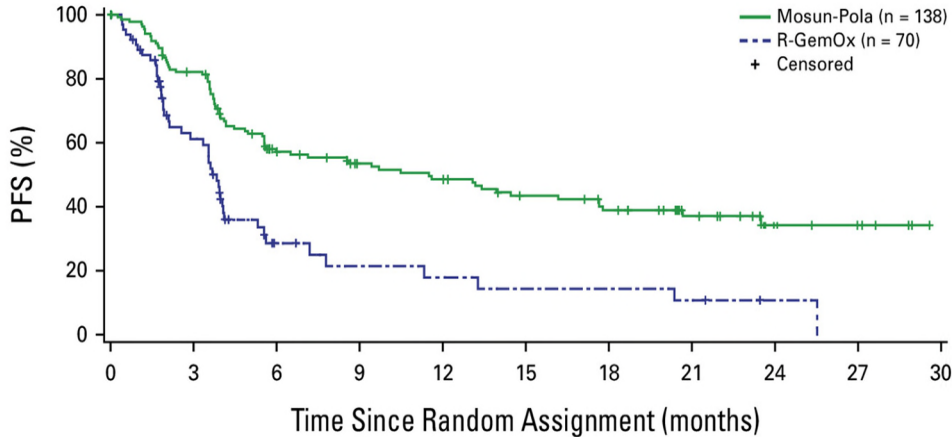
vs 13.6 mo
Median OS

NR

vs 9.5 mo
DOCR

- Transplant-ineligible R/R LBCL (N=208) • outpatient SC/IV dosing
- Safety: CRS in 25.9% (grade ≥3 0.7%); grade ≥3 AEs ~52% in both arms

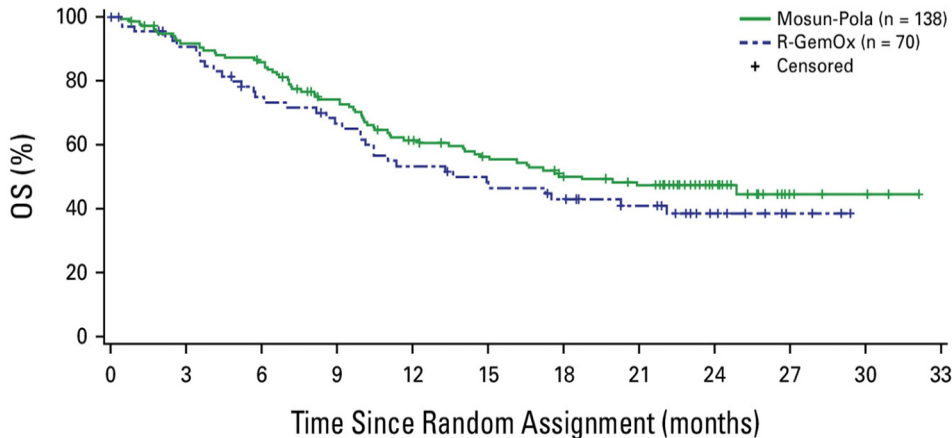
B



Number at risk (censored)

Mosun-Pola	138 (0)	108 (6)	65 (17)	54 (24)	49 (24)	40 (28)	34 (30)	20 (43)	8 (54)	5 (57)	NE
R-GemOx	70 (0)	33 (14)	9 (22)	6 (23)	5 (23)	4 (23)	4 (23)	3 (23)	1 (25)	NE	NE

C



Number at risk (censored)

Mosun-Pola	138 (0)	122 (5)	113 (6)	93 (11)	75 (13)	65 (17)	55 (20)	50 (22)	24 (48)	5 (66)	3 (68)	NE
R-GemOx	70 (0)	58 (6)	46 (8)	40 (9)	32 (9)	27 (10)	24 (11)	19 (15)	11 (22)	3 (30)	NE	NE



POLARGO (Phase III): Pola-R-GemOx vs R-GemOx

52.7%

vs 24.6% ($P < .0001$)
ORR

40.3%

vs 19.0%
CR rate

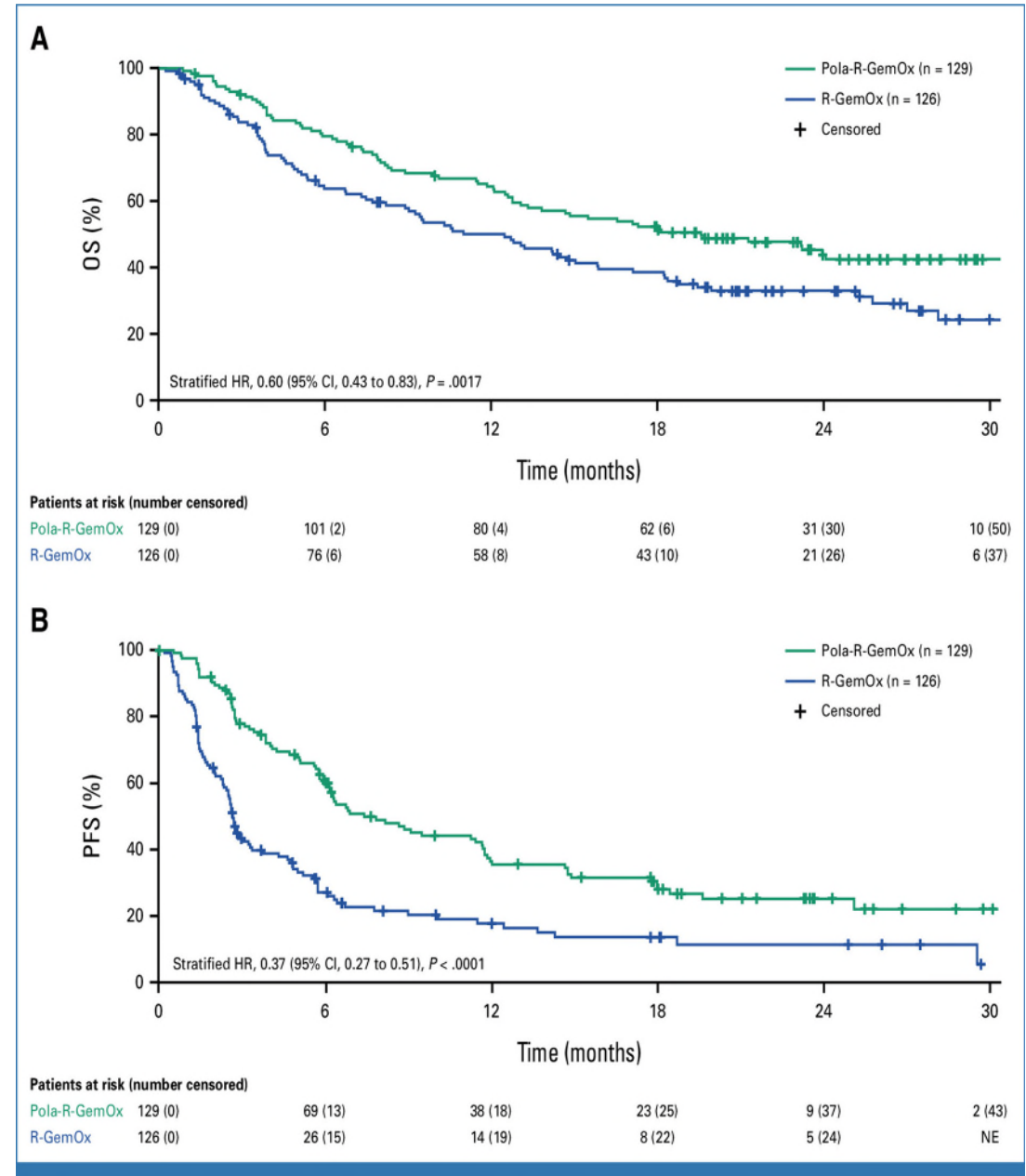
7.4 mo

vs 2.7 mo ($P < .0001$)
Median PFS

19.5 mo

vs 12.5 mo (HR 0.60)
Median OS

- Transplant-ineligible R/R DLBCL (N=255) • IV, 8 cycles
- 40% reduction in risk of death vs R-GemOx alone
- Safety: Gr $\geq$ 3 thrombocytopenia/neutropenia 34% each; neuropathy 57% (mostly gr1)



How to Choose? Regimen Comparison

	Regimen ^{df}	ORR	CR	Median PFS	DOR	Median OS	Administration	Key safety signal
★	1. Epcoritamab mono (EPCORE NHL-1)	63.1%	40.1%	4.4 mo	17.3 mo	18.5 mo	SC, continuous	CRS ~50% (gr ≥3 in 2.5%)
★	2. Glofitamab mono (NP30179)	52%	39%	12-mo PFS 37%	18.4 mo	12-mo OS 50%	IV, fixed-duration (12 cycles)	CRS 63% (gr ≥3 in 4%)
	3. Epcor-GemOx (EPCORE NHL-2)	85%	61%	12-mo PFS 44%	11.7 mo DOCR: 23.5 m	12-mo OS 56.6%	SC, continuous Epcor Gem-ox 4 cycles (8 doses)	CRS 54% (gr ≥3 in 1%)
	4. Glofit-R-GemOx (STARGLO)	68.3%	58.5%	14.4 mo	NR	25.5 mo	IV, fixed Glofit 12 cycles; R-Gem-Ox 8 cycles	CRS 44.8% (gr ≥3 in 2.3%)
	5. Mosun-Pola (SUNMO)	70.3%	51.4%	11.5 mo	15.6 mo	18.7 mo	SC/IV, fixed-duration, 8-17 cycles Mosun, 6 Pola	CRS 26% (gr ≥3 in 0.7%)
	6. Pola-R-GemOx (POLARGO)	52.7%	40.3%	7.4 mo	11.8 mo	19.5 mo	IV, 8 cycles	Neuropathy 57% (Gr 3 in 3.9%), cytopenias
★	7. Tafasitamab + lenalidomide (L-MIND)	60%	43%	12.1 mo	21.7 mo	33.5 mo	IV + oral, Tafa until progression; Len 12 cycles	Neutropenia; infections
★	8. Loncastuximab tesirine (LOTIS-2)	48.3%	24.8%	4.9 mo	10.3 mo	9.5 mo	IV monotherapy, q3wk up to 1 year	Edema/effusions; skin toxicity, cytopenias

All are category 2A or greater within NCCN guidelines

★ indicates FDA approved.

Important to remember, these regimens cannot be directly compared; different populations were represented in these studies.

Managing Bispecific Antibody Toxicities in Older Adults



BEFORE TREATMENT

Patient optimization

- Geriatric assessment; check baseline IgG
- Local lodging, transportation, and caregiver support
- Patient education on CRS/ICANS (what to do, who to call, etc)



CYCLE 1, STEP-UP

CRS

- Peaks with step-up or first full dose
- Debulking when possible (ie. Obin prior to glofit, Gem-Ox prior to bsAB)
- Administer Dex and Tylenol early



ONGOING THERAPY

Infections/cytopenias

- Give IVIG for hypogammaglobulinemia
- HSV/PJP prophylaxis
- G-CSF support; check CBC each cycle
- Vaccinate before starting when feasible



SITE REQUIREMENTS

Facility readiness

- 24/7 access to an MD/APP experienced in CRS/ICANS management
- Direct-admission/hospitalization capacity
- On-site tocilizumab and corticosteroids



CYCLES 1-2

ICANS

- Less frequent/severe than with CAR-T
- ICE score; distinguish from baseline delirium
- Dexamethasone per protocol if it occurs



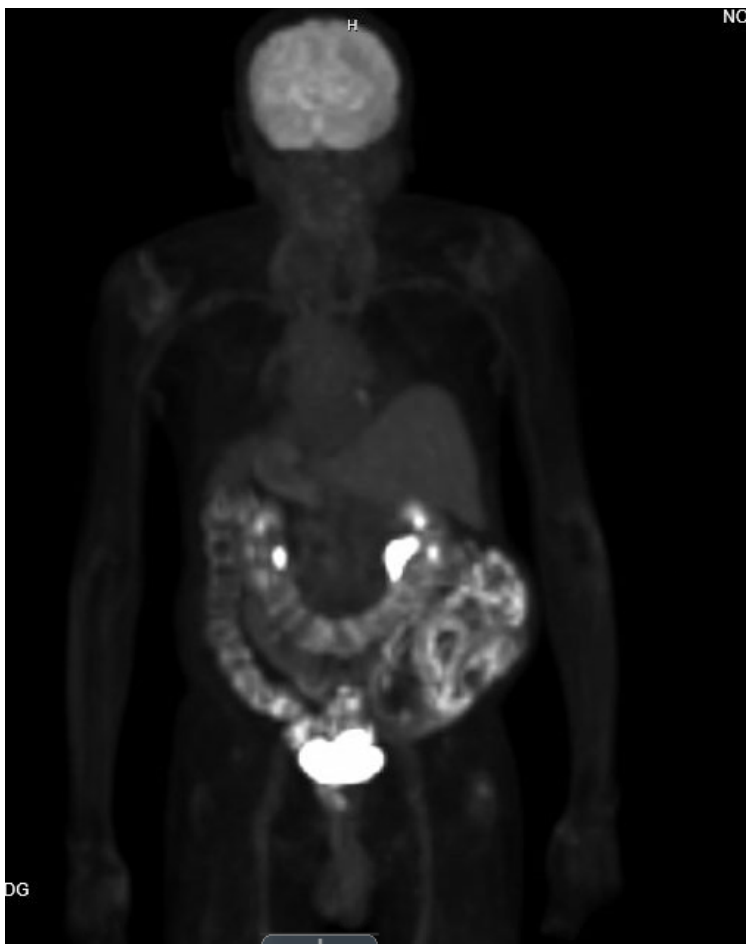
THROUGHOUT COURSE

Function and logistics

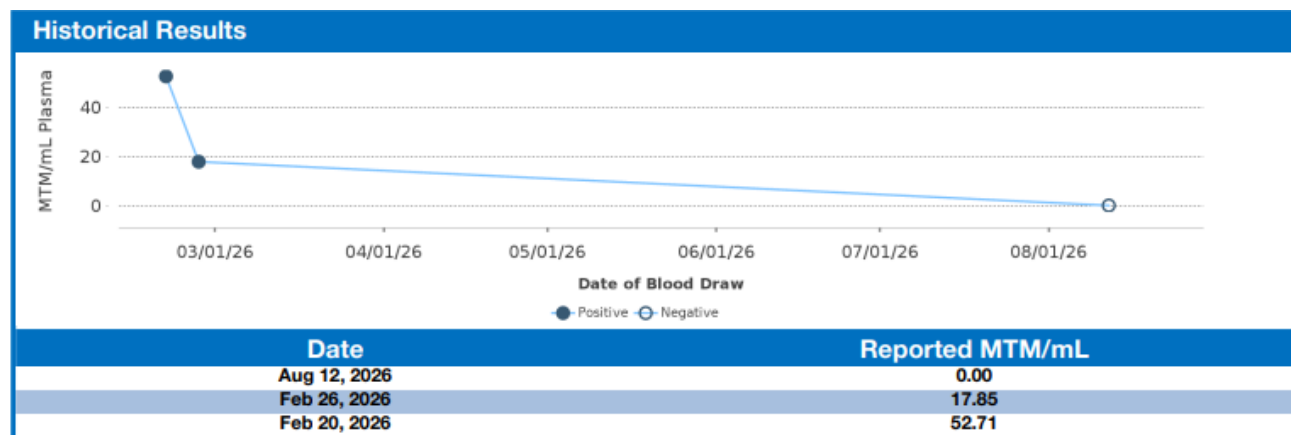
- Lower administration burden than CAR-T
- Assess transportation, caregiver support
- Reassess frailty and goals of care

Key point: Severe (grade ≥ 3) CRS is less common with bispecifics than with CAR-T, but step-up dosing should only be given at centers with the infrastructure to support it

6 months of glofitamab



In CR – with MRD negative



Conclusions

- Age alone shouldn't drive treatment decisions.
- CAR-T remains feasible and effective in carefully selected older adults, with liso-cel showing the most favorable toxicity profile.
- Bispecific antibodies have reshaped the post-CAR-T relapse landscape, offering off-the-shelf, largely outpatient options.
- Combination regimens (bispecific + GemOx, Pola + Mosun/R-GemOx) outperform R-GemOx alone
- Treatment selection should balance efficacy, toxicity profile, administration burden, and the patient's goals of care - there is no single right answer.

Questions

Thank You

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