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Management of DLBCL in the Elderly Patient

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Division of Hematology – Lymphoma Section

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Disclosures

- **AdBoard:** Amgen, Kite, SeaGen, Epizyme, Janssen, BeiGene, Abbvie, Incyte, TG Therapeutics, ADC Therapeutics, Lilly, Genentech
- **Research Funding:** Loxo, BeiGene, Incyte

Case #1: 88 y/o Male with Neck Lymphadenopathy

Past Medical History:

- Obesity | Type 2 DM (HbA1c 6.7, not on insulin) | Hypertension
- CAD with CHF s/p PCI (mild LVH, EF 65%, grade 1 diastolic dysfunction)
- SVT (2005, s/p ablation) | GERD | Diverticulitis | BPH | Gout
- CKD with proteinuria (2g in 2013, CrCl 50 mL/min)
- Hemorrhagic stroke with seizures (2001) | h/o VP shunt
- Parkinson's disease

Case #1: Clinical Course

- Usual state of health until he notices a non-tender neck mass
- Excisional LN biopsy → Diffuse Large B-Cell Lymphoma (GCB phenotype)
 - Ki67: 90% | FISH: negative for IGH-BCL2, BCL6, MYC, IGH-MYC rearrangements
- Admitted for constipation → OSH "overdose of laxatives" → volume depletion, AKI, functional decline; VP shunt malfunction suspected

Labs at Transfer to Sylvester:

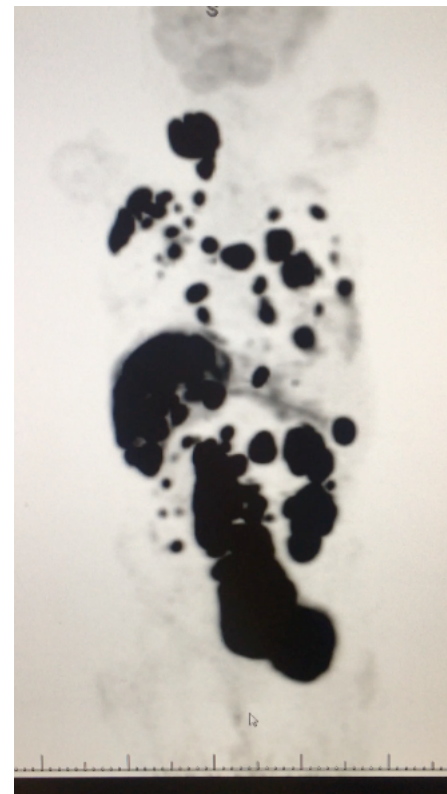
- Creatinine 2.7 (baseline 1.3 mg/dL) | Uric acid 10.2 mg/dL | Calcium 11.3 mg/dL | Albumin 2.9 g/dL
- Physical exam: BP 105/50, HR 110, O2 sat 94%, lethargic, dry mucosae
- Palpable cervical, axillary, inguinal lymphadenopathy | LLQ palpable tender mass

Case #1 — Baseline PET/CT

Extensive FDG-avid disease:

- Bilateral cervical, axillary, mediastinal
- Large retroperitoneal / perinephric mass
- Inguinal lymphadenopathy

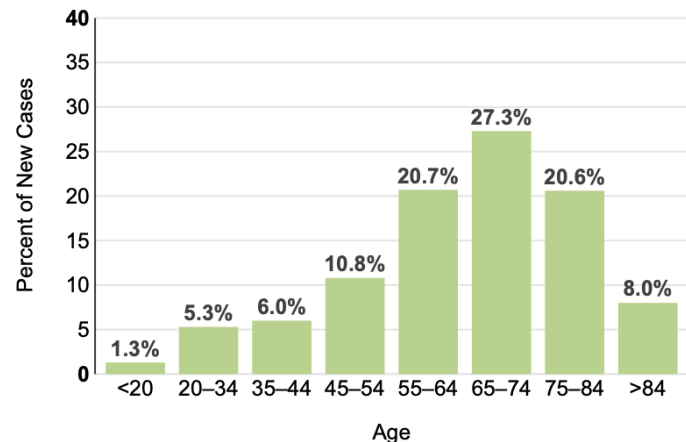
What would you do?



Why This Matters: DLBCL Is a Disease of the Elderly

Incidence rises sharply with age:

- Incidence increasing as population ages globally
- Median age at diagnosis: 66 years; ~40% are >70 at diagnosis
- Same morphology and clinical presentation as younger patients



SEER 21 2018-2022, All Races, Both Sexes

Biology & Treatment Challenges in Elderly DLBCL

Why Treatment Is Harder in the Elderly:

Comorbidities

Cardiac, renal, neurologic, endocrine

Decreased Organ Function

Reduced GFR | Low EF

Altered Drug Metabolism

CYP450 changes, reduced albumin → increased free drug levels, polypharmacy

More Aggressive Biology

ABC/non-GCB predominates in elderly → inferior R-CHOP outcomes

Underrepresented in clinical trials

Source: [Mareschal et al., Blood 2017](#)

ABC increases ~13.7% per decade | Source: [Mareschal et al., Blood 2017](#)

Cell of Origin Shifts with Age:

Age Group	ABC/Non-GCB %	GCB %
50–60 years	~28%	~72%
60–70 years	~42%	~58%
70–80 years	~55%	~45%
≥80 years	~67%	~33%

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SECTION

Geriatric Assessment

Evaluating the Elderly DLBCL Patient

What Is "Elderly" in DLBCL?

There is no universal definition — it depends on the context:

Age Cutoff	Context	Examples
>60 years	Original R-CHOP trials	GELA, LNH03-6B, RICOVER-60
>65 years	Geriatric assessment studies	FIL CGA, NCCN geriatric thresholds
>70 years	Practical treatment decisions	POLARIX subgroup, CAR-T eligibility
>80 years	Very elderly — no benefit from intensive Tx	R-miniCHOP standard (LYSA), MorningSun

Key principle: Chronological age alone is insufficient — functional status and fitness are more important than birthdate.

Source: [NCCN Guidelines 2024](#); [Tucci et al., JCO 2015](#)

Polypharmacy and Key Comorbidities

Polypharmacy (≥ 5 medications)

- Gong et al. (JNCCN 2025, n=5,527): Polypharmacy independently associated with worse OS in elderly DLBCL (HR 1.23, p=0.01)
- Common drug interactions with R-CHOP: CYP3A4 inhibitors (azoles, macrolides), anticoagulants, PPIs
- Medication reconciliation before each cycle is essential

Key Comorbidities Affecting Treatment

- Cardiovascular – EF, arrhythmias, hypertension
- Renal: MTX, TLS risk
- Neuro: Pre-existing neuropathy
- Endocrine: hyperglycemia, hypocortisolism

Source: [Gong et al., JNCCN 2025](#); [Tsai et al., SEER-Medicare 2014](#)

FIL Simplified Geriatric Assessment (sGA) Components

Domain	Tool	What It Measures	Scoring
Activities of Daily Living	ADL (Katz Index)	Bathing, dressing, toileting, transferring, continence, feeding	0–6 (6 = fully independent)
Instrumental ADL	IADL (Lawton)	Phone use, shopping, cooking, housekeeping, laundry, transport, medications, finances	0–8 (8 = fully independent)
Comorbidity	CIRS (Cumulative Illness Rating Scale)	14 organ systems rated 0–4 for severity; key threshold: grade 3-4 in any domain	Grade 3 = unfit Grade 4 = frail

FIL Elderly Project validation (Merli et al., JCO 2021, n=1,163):

- sGA independently predicted OS and PFS beyond IPI and ECOG-PS
- Fit: 2-yr OS 78% vs. Unfit: 66% vs. Frail: 46% (p<0.001)
- ECOG-PS alone missed ~20% of patients with geriatric impairments

Source: [Merli et al., JCO 2021](#)

FIL Simplified Geriatric Assessment (sGA)

Developed by the Italian Lymphoma Foundation (Fondazione Italiana Linfomi)

FIT

ADL 6, IADL 8, CIRS 0
Age \leq 80

Full-dose

2-yr OS: ~70-75%

UNFIT

ADL 5 or IADL 6-7
or CIRS grade 3 in 1 domain

Attenuated chemo
or
Novel combinations

2-yr OS: ~50-60%

FRAIL

ADL \leq 4 or IADL \leq 5
or CIRS grade 4 any domain
or Age $>$ 80

**Palliative or low-
intensity approaches**

2-yr OS: ~30-40%

Source: [Tucci et al., JCO 2015](#); [Merli et al., JCO 2021](#)

Simple Bedside Assessments

Hand Grip Strength

- Simple, reproducible, <1 minute
- Cutoffs (EWGSOP2): <27 kg men, <16 kg women
- Liu et al. (Blood 2019, n=448): Low grip strength predicted inferior OS (HR 1.82, p=0.003)
- Predicts treatment toxicity and early discontinuation
- Xue et al. (ASH 2024): Correlated with grade 3–4 toxicity in elderly lymphoma patients

Timed Up and Go (TUG)

- Stand from chair, walk 3m, turn, return, sit
- Normal: <12 seconds
- Impaired: ≥ 20 seconds
- Torka et al. (JCO 2025, n=194): Impaired TUG predicted worse PFS (HR 1.75) and OS (HR 2.1) in elderly lymphoma
- Assesses balance, gait speed, lower extremity strength — integrates multiple domains

Source: [Liu et al., Blood 2019](#); [Torka et al., JCO 2025](#)



SECTION

First-Line Treatment

Standard Therapy, Dose Adjustments, and Targeted Additions

Elderly – platform for treatment development

GELA trial (Coiffier et al., NEJM 2002, patients 60–80 years):

- R-CHOP vs CHOP: CR 76% vs 63%, 2-yr OS 70% vs 57%

RICOVER-60 (Pfreundschuh et al., 60–80 years):

- 6×R-CHOP-14 optimal: 3-yr EFS 66.5%, OS 78.1%
- 8 cycles NOT better than 6 cycles in elderly

LNH03-6B (Delarue et al., Lancet Oncol 2013, patients >60 years):

- Dose-dense R-CHOP-14 vs standard R-CHOP-21: No benefit in elderly
- 10-yr PFS ~40%, 10-yr OS ~50%
- More toxicity with dose-dense approach without survival benefit

Source: [Coiffier et al., NEJM 2002](#); [Delarue et al., Lancet Oncol 2013](#)

Outcomes Worsen Dramatically with Advancing Age

Age Group	Standard Tx	2-yr PFS	2-yr OS	Key Issue
60–70	R-CHOP×6	~55-60%	~65-70%	Dose reductions common
70–80	R-CHOP (adjusted)	~45-50%	~55-60%	Toxicity-related deaths rise
>80	R-miniCHOP	~47%	~59%	No benefit from intensive Tx

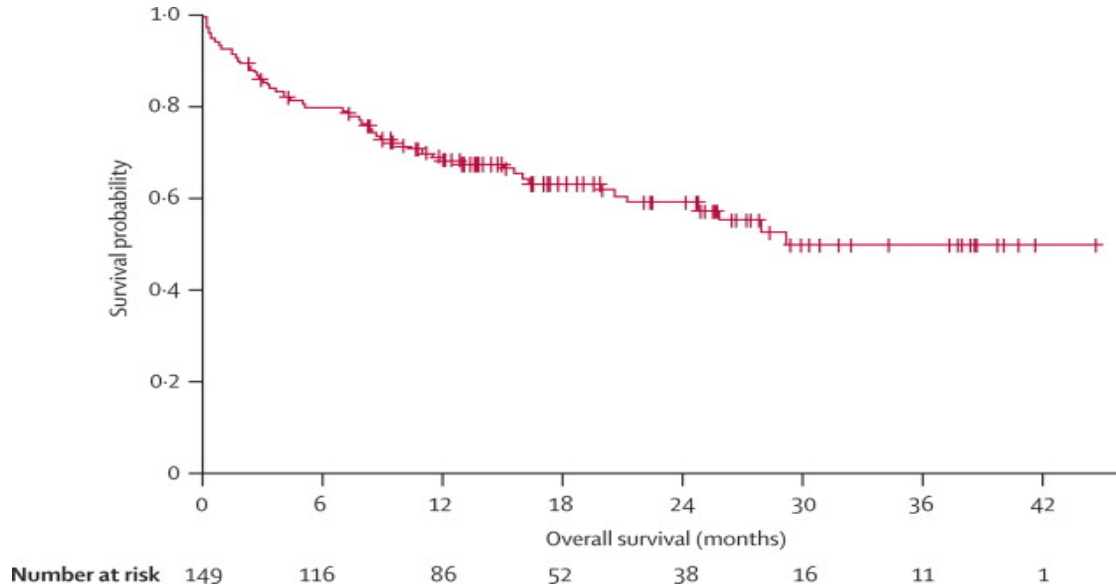
Key concept: Patients >80 do NOT benefit from full-dose chemotherapy. Dose intensification increases toxicity-related mortality without improving lymphoma outcomes.

- LNH03-6B: 10-year OS in patients >70 receiving dose-dense R-CHOP was not superior to standard R-CHOP
- Treatment-related mortality increases sharply after age 75: ~10–15% of patients >80 die from treatment toxicity

Source: [Peyrade et al., Lancet Oncol 2011](#); [Delarue et al., Lancet Oncol 2013](#)

R-miniCHOP: Overall Survival — Phase II Results

Peyrade et al. (LYSA, Lancet Oncol 2011) — n=149 patients, all >80 years



Regimen:

- Rituximab 375 mg/m²
- Cyclophosphamide 400 mg/m²
- Adriamycin 25 mg/m²
- Vincristine 1 mg (flat)
- Prednisone 40 mg/m² d1-5

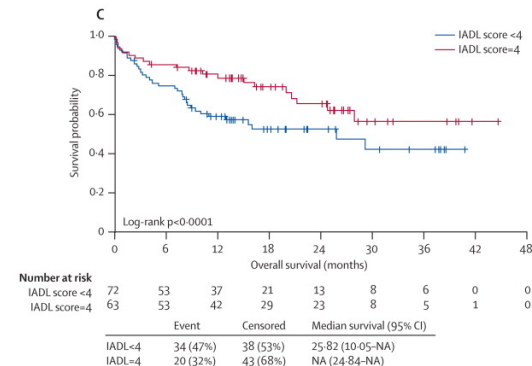
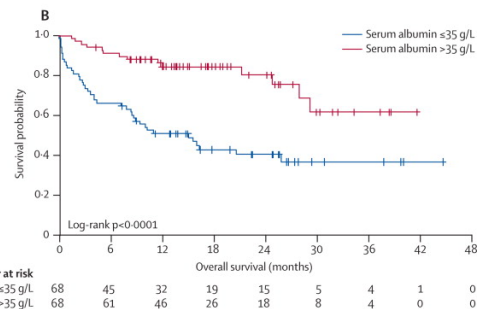
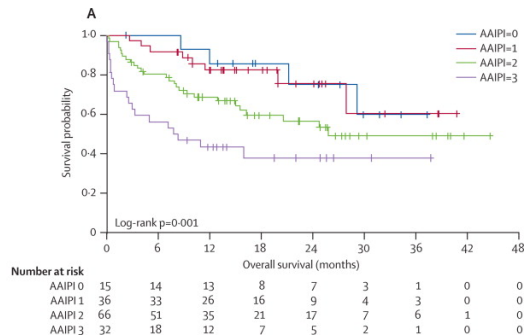
Results:

- ORR 74% | CR 63%
- 2-yr PFS: 47% | 2-yr OS: 59%
- Gr 3-4 neutropenia: 59% | TRM: 7%

Source: [Peyrade et al., Lancet Oncol 2011](#)

R-miniCHOP: Outcomes by IPI, Albumin, and IADL

Lancet Oncol 12:460, 2011 — Survival varies by functional and nutritional status



Results:

- Outcomes vary significantly by IPI risk score
- Albumin level is an independent prognostic factor
- IADL (instrumental activities of daily living) predicts survival
- Geriatric assessment tools capture what IPI alone misses in the very elderly
- Key takeaway: Fitness and function matter as much as disease risk

POLARIX: Pola-R-CHP in Elderly Subgroup

POLARIX trial (Tilly et al., NEJM 2022): Pola-R-CHP vs R-CHOP

Phase III, n=879, previously untreated DLBCL, IPI ≥ 2

Overall Population

- 2-yr PFS: 76.7% vs 70.2% (HR 0.73)
- OS: No significant difference
- Modest overall benefit

Patients ≥ 70 years

- **2-yr PFS: 77.1% vs 67.0% (HR 0.64)**
- 2-yr OS: 86.2% vs 82.8%
- **Largest benefit in elderly subgroup**

Clinical implications:

- Polatuzumab vedotin (anti-CD79b ADC) replaces vincristine in Pola-R-CHP
- Better PFS in elderly - eliminating vincristine neurotoxicity? Non-GCB subtype?
- Pola-R-CHP is now a preferred option

Source: [Tilly et al., NEJM 2022](#)

PHOENIX Trial: A Cautionary Tale for Elderly Patients

Younes et al. (Lancet 2019): Ibrutinib + R-CHOP vs placebo + R-CHOP in non-GCB DLBCL

Outcome	Age <60	Age ≥60
EFS (HR)	0.579 (favors ibrutinib)	1.228 (HARMS elderly)
OS (HR)	0.330 (favors ibrutinib)	1.440 (HARMS elderly)
SAEs	Lower	63.4% vs 38.2%
R-CHOP completion	Similar	73.7% vs 88.8%

Lesson: Adding ibrutinib to R-CHOP in elderly patients caused more toxicity, leading to R-CHOP dose reductions and delays, resulting in WORSE lymphoma outcomes. The toxicity of the targeted agent undermined the delivery of effective backbone chemotherapy.

Source: [Younes et al., Lancet 2019](#)

Practical Dose Modifications in Elderly DLBCL

Standard modifications:

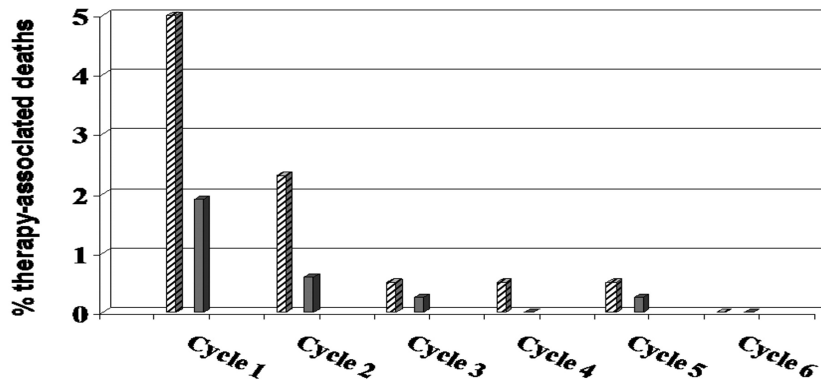
- Vincristine: Cap at 1 mg flat dose (or omit) in patients >70 with pre-existing neuropathy
- Doxorubicin: Careful evaluation of cardiac and overall CV risk
- Cyclophosphamide: Reduce 25–50% if CrCl <50 mL/min
- G-CSF: Mandatory in all patients ≥65 receiving R-CHOP (or R-miniCHOP)

Essential supportive measures:

- Hydration and TLS prevention are critical:
 - Reduced thirst perception and renal reserve
 - IV/PO fluid intake: Aggressive pre-treatment hydration given frequent renal impairment
 - Allopurinol: Start 2-3 days before treatment
 - Rasburicase: Consider for high tumor burden or elevated baseline uric acid
 - Frequent renal function monitoring during cycle 1
- Prednisone:
 - Glycemia, hypertension, insomnia
 - Adrenal insufficiency

Pre-Phase & Staggered Cycle 1: Easing Into Treatment

Why pre-phase?



Most treatment-associated deaths in elderly occur during Cycle 1 (Blood 116:5103, 2010). Pre-phase reduces this risk.

Source: [Pfreundschuh et al., Blood 2010](#)

Staggered R-mini-CHP-Pola (Dr. Alencar's Cycle 1):

Days 1–5: Prednisone 40 mg/m²

Pre-phase effect: steroid debulking begins

Day 4: Cyclophosphamide + Doxorubicin added

Cytotoxics after partial steroid debulk

Day 5: Rituximab + *Polatuzumab* (last)

Less bulk → lower infusion reaction risk & TLS risk

Can be delivered over days OR split weekly (less urgency → more flexibility).

The key: 'ease into' Cycle 1.

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SECTION

Non-Chemotherapy Frontline

Targeted Agents Replacing Cytotoxic Therapy

Chemo-Free Frontline for Elderly/Unfit DLBCL: The Mosunetuzumab Spectrum

Feature	IV Mosun Mono (GO40554)	SC Mosun Mono (MorningSun)	M-Pola (mosun + pola)
Study / Phase	Phase 1/2, single-arm	Phase 2 basket	Phase Ib/II, NCT03677154
Population	Elderly/unfit 1L DLBCL	Age ≥80 or 65–79 CIT-ineligible 1L	Elderly/unfit 1L DLBCL
N	22 evaluable	49	108 treated; 90 evaluable
Median Age	~80s	82.5 yrs (71–101)	Elderly/unfit range
Route / Schedule	IV step-up C1; q21d ×8	SC step-up C1; fixed-duration q28d	SC mosun + IV pola 1.8 mg/kg q28d ×6
ORR	63.5%	73.5%	~80% (BOR)
CR Rate	45.5%	59.2%	~61% BOR; 45% EOT
12-mo PFS / OS	Not mature	PFS 71.3% / OS 74.7%	Not yet reported
G3/4 AEs	14%	~65% (manageable)	43%; neutropenia 28%
Serious AEs	None → disc.	Not CRS/infection-driven	41%; CRS 14%, infect. 21%

⚠ **M-Pola COVID-19 signal:** COVID-19 AEs in 10% of patients — underscores infection vulnerability in this immunosuppressed elderly population.

Source: [Olszewski et al. \(GO40554\)](#); [MorningSun \(ASH 2024\)](#); [M-Pola NCT03677154](#)

Emerging Chemo-Free Frontline Regimens

Regimen	Population	ORR / CR	PFS / OS	Key Finding
ZR2 (zanubrutinib+R+len)	≥75 years (Blood 2025)	CR: 65%	2-yr PFS: 67.1% 2-yr OS: 82.4%	Outperforms historical R-miniCHOP
Pola-ZR (pola+zanubrutinib+R)	Median age 73 Frail/elderly	CR: 83%	1-yr OS: 95.8%	Exceptionally high CR in frail
Epcoritamab (EPCORE DLBCL-3)	1L elderly/unfit	ORR: 73%	1-yr PFS: 54%	Continuous dosing; CRS manageable

Paradigm shift: Chemo-free regimens are achieving CR rates of 60–83% in elderly/frail patients. These approaches are rapidly moving into practice and clinical trials.

First-Line Treatment Algorithm – How I do it?

FIT (age 60s-70s)

Adv stage – Pola-R-CHP ×6

- Mandatory G-CSF
- 70-80 – prednisone 60 mg/d

Limited stage – R-CHOP

- Vincristine 1 mg
- PET guided adjustment when possible

UNFIT (age 60+)

R-miniCHP-pola ×6

(standard for >80)

R-pola:

PET2 – intensify?

2 additional doses of ritux

Limited stage – R-mini-CHOP

- Vincristine 1 mg
- PET guided adjustment when possible
- Greater consideration for radiation

FRAIL

R-pola x 6

PET2 – intensify?

- Bispecifics

Best supportive care

Case 2: 88 y/o Male with DLBCL — Presentation

Past Medical History:

- IgG kappa MGUS
- Atrial fibrillation on Eliquis (apixaban)
- CAD s/p stent placement (2014)
- Stage IV CKD — baseline CrCl ~30 mL/min
- Dyslipidemia | Hypertension
- Excised melanoma | Bilateral knee replacement with quadriceps repair

Case 2: Workup & Diagnosis (May–June 2024)

May 2024:

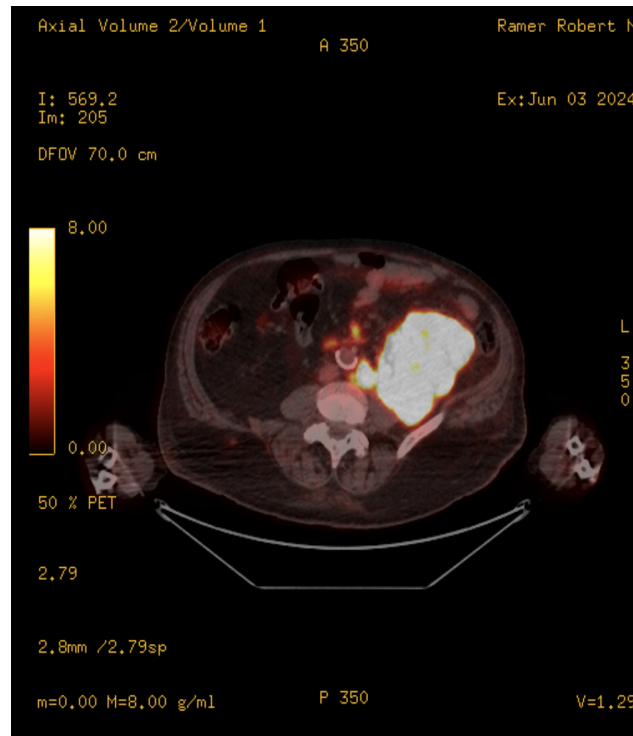
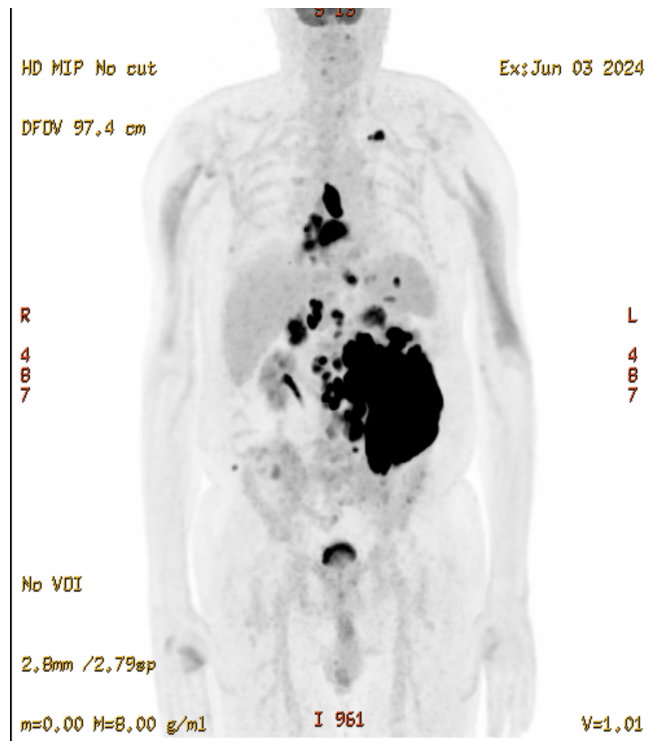
- Weakness → ER: Hgb 6.7 g/dL, PLT 97k, WBC 7.5, Cr 2.1 mg/dL, FOBT (+)
- EGD: 1 cm ulcer with large adherent clot
- CT A/P: 16 × 11.7 cm left retroperitoneal mass extending to L kidney; L periaortic LAD, multiple kidney cysts
- **L retroperitoneal mass biopsy → non-GCB DLBCL**
 - (+) PAX5, CD20 (subset, weak), CD79a, BCL6 (80%), MUM-1 (60%), BCL-2 (90%)
 - FISH: (+) BCL6 rearrangement | Ki67: 95%

June 2024:

- PET/CT: Supraclavicular, mediastinal, retroperitoneal LAD; 13 × 11 cm perinephric mass; gastric fold uptake
- Echo: EF 65–70%, mild-moderate aortic stenosis

Case 2 — Baseline PET/CT (June 2024)

Massive left retroperitoneal/perinephric mass (13 × 11 cm) with extensive nodal disease



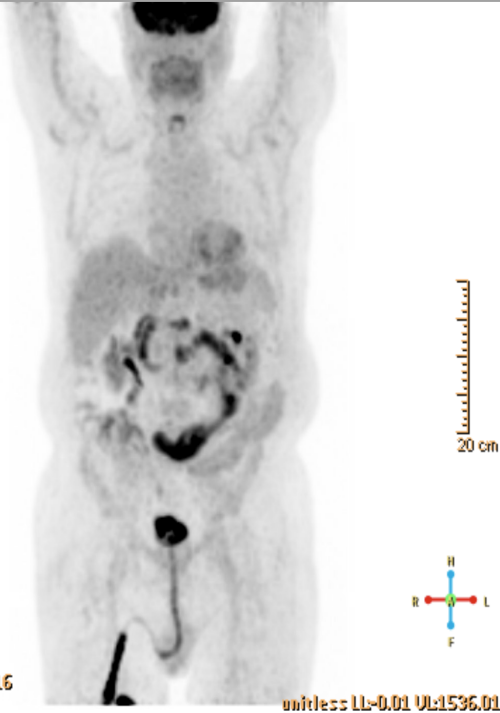
Case #2 – Treatment Course

- Jun 2024: therapy initiated
 - Cycle 1: R-mini-CHOP x1 — admitted with AKI
 - Cycle 2: R-pola — 3-week delay (rehab, COVID)

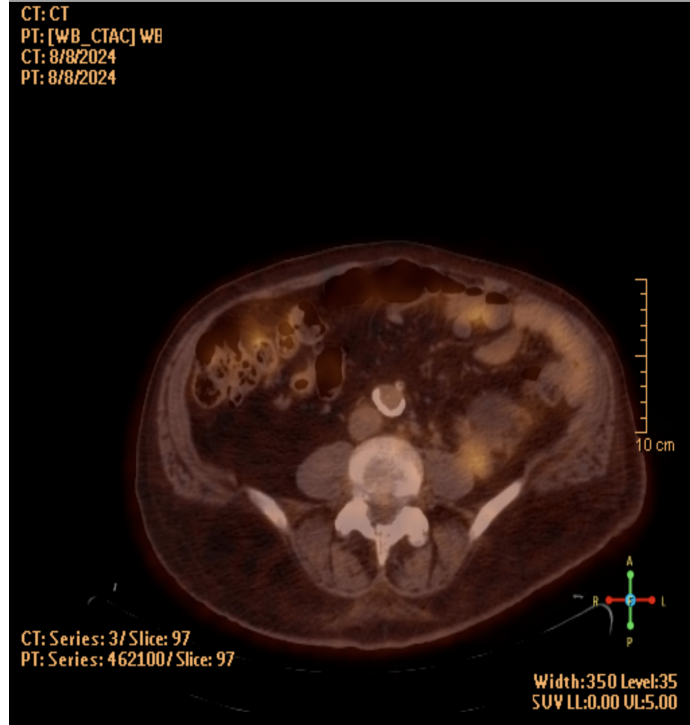
Case 2 — PET2 (August 2024): Deauville 3

After C1 R-mini-CHOP + C2 R-Pola — Deauville 3

[WB_CTAC] WB
8/8/2024



CT: CT
PT: [WB_CTAC] WB
CT: 8/8/2024
PT: 8/8/2024



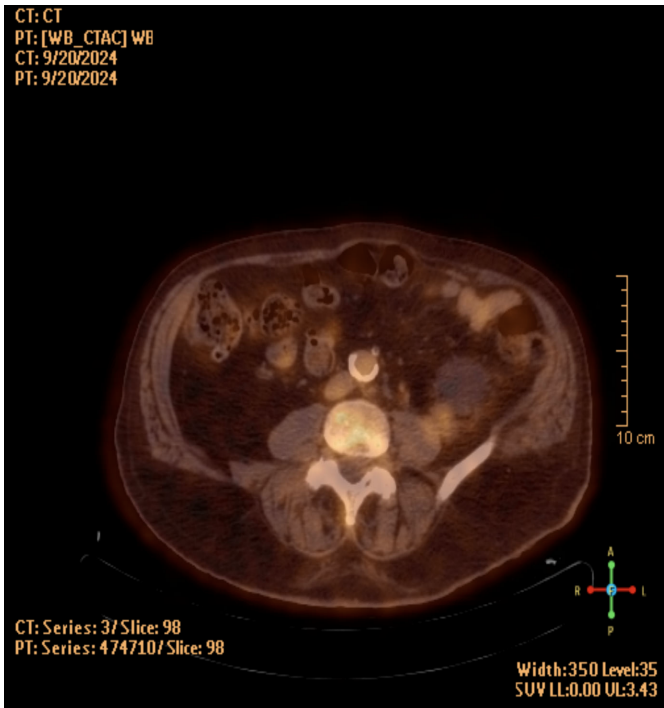
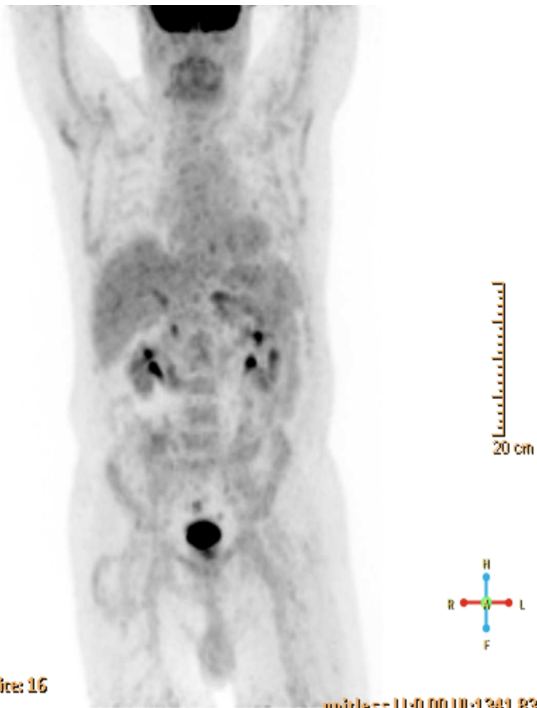
Case #2 – Treatment Course

- Jun 2024: therapy initiated
 - Cycle 1: R-mini-CHOP x1 — admitted with AKI
 - Cycle 2: R-pola — 3-week delay (rehab, COVID)
- Aug 2024 (PET2): Deauville 3
 - Cycles 3-4: R-pola

Case 2 — PET4 (September 2024): Deauville 3, Improving

After C3–C4 R-Pola — Further metabolic improvement; continued response without additional cytotoxics

[WB_CTAC] WB
9/20/2024

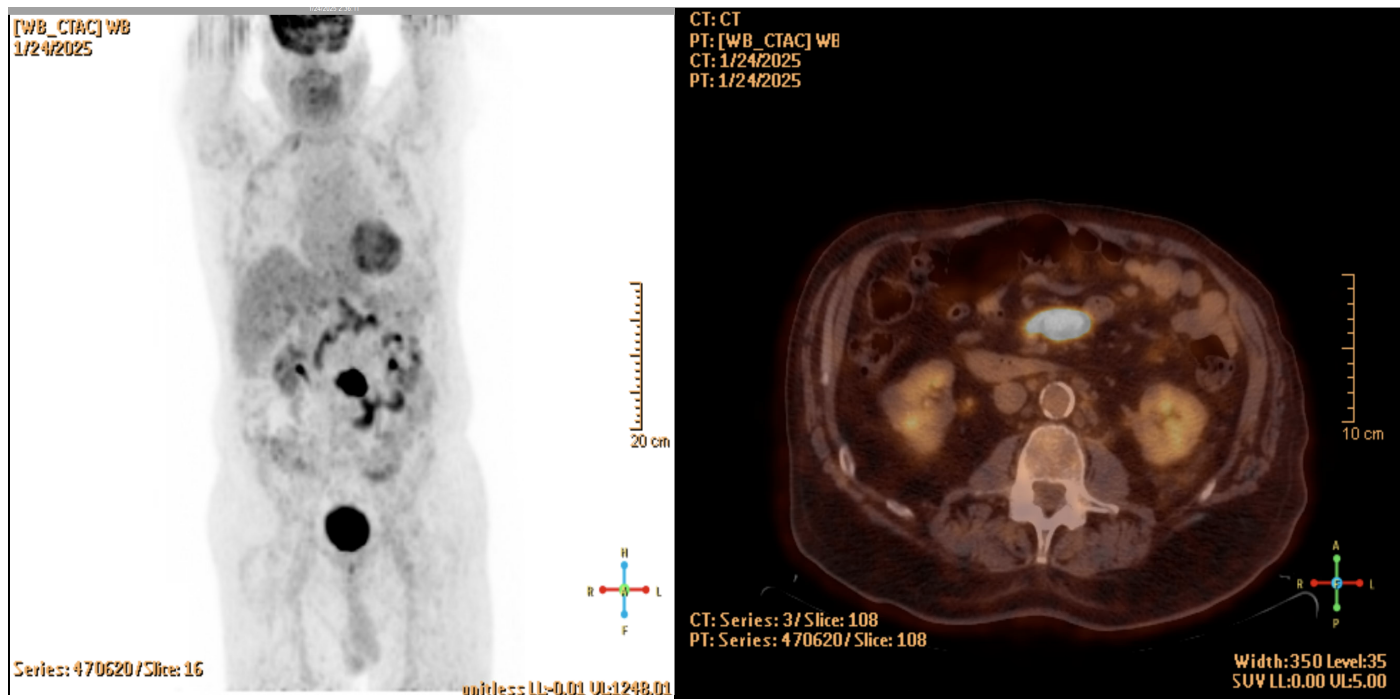


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- Aug 2024 (PET2): Deauville 3
 - Cycles 3-4: R-pola
- Sep 2024 (PET4): Deauville 3, improved — ongoing response
 - Cycles 5-6: R-pola
 - Cycles 7-8: Rituximab

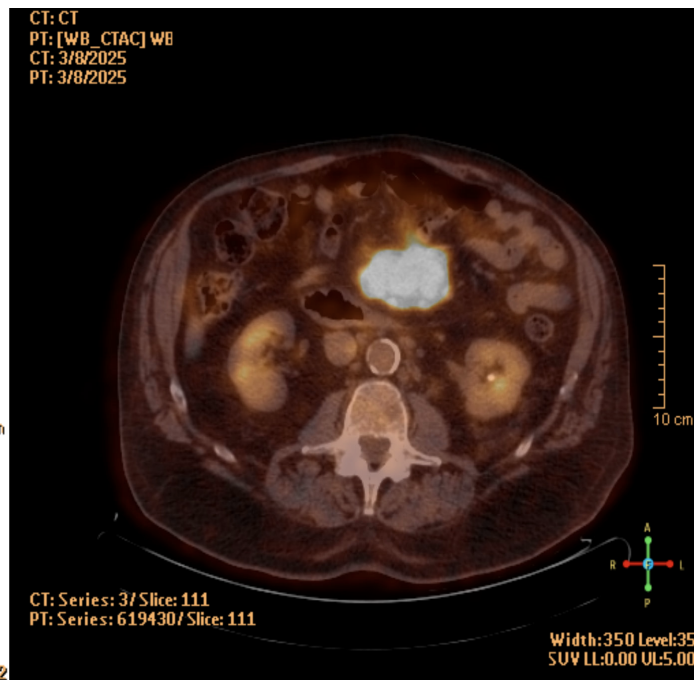
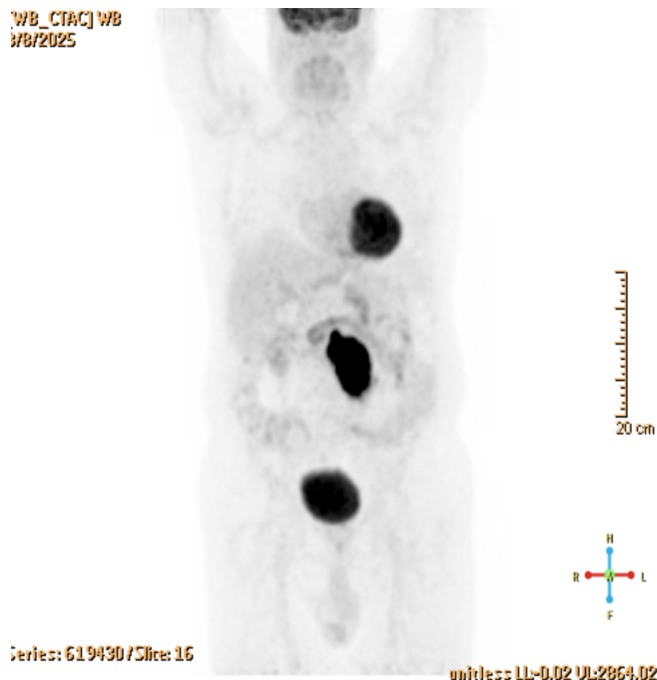
Case 2 — PET8 (January 2025): Progressive Disease?

New FDG-avid masses — suspected progression, but too difficult to biopsy to confirm



Case 2 — Follow-up PET/CT (March 2025): Clear PD

Confirmed progressive disease — multiple large, intensely FDG-avid masses



Case #2 – Treatment Course

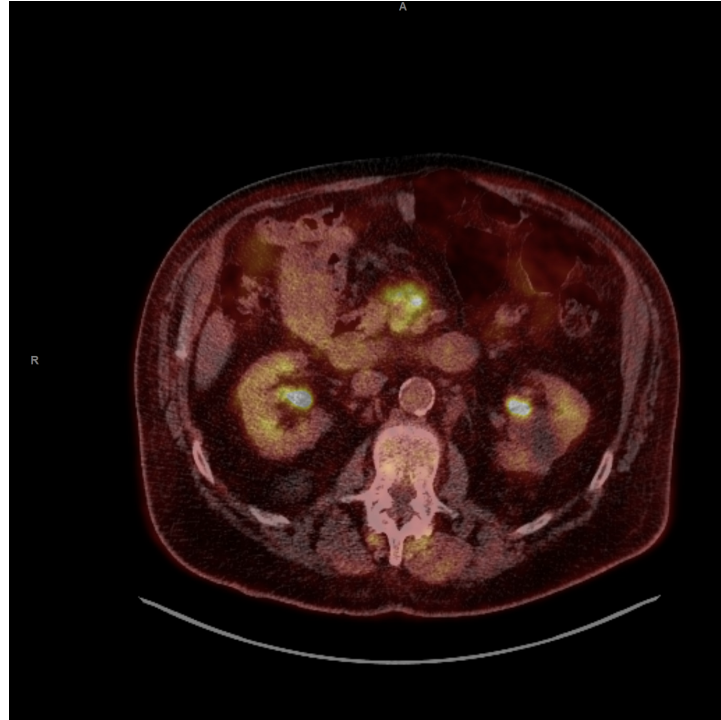
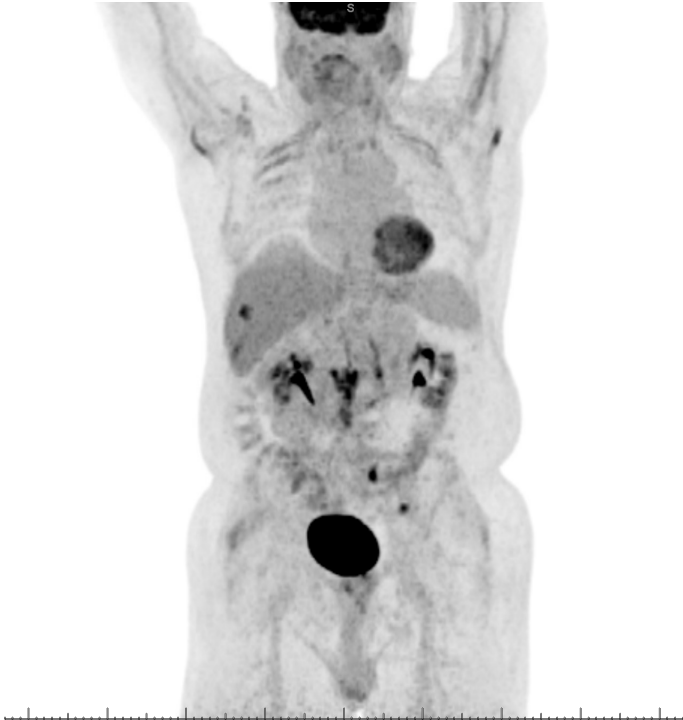
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 - Cycles 3-4: R-pola
- Sep 2024 (PET4): Deauville 3, improved — ongoing response
 - Cycles 5-6: R-pola
 - Cycles 7-8: Rituximab

- Jan 2025 (PET after cycle 8): Possible progression — biopsy too difficult
- Mar 2025 (Follow-up PET): Clear progression — disease relapse confirmed

- Mar 2025: mosunetuzumab

Case 2 — PET2 (April 2025): Deauville 4 PR

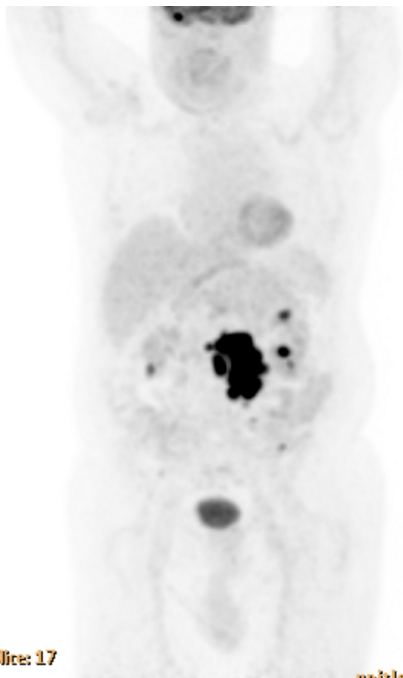
Significant clinical and radiologic response



Case 2 — PET5 (June 2025): PD

Clear disease progression

[WB_CTAC] WB
6/24/2025



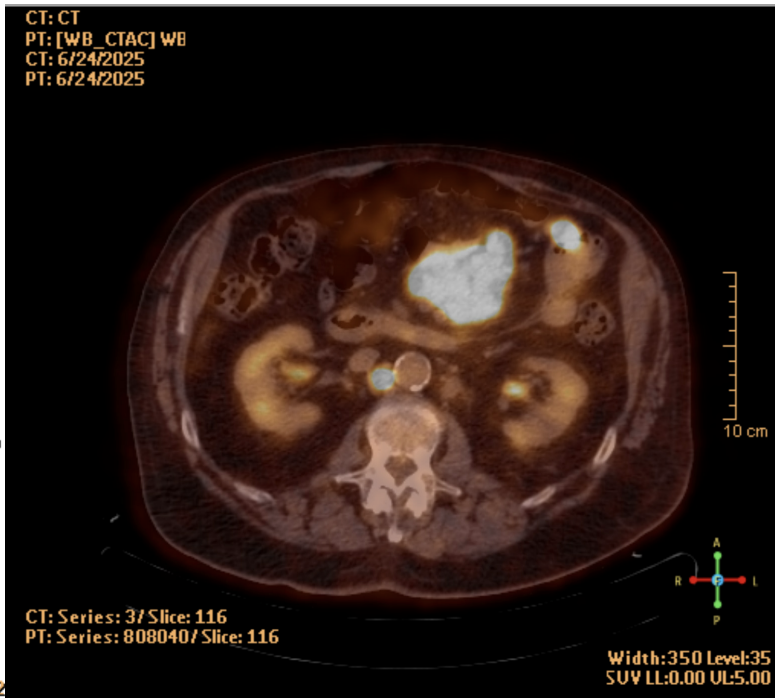
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10 cm



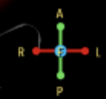
CT: CT
PT: [WB_CTAC] WB
CT: 6/24/2025
PT: 6/24/2025



CT: Series: 3 / Slice: 116
PT: Series: 808040 / Slice: 116

Width: 350 Level: 35
SUV LL: 0.00 UL: 5.00

10 cm



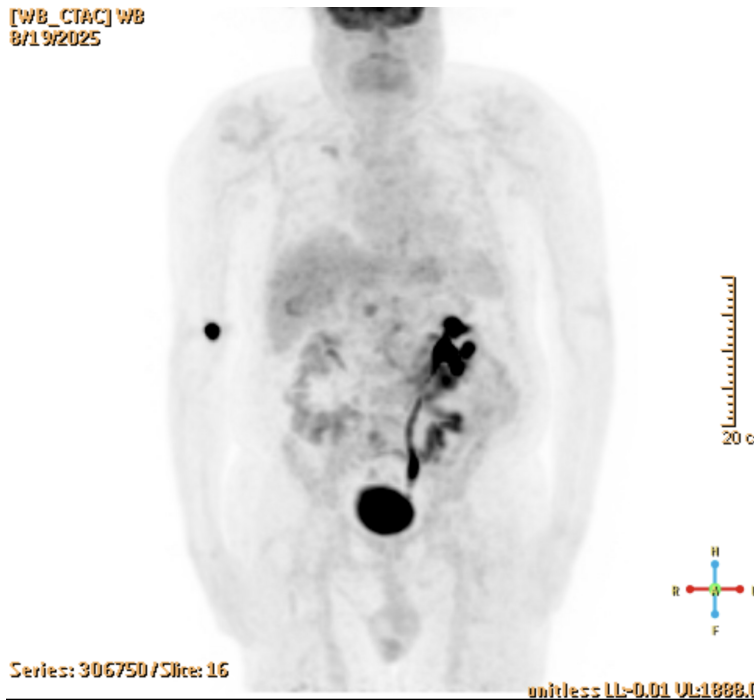
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- Mar 2025 (Follow-up PET): Clear progression — disease relapse confirmed
- Mar 2025: mosunetuzumab x 6
 - April 2025 - PET2 - Deauville 4 PR
 - June 2025 - PET5 - PD
- July 2025 - loncastuximab

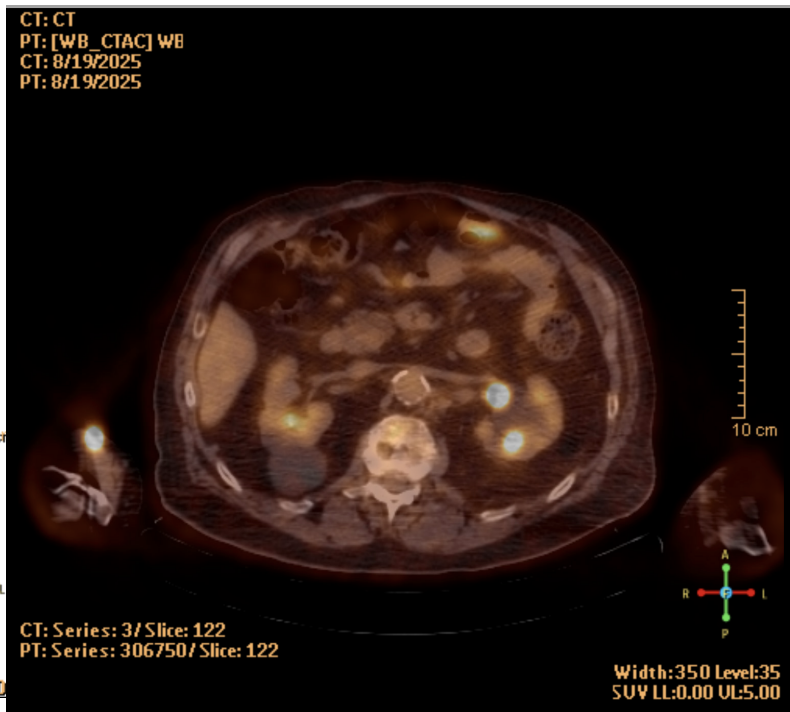
Case 2 — PET2 (August 2025): Deauville 3 CR

Complete metabolic response with excellent tolerability

[WB_CTAC] WB
8/19/2025



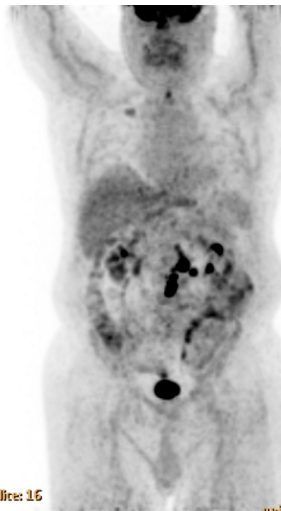
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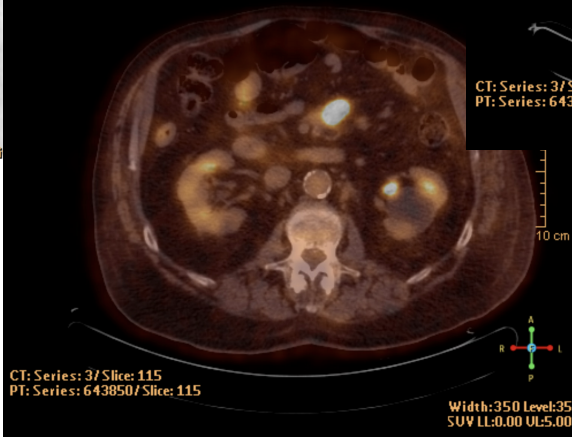
Case 2 — PET5 (October 2025): PD

Fast progression with fast decline

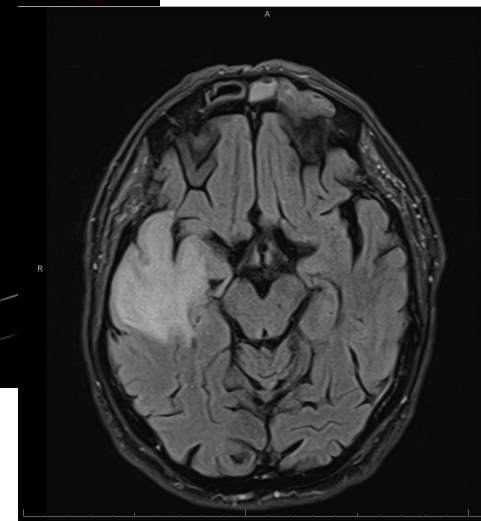
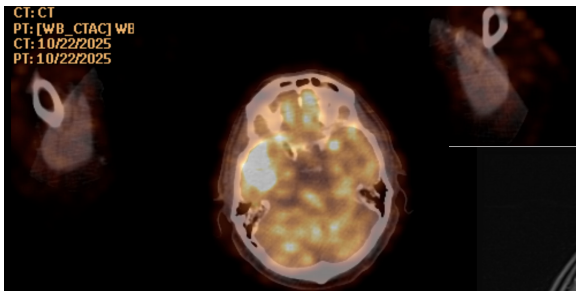
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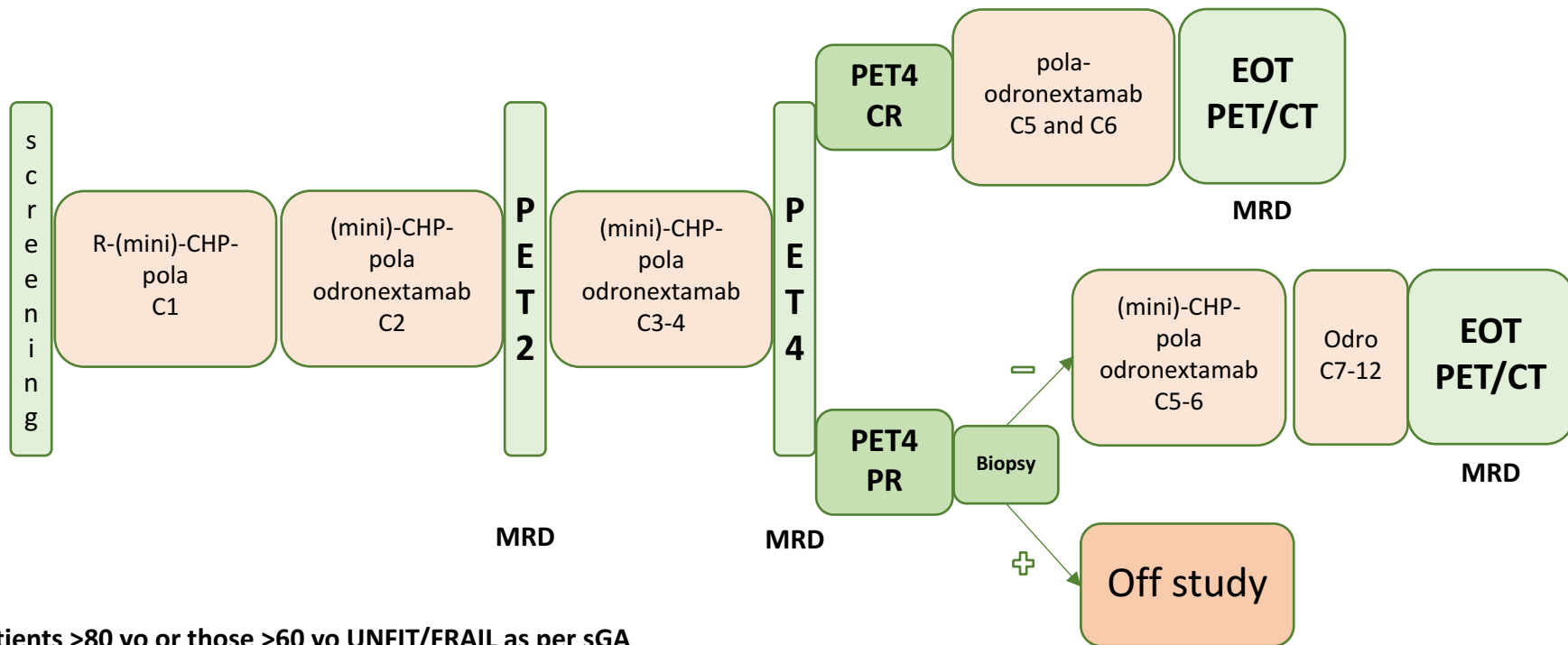
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PT: 10/22/2025



Frontline study in >60-year-old with DLBCL



Patients >80 yo or those >60 yo UNFIT/FRAIL as per sGA



SECTION

Relapsed/Refractory DLBCL

Management When Standard Therapy Fails

The Challenge: R/R DLBCL in the Elderly

The problem:

- ~40% of elderly DLBCL patients relapse or are refractory to first-line therapy
- Most elderly patients are NOT candidates for autologous stem cell transplant (ASCT)
- Historical median OS for transplant-ineligible R/R DLBCL: ~6 months

The good news:

Multiple new therapeutic options have transformed the R/R landscape:

- CAR-T cell therapy (even in selected elderly patients)
- Bispecific antibodies (glofitamab, epcoritamab, mosunetuzumab)
- Antibody-drug conjugates (polatuzumab vedotin, loncastuximab tesirine)
- Targeted combinations (tafasitamab + lenalidomide)

CAR-T Cell Therapy: Age Is Not a Contraindication

Key message: Older patients CAN receive CAR-T with good outcomes

Study	Product	Elderly Data	Key Results
ZUMA-7 (2L)	Axi-cel	≥65 years subgroup	EFS 21.5 vs 2.5 mo (vs SoC) CR 75%
PILOT (2L)	Liso-cel	Median age 74 46% were ≥75y	ORR 80%, CR 54% DCR not reached
TRANSCEND (3+L)	Liso-cel	Transplant-ineligible	Lowest CRS/ICANS rates Preferred in elderly

Considerations in elderly:

- Liso-cel preferred for older patients due to lower CRS/ICANS rates
- Geriatric assessment before CAR-T essential (fitness, cognition, caregiver)
- Higher ICANS risk in elderly (but similar CRS)
- No formal upper age limit — fitness matters more than age
- Attempt to have some disease control

Source: [ZUMA-7, Locke et al. NEJM 2022](#); [PILOT, Sehgal et al. Lancet 2024](#)

Bispecific Antibodies in R/R DLBCL

Agent	Trial	ORR / CR	Durability	Key Feature
Glofitamab	Phase I/II	52% / 39%	12-cycle fixed duration	Fixed duration (stops at 12 cycles)
Epcoritamab	EPCORE NHL-1 (3-yr data)	59% / 41%	53% of CR patients PFS at 3 years	SC; durable CRs; continuous dosing
STARGLO (glofit+GemOx)	Phase III (63% ≥65y)	85% / 61%	OS 25.5 vs 12.9 mo vs R-GemOx	OS benefit proven in phase III

Advantages for elderly patients:

- No chemotherapy backbone required (can be used as single agents)
- Manageable CRS (mostly grade 1–2, limited to first doses)
- Outpatient administration feasible (especially epcoritamab SC)
- No age-related efficacy differences in subgroup analyses
- Key option for patients not eligible for CAR-T

Other R/R Options for Elderly DLBCL

Agent	Trial	ORR / CR	Median OS	Elderly Note
Loncastuximab tesirine	LOTIS-2	48% / 25%	9.5 mo	≥70y: better PFS (7.4 vs 3.8 mo)! No CRS/ICANS Issue with steroids
Tafasitamab + lenalidomide	L-MIND	60% / 43%	33.5 mo	Median age 72; best for 2L non-primary refractory
Pola-BR	GO29365	63% / 53%	12.4 mo	68% of cohort ≥65y; well tolerated
Selinexor	SADAL	28%	9 mo	Limited role; generally de-favored vs bispecifics

Source: [GO29365, Sehn et al.](#); [LOTIS-2, Caimi et al. Lancet Oncol 2021](#); [L-MIND, Salles et al.](#)

R/R DLBCL in Elderly: Treatment Algorithm

Step 1: Fitness Assessment

- Fit for CAR-T? (geriatric assessment, cognition, caregiver, logistics)

Step 2: If CAR-T eligible

- Liso-cel preferred in elderly (≥ 70 –75y) for lowest CRS/ICANS profile
- Axi-cel preferred for response

Step 3: If NOT CAR-T eligible

- Bispecific antibody (glofitamab or epcoritamab) — best data, durable responses
- Tafasitamab + lenalidomide for 2L non-primary refractory (no CRS/ICANS)
- Loncastuximab tesirine (outpatient, no CRS, good in ≥ 70 y)

At all stages: Clinical trial participation strongly recommended

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SECTION

Summary and Conclusions

Key Takeaways for Clinical Practice

Key Takeaways

- 1. Assess fitness, not just age:** sGA (FIL), hand grip, TUG, polypharmacy assessment before decision
- 2. Match treatment to fitness:** Intensity vs exposure, early 2L
- 3. Don't add toxicity:** more likely to replace than add.
- 4. Bispecifics are changing the landscape:** chemo-free options with 60–74% ORR in the very elderly
- 5. CAR-T is not age-limited:** Liso-cel preferred in elderly for R/R; geriatric assessment essential
- 6. Enroll in clinical trials:** Elderly patients remain underrepresented. Every patient should be considered for trial enrollment.

BY THE WAY...

Case #1 End-of-Treatment PET

That 88-year-old with 11 comorbidities, AKI, hypercalcemia, and a VP shunt



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Thank You

Questions?

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