



# The young side of **LYMPHOMA**

gli under 40 a confronto

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## **Ruolo della radioterapia nel trattamento del DLBCL dell'anziano**

Fabio Matrone

*Division of Radiation Oncology  
Centro di Riferimento Oncologico di Aviano CRO IRCCS  
Aviano (PN), Italy*



**Disclosures of Fabio Matrone**

| Company name | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
|--------------|------------------|----------|------------|-------------|-----------------|----------------|-------|
| none         |                  |          |            |             |                 |                |       |
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## An 82-years-old man with DLBCL



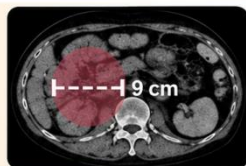
**82 years old**  
Fully independent  
ECOG PS 1



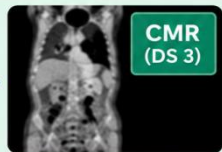
Relevant  
**cardiovascular**  
comorbidity



**Stage II DLBCL**  
Abdominal bulky disease:  
**9 cm**  
LDH normal  
No extranodal involvement  
**R-IPI 1**



**4 cycles of R-COMP**  
(rituximab + cyclophosphamide,  
vincristine, prednisone +  
liposomal doxorubicin)  
Good response to treatment



**Progressive fatigue**  
and **declining**  
treatment **tolerance**



Ongoing clinical  
concerns related  
to comorbidity



Hematologist is **reluctant** to deliver  
further anthracycline-containing therapy

## What would you do next?

- A. Complete 6 cycles of R-COMP
- B. Stop systemic therapy and give ISRT
- C. Stop treatment and observe
- D. Individualize according to frailty/comorbidity

## Age is not the question. Fitness is.

| <b>FIT</b>                                  | <b>UNFIT</b>                     | <b>FRAIL</b>                              |
|---------------------------------------------|----------------------------------|-------------------------------------------|
| Standard curative approach                  | Adapt treatment intensity        | Individualized goals                      |
| Full-dose systemic therapy<br>when feasible | Dose-adapted systemic<br>therapy | Attenuated / symptom-<br>oriented therapy |
| RT = selective                              | RT = selective                   | RT = selective                            |

## Chronological age $\neq$ biological age

*Comorbidity • functional status • cognition • nutrition • social support*

Tucci A et al. Leuk Lymphoma. 2015;56:921–926.  
Thieblemont et al. HemaSphere 2025; 9:e70207.

## Why may RT matter MORE in older patients?

**LESS systemic treatment tolerance**

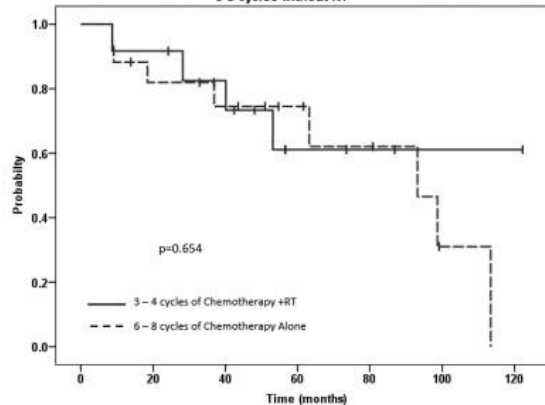


**FEWER salvage opportunities**



**HIGHER value of durable local control**

PFS Among Early Stage Patients Treated with 3-4 cycles of chemotherapy with RT versus 6-8 cycles without RT



3-year PFS: 82.5% vs 81.9%;  $p=0.654$

### What do we know in the very elderly?

DLBCL patients  $\geq 80$  years

$n = 131$  | median age 83

Early-stage subgroup:

3-4 cycles chemotherapy + RT ( $n=12$ )

vs

6-8 cycles chemotherapy alone ( $n=17$ )

→ No significant difference in DFS, PFS or OS

Retrospective analysis — hypothesis-generating

## RT may be treatment-sparing — not simply treatment-adding.

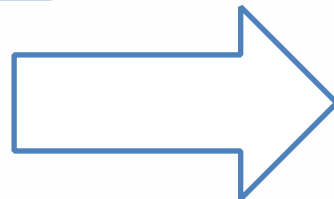
Pinnix CC et al. Adv Radiat Oncol. 2017;2:370-380.

Parikh RR, Yahalom J. Leuk Lymphoma. 2017;58:614-622.

## Early-stage DLBCL: when can we safely omit RT?

### EVIDENCE FOR OMISSION

- **FLYER** (*Poeschel et al. Lancet 2019*)  
4 × R-CHOP  
Young, favorable, non-bulky patients
- **Excellent outcomes without RT**
- **S1001** (*Persky et al. J Clin Oncol 2020*)  
PET-adapted strategy  
3 R-CHOP → iPET-negative → R-CHOP, no RT
- **Excellent long-term disease control**



### THE ELDERLY GAP

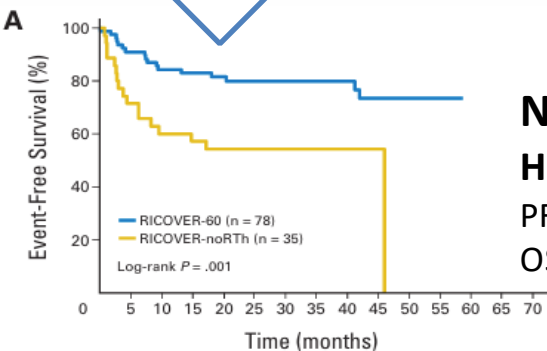
- ≥80 years
- Bulky disease
- Reduced chemotherapy tolerance

**Can we extrapolate these de-escalation strategies to our 82-year-old patient?**

# Bulky disease: is SIZE alone enough to prescribe RT?

## THEN

- **RICOVER-60** (Held G et al. J Clin Oncol. 2014;32:1112–1118).
- 61-80 years 6 x R-CHOP-14 + 2R  
Bulky  $\geq 7.5$  cm  
 $\pm$  IFRT 36 Gy



**PET changed the question**

**No RT  $\rightarrow$  worse EFS**  
**HR 2.1 (95% CI 1.3–3.5),  $p=.005$**   
PFS: HR 1.8,  $p=.058$   
OS: HR 1.6,  $p=.127$

## NOW

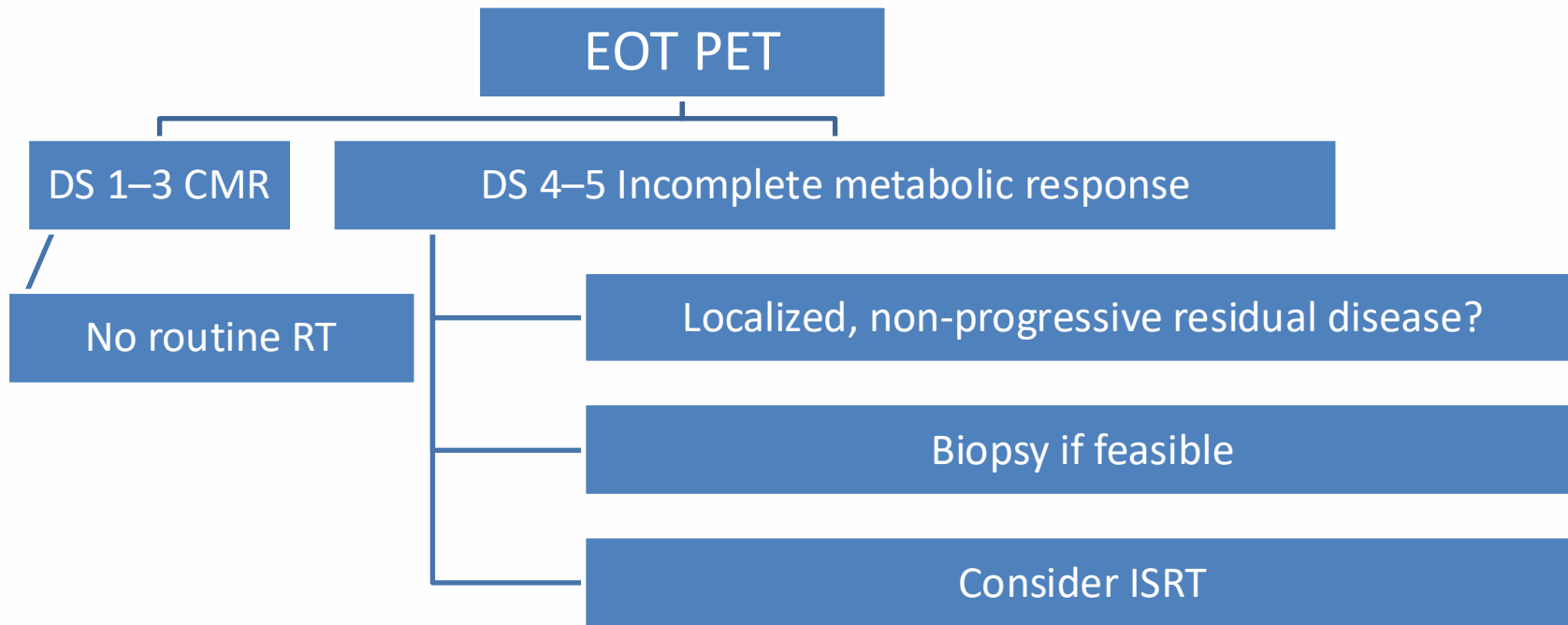
- Baseline bulk  
+
- Metabolic response

## Who actually needs RT?

- Bulk identifies risk
- PET may identify residual risk

Thieblemont et al. HemaSphere 2025; 9:e70207.

## EOT PET-positive: systemic failure or local opportunity?



**PET should help SELECT RT — not simply predict prognosis.**

Freeman CL et al. Blood. 2021;137:929–938.

Thieblemont et al. HemaSphere 2025; 9:e70207.

# Frail ≠ palliative

## WHAT IS THE GOAL?

| GOAL                     | WHEN                                     | RT APPROACH                  |
|--------------------------|------------------------------------------|------------------------------|
| Selected curative intent | Highly selected localized disease        | Individualized definitive RT |
| Durable local control    | Limited systemic options                 | Short-course RT              |
| Symptom control          | Advanced disease/limited life expectancy | Very short / low-dose RT     |

**Match RT intensity to the patient's goal — and reserve.**

Lugtenburg PJ, Mutsaers PGJ. Blood. 2023;141:2566–2575.

Yahalom J et al. Blood. 2020;135:1829–1832.

Tucci A et al. Leuk Lymphoma. 2015;56:921–926.

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Stopping CT+ISRT is a reasonable treatment-sparing option

Not PET-driven. Patient-driven.



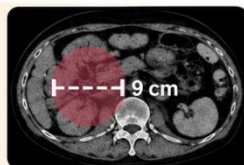
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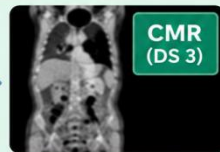
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## TAKE-HOME MESSAGES

### 1. Age alone should never drive RT decisions

- *Fitness, disease biology and systemic treatment tolerance matter.*

### 2. RT should be selective, not routine

- *Bulk identifies risk – metabolic response refines treatment selection.*

### 3. RT can be part of a treatment-sparing strategy in selected older patients

- *Treatment tailoring ≠ therapeutic nihilism. It means using RT smarter, not necessarily more.*

**“Less treatment” or “smarter treatment”?**

Thurner L et al. Hematol Oncol. 2025;43(S3):43(S3):e157\_70093.

Thieblemont C et al. HemaSphere. 2025;9:e70207.