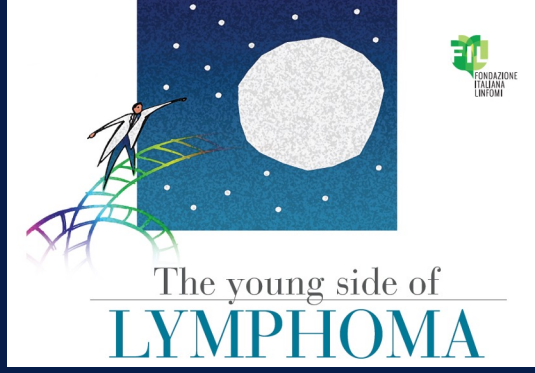



# DLBCL TALK: efficacia e gestione di epcoritamab nella pratica clinica italiana nei pazienti recidivati refrattari

Dott. Francesco Malaspina

IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) "Dino Amadori",
Meldola, Italy

CODICE VEEVA: IT-TDLBCL-250059

# DISCLOSURES

**Relevant Financial Relationships**:

- employed as an hematologist at IRCCS IRST “Dino Amadori”, Meldola (FC), Italy
- received compensation from Sobi
- received compensation from Abbvie

**Relevant Non-Financial Relationships**:

- member of the Medical-Scientific Board of IRCCS IRST “Dino Amadori”

# 3L+ DLBCL Treatments: the Dilemma

CAR-T Naive and Eligible?

yes

- Axi-Cel
- Liso-Cel
- Tisa-Cel

± bridge therpay

no

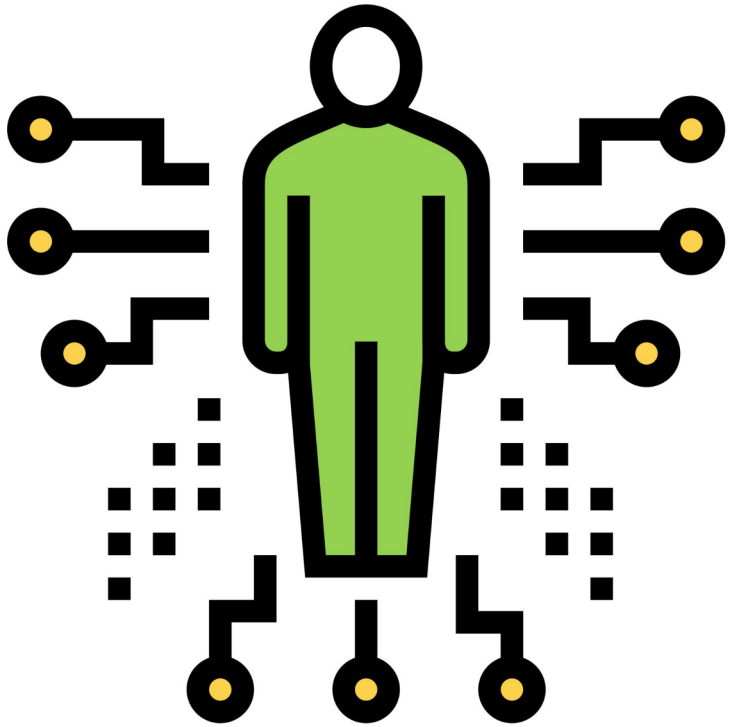
- Tafa-Len
- Lonca
- R-Pola-Benda
- Glofitamab
- Epcoritamab
- CIT (R-Gemox, R-ICE, R-Benda, etc…)
- ASCT and HSCT
- Clinical Trials

# A Case for Bispecifics

2016 - 35, M

Non fumatore

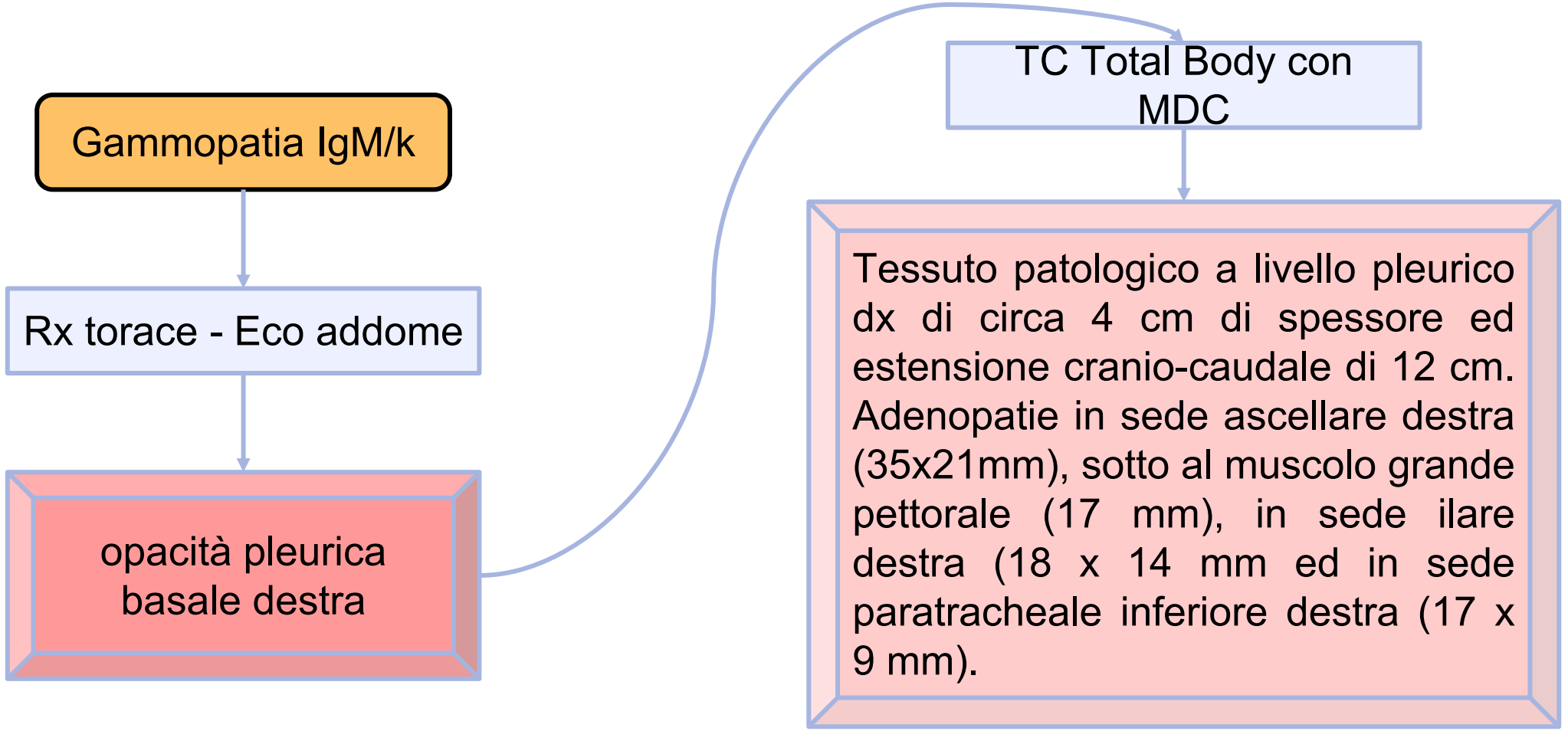
Non allergie note



Sempre in ABS

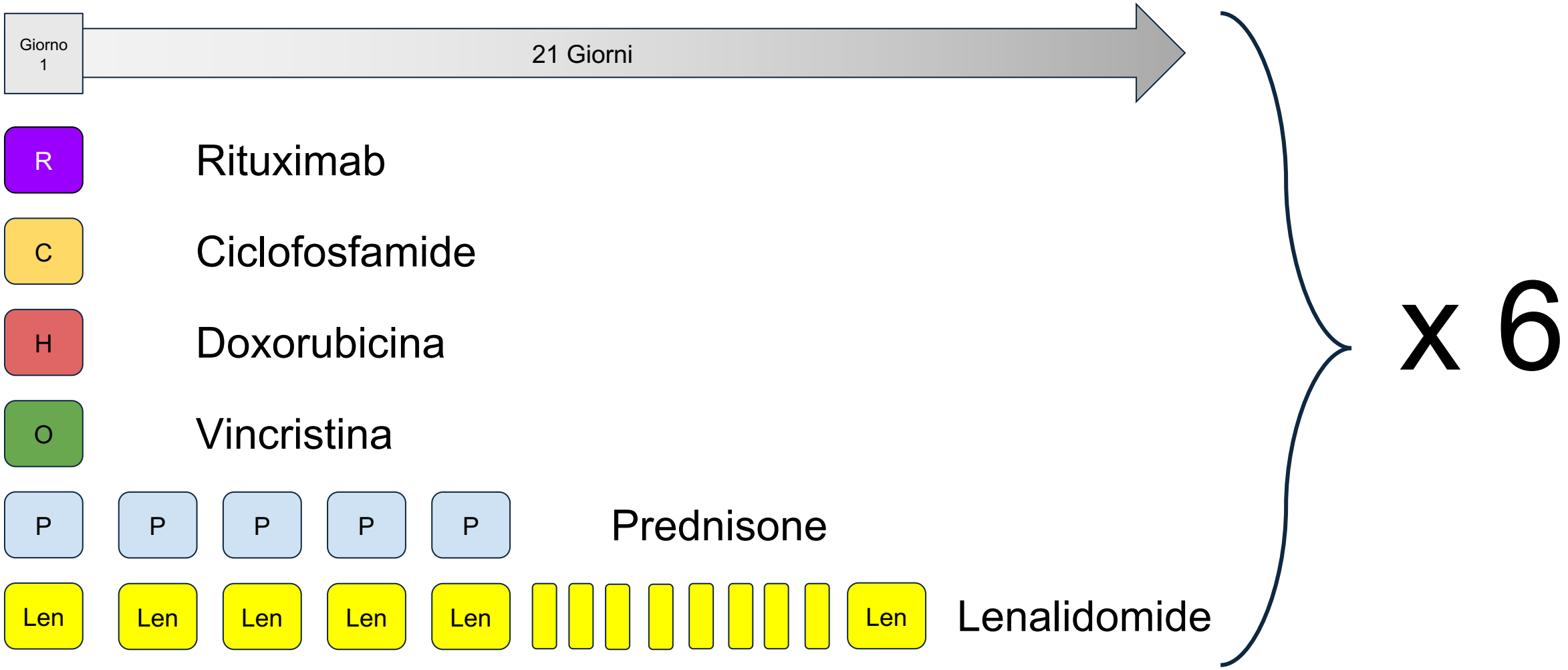
Nessuna terapia domiciliare cronica

# Esordio

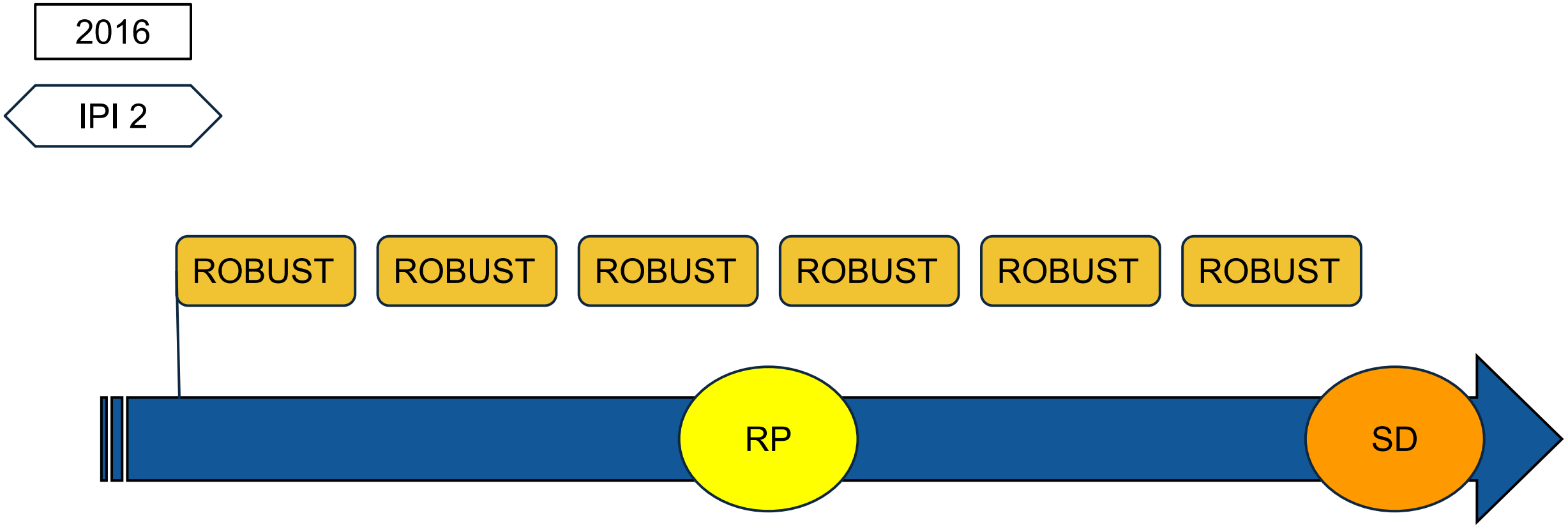

Gammopatia IgM/k
Rx torace - Eco addome
opacità pleurica basale destra
TC Total Body con MDC
Tessuto patologico a livello pleurico dx di circa 4 cm di spessore ed estensione cranio-caudale di 12 cm. Adenopatie in sede ascellare destra (35x21mm), sotto al muscolo grande pettorale (17 mm), in sede ilare destra (18 x 14 mm ed in sede paratracheale inferiore destra (17 x 9 mm).

# Protocollo ROBUST

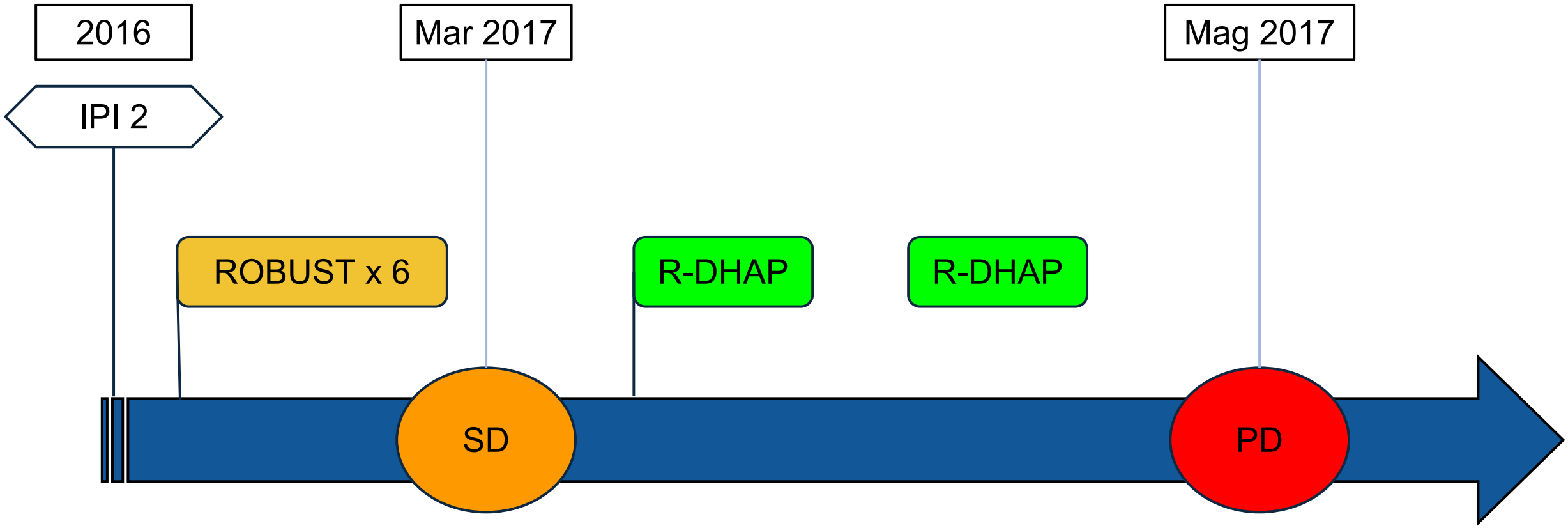




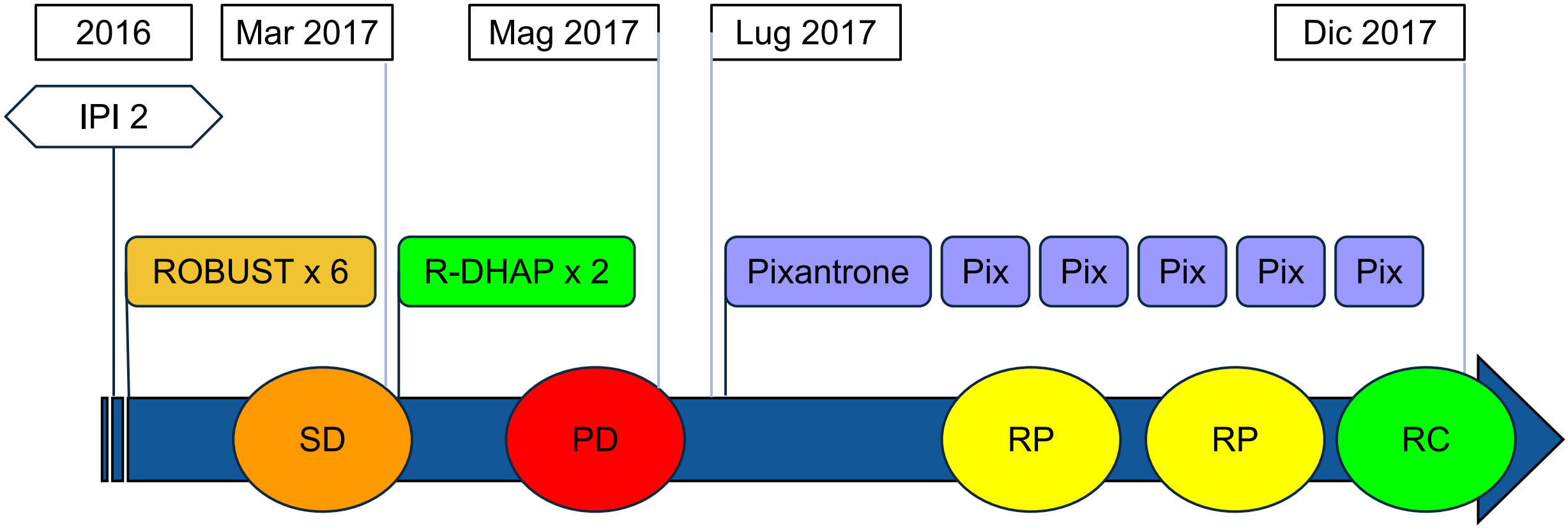
# Terapia e risposta alla I Linea



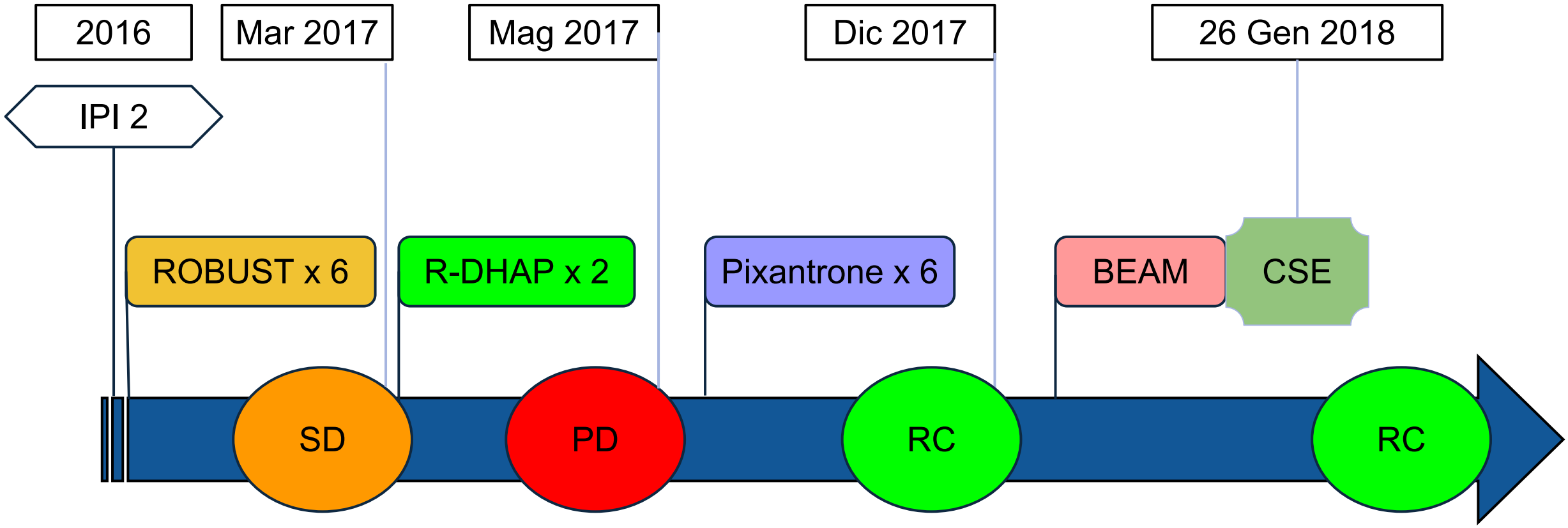
# Terapia e risposta alla II Linea



# Terapia e risposta alla III Linea



# Terapia e risposta alla III Linea



# Recidiva



Ottobre 2024

Comparsa di epigastralgia da circa 3 mesi

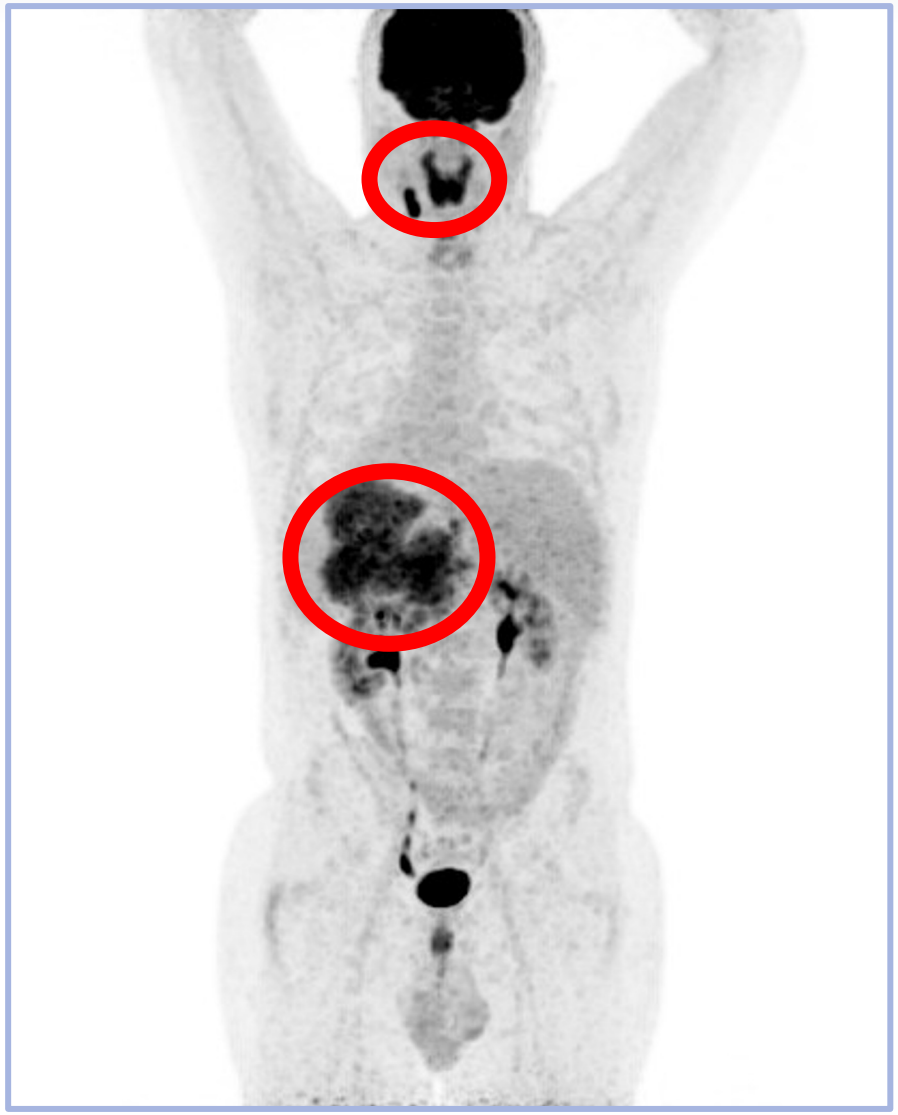
Calo ponderale di 10 Kg in 6 mesi

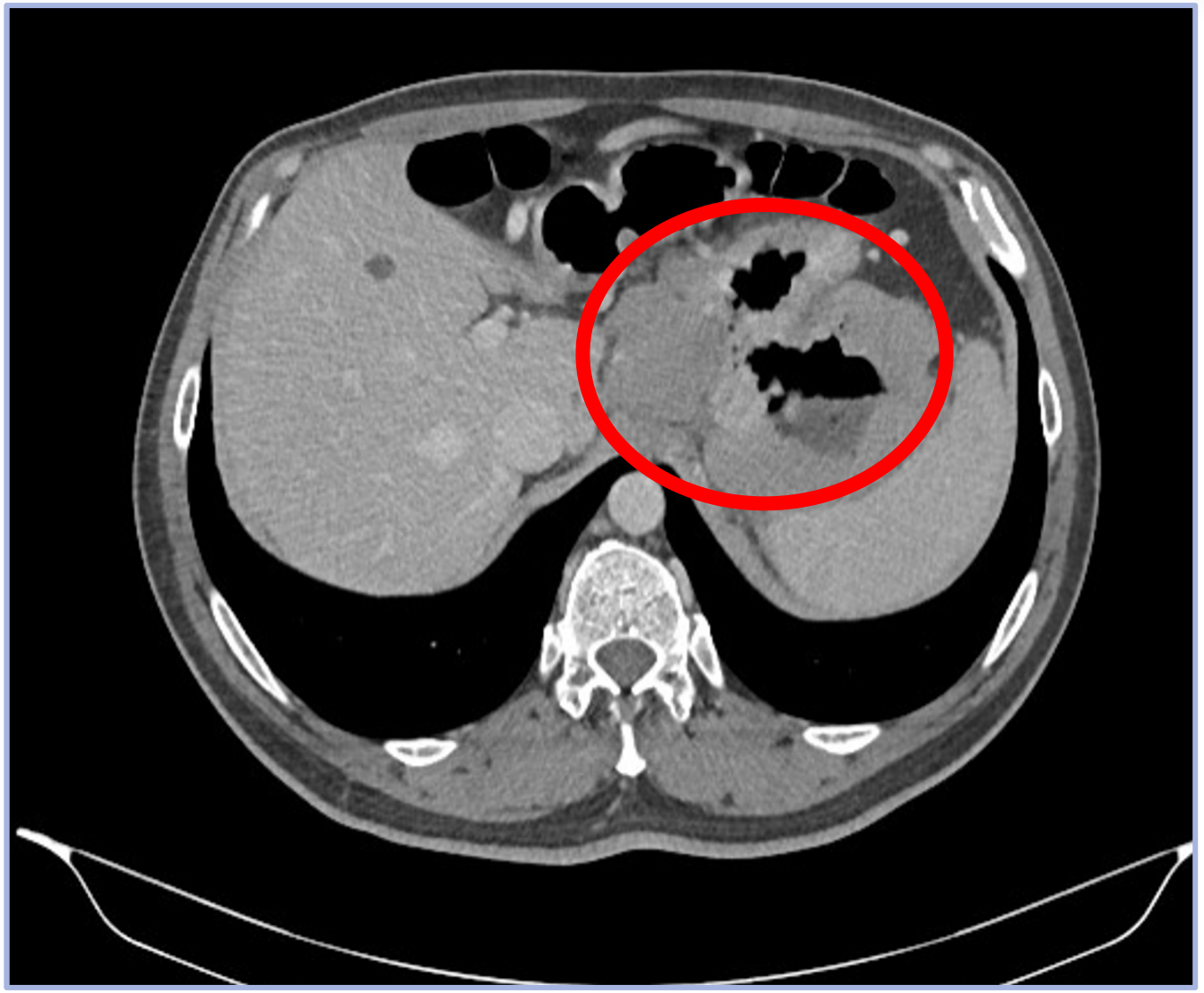
Stomaco: al fondo e al corpo prossimale, versante grande curva e parete anteriore, presenza di voluminosa ulcera a fondo fibrinoso di circa 5-6 cm con bordi rilevati ed irregolari e coagulo adeso sul fondo della lesione

Localizzazione gastrica di linfoma B a grandi cellule.
Alle indagini immunoistochimiche le cellule neoplastiche sono risultate positive per CD20 e Bcl2 con focale espressione di Bcl6, Mum1 e CD10 e negative per CD30, EBV. c-Myc presente nel 30% degli elementi. ki67 60%.
Riarrangiamento di MYC (regione 8q24): ASSENTE

# Caratteristiche malattia alla recidiva





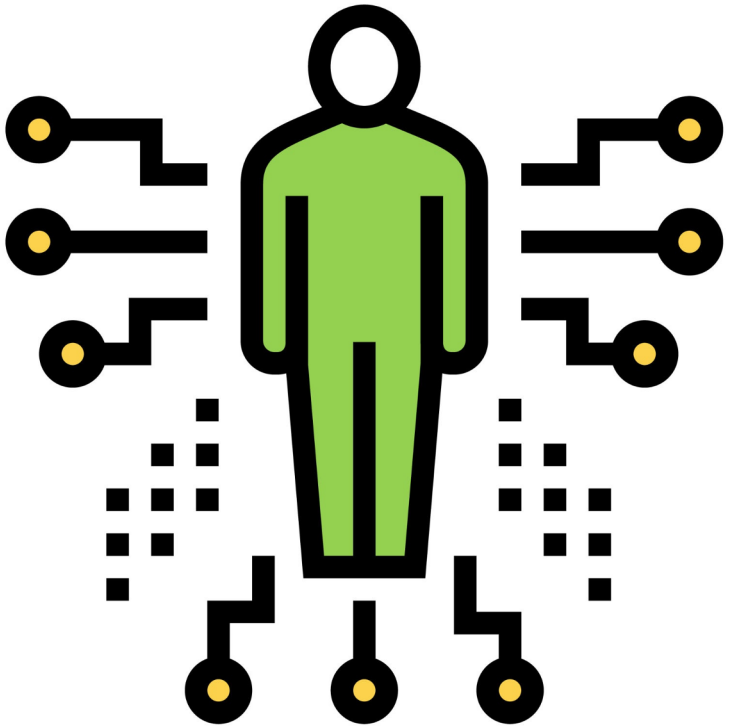


# Caratterizzazione del paziente alla recidiva

2024 - 43, M

Non fumatore

Allergia: allopurinolo, cefazolina, trimetoprim / sulfametoxazolo



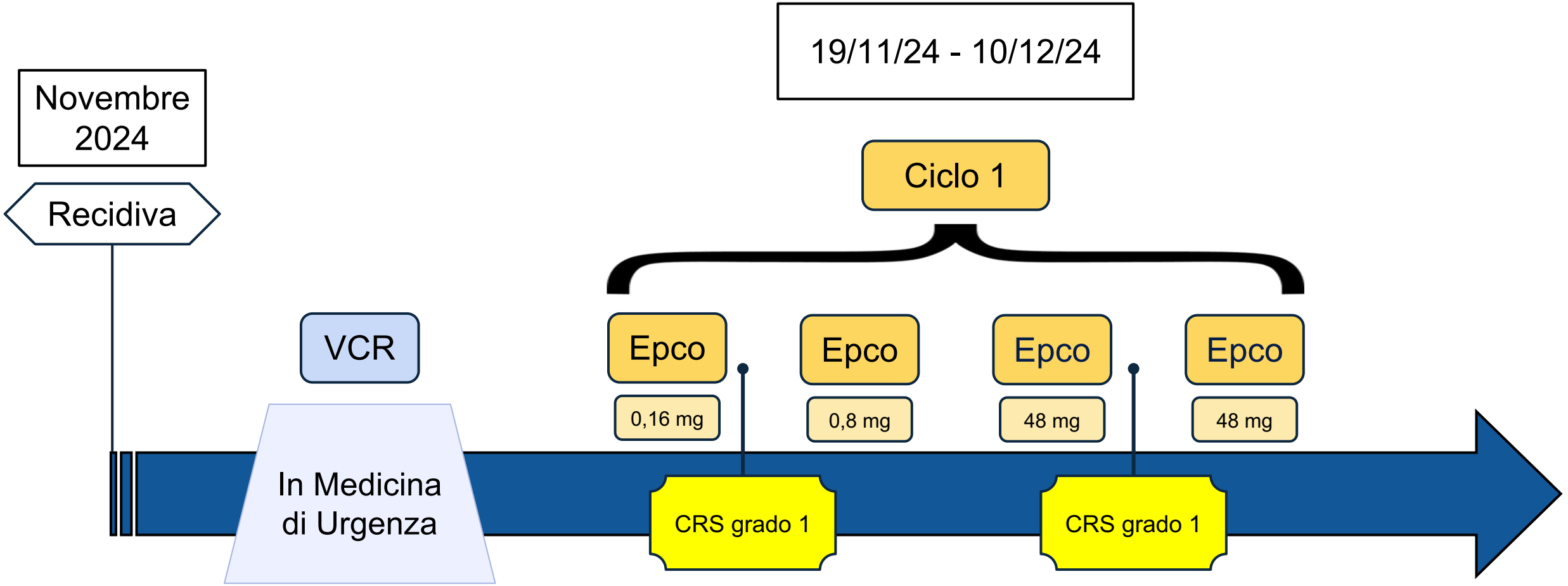
2018: Exeresi granuloma piogenico ginocchio dx

2018: Tiroidectomia per adenocarcinoma tiroide

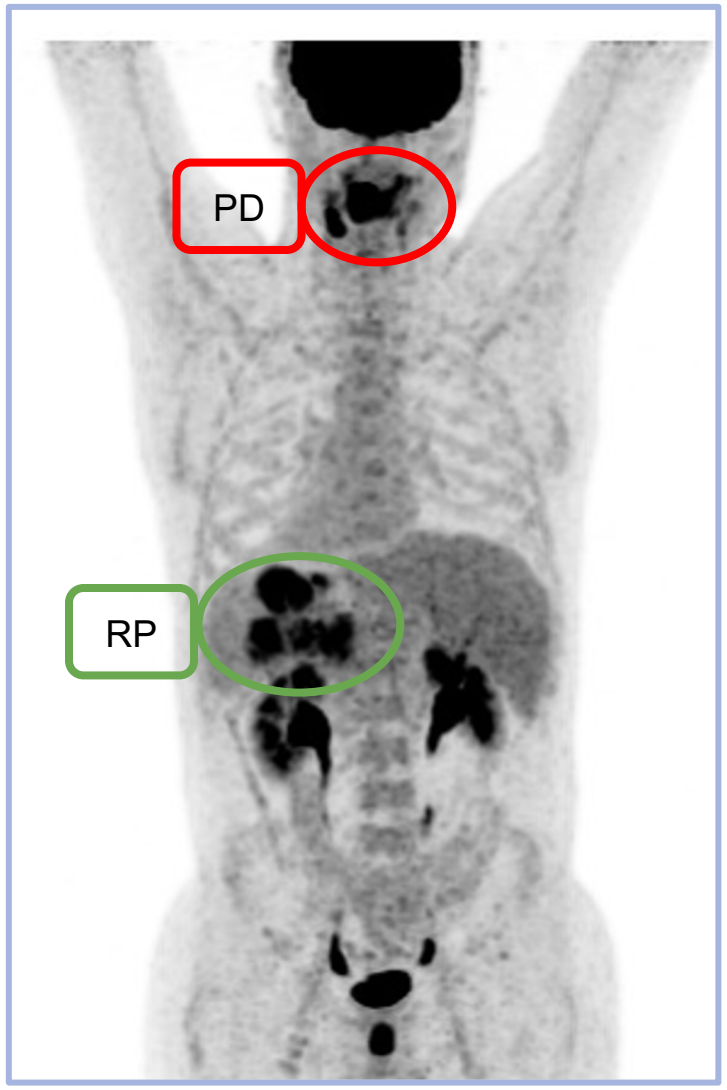
2024: mononucleosi

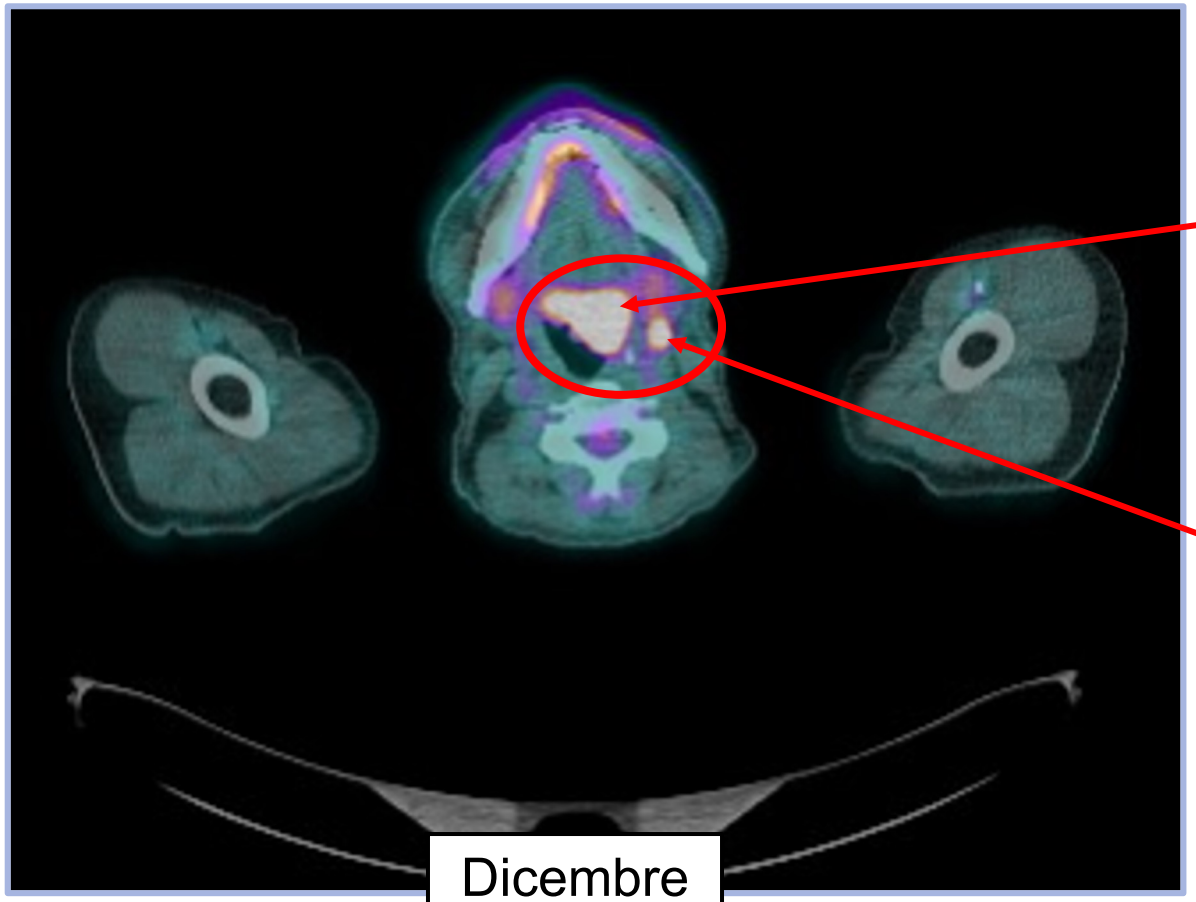
Nessuna terapia domiciliare cronica


TREATMENT CHOICE
3L+ R/R DLBCL
POLATUZUMAB-BR
CD79b ADC
TAFA-LEN
CD19 Ab/IMID
AXI-CEL/TISA-CEL
CAR T-CELL THERAPY
GEMOX/R-ICE
CHEMO-IMMUNOTHERAPY
LONCA
CD19 ADC
OTHER TRIALS
CLINICAL STUDIES
SELECT YOUR FIGHTER
START


19/11/24 - 10/12/24
Novembre 2024
Recidiva
Ciclo 1
VCR
Epco
0,16 mg
Epco
0,8 mg
Epco
48 mg
Epco
48 mg
In Medicina di Urgenza
CRS grado 1
CRS grado 1

# +1 mese



SUVmax = 26.6
prec. = 16.5

SUVmax=20.8
prec. = 16.5

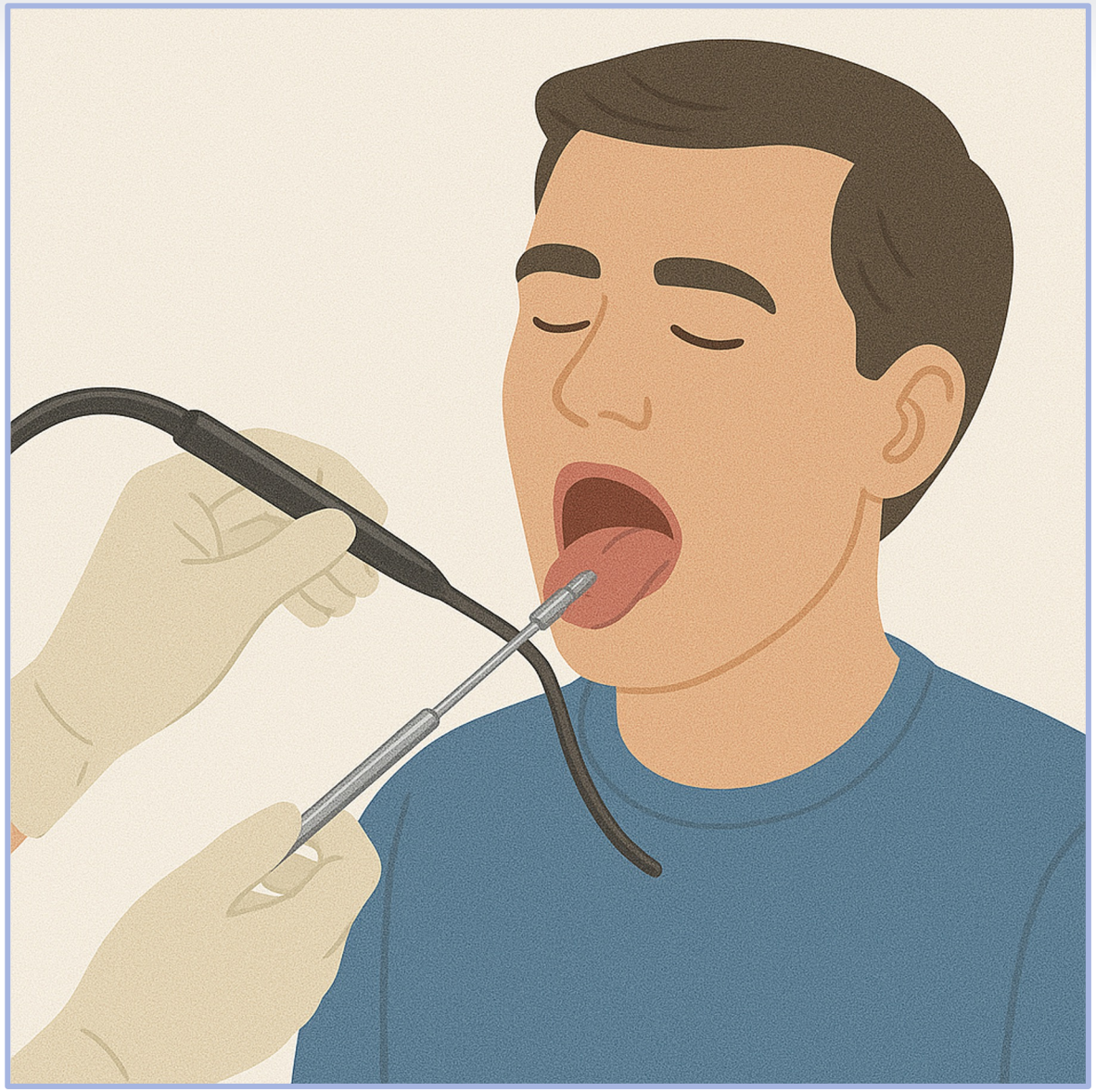
Dicembre
2024

Biopsia lingua (03/01/25):

Localizzazione della nota malattia linfomatosa (DLBCL).

Le cellule neoplastiche sono risultate CD20+, CD3- e citocheratine - all'indagine immunoistochimica.

L'indice proliferativo (Ki-67) è pari al 95%.

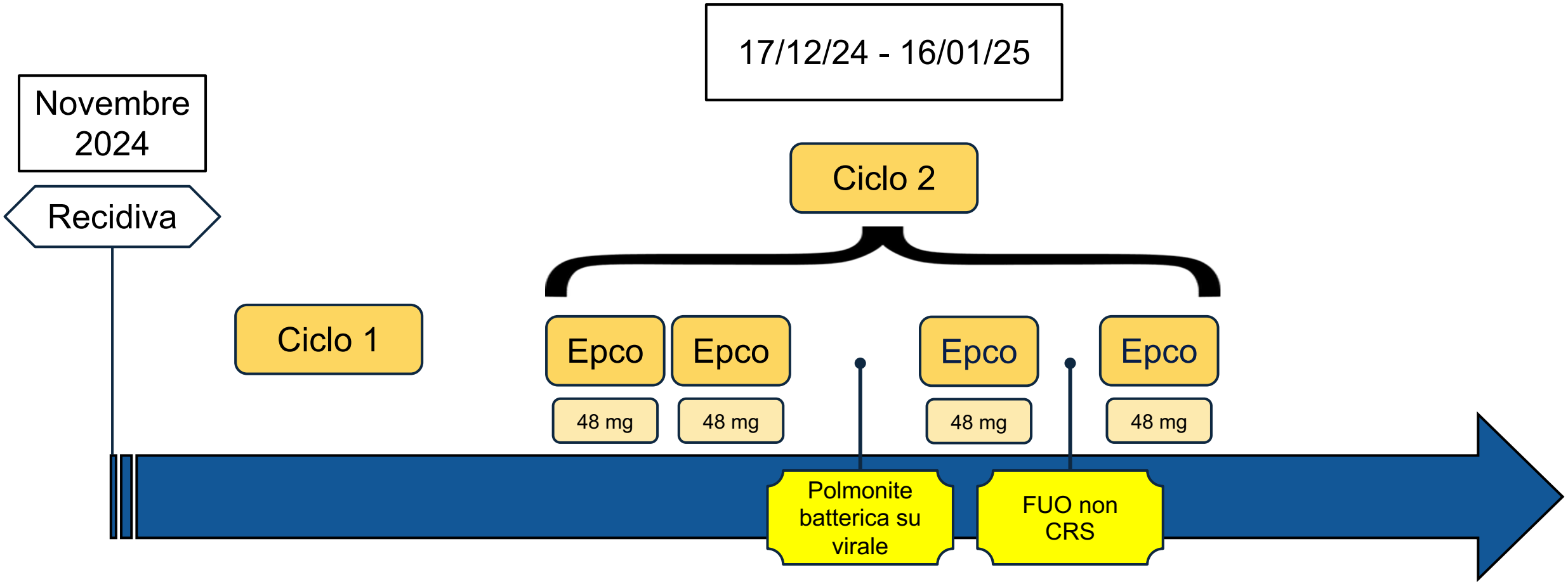


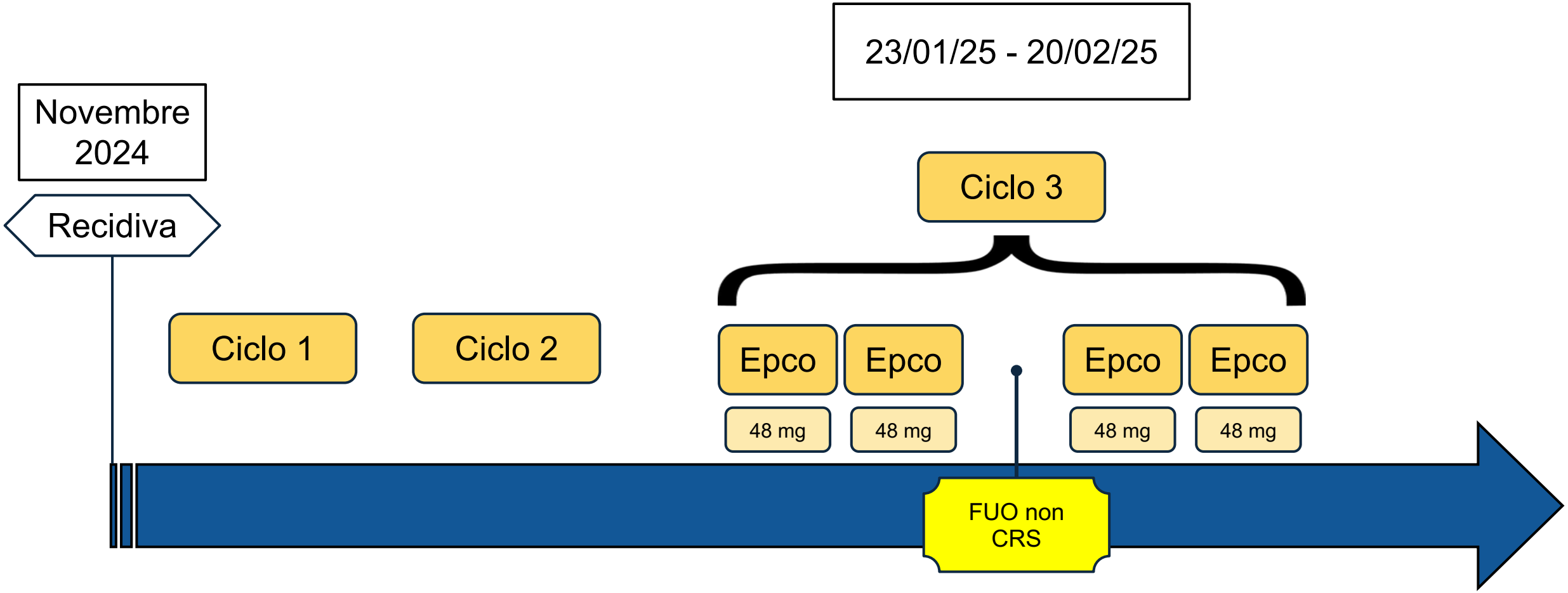
09/12/24 Stomaco: profonda ulcera con bordi rilevati che presenta dimensioni notevolmente ridotte rispetto alla precedente indagine (circa 25 vs 50-60 mm) e fondo in fase di riepitelizzazione

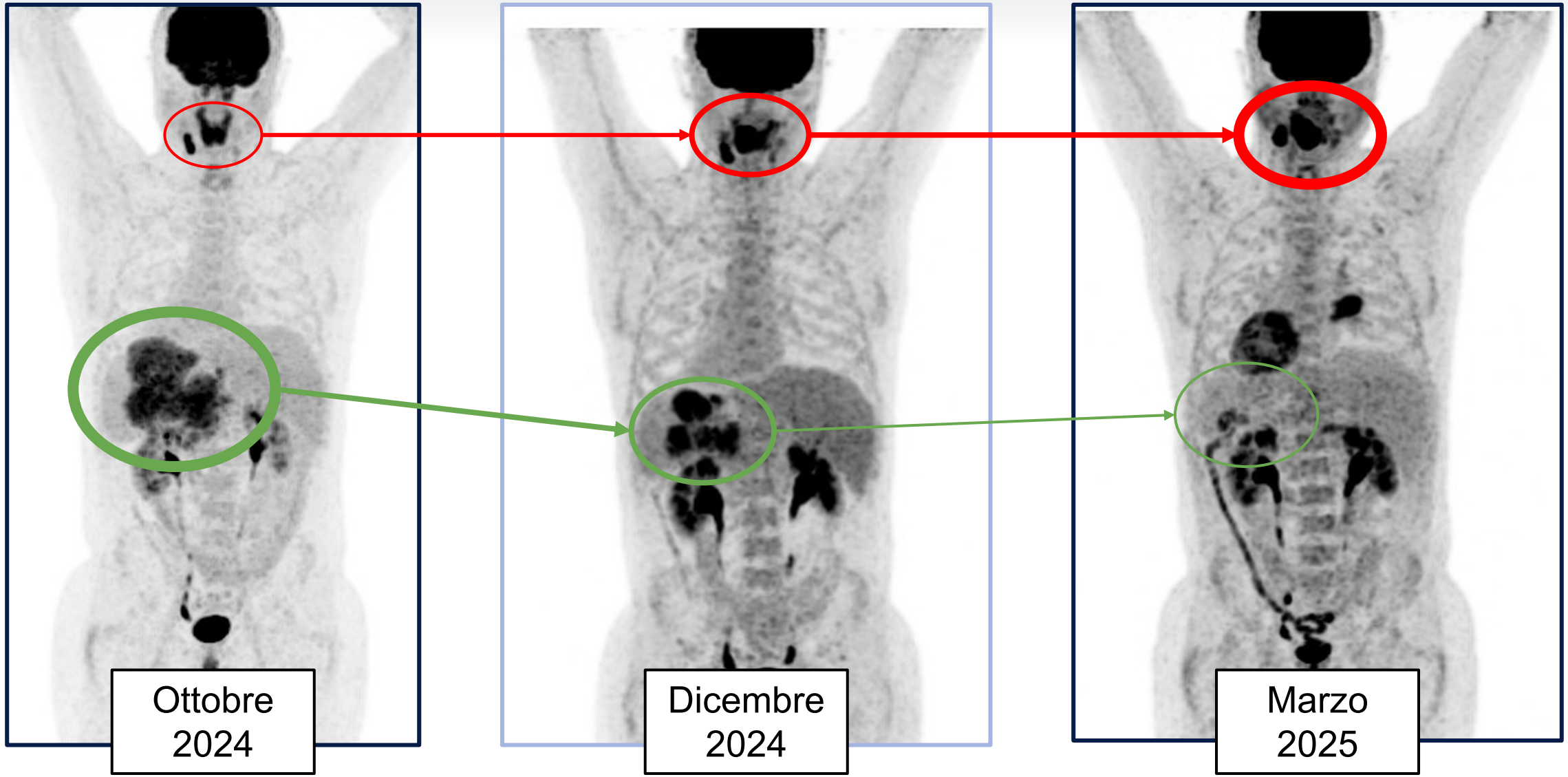
Localizzazione gastrica di linfoma di derivazione dai linfociti B periferici.

Alle indagini immunoistochimiche le cellule sono risultate positive per CD20.


CONTINUE?
Yes or No?
NO
YES
SELECT YOUR ACTION
START

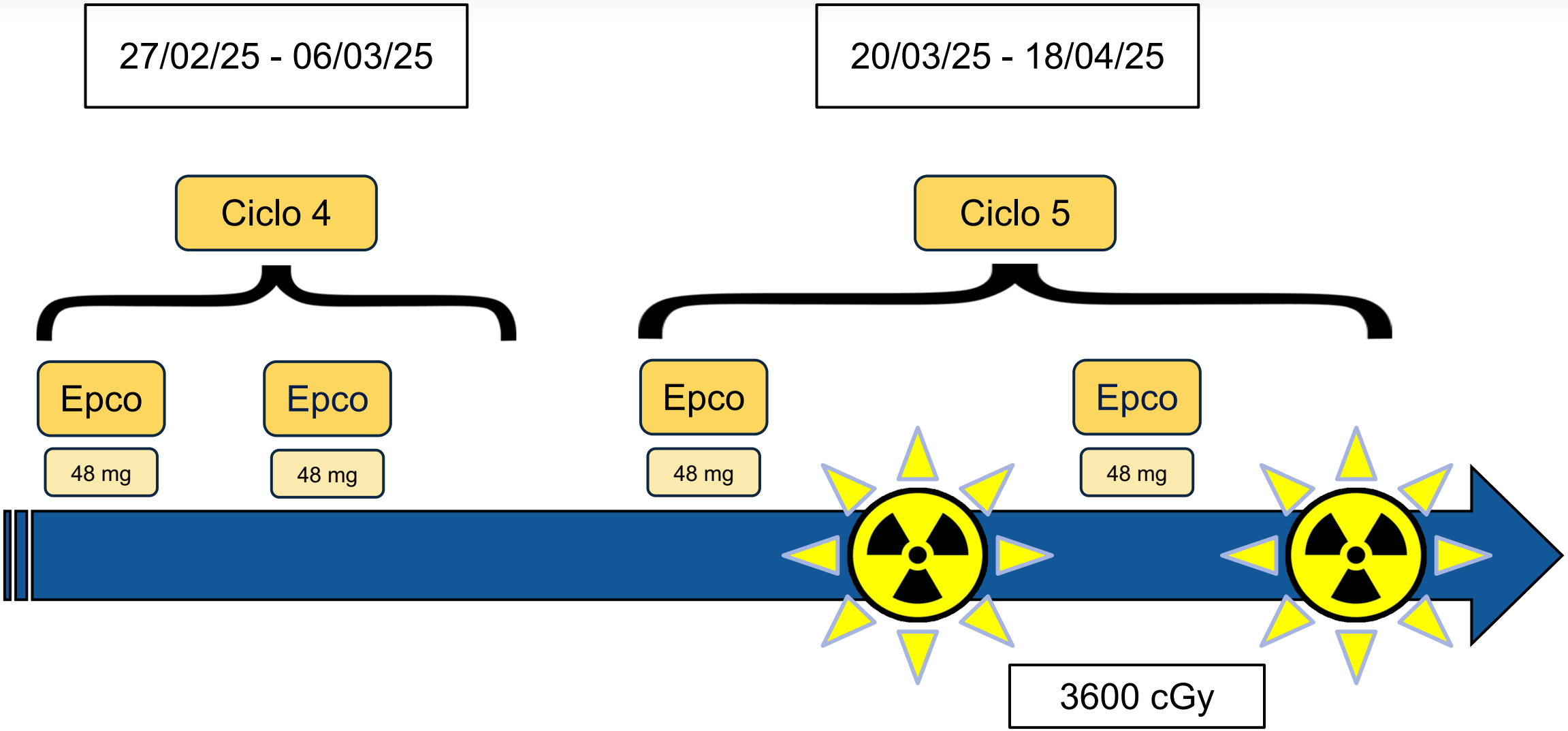

17/12/24 - 16/01/25
Novembre 2024
Recidiva
Ciclo 2
Ciclo 1
Epco
Epco
Epco
Epco
48 mg
48 mg
48 mg
48 mg
Polmonite batterica su virale
FUO non CRS

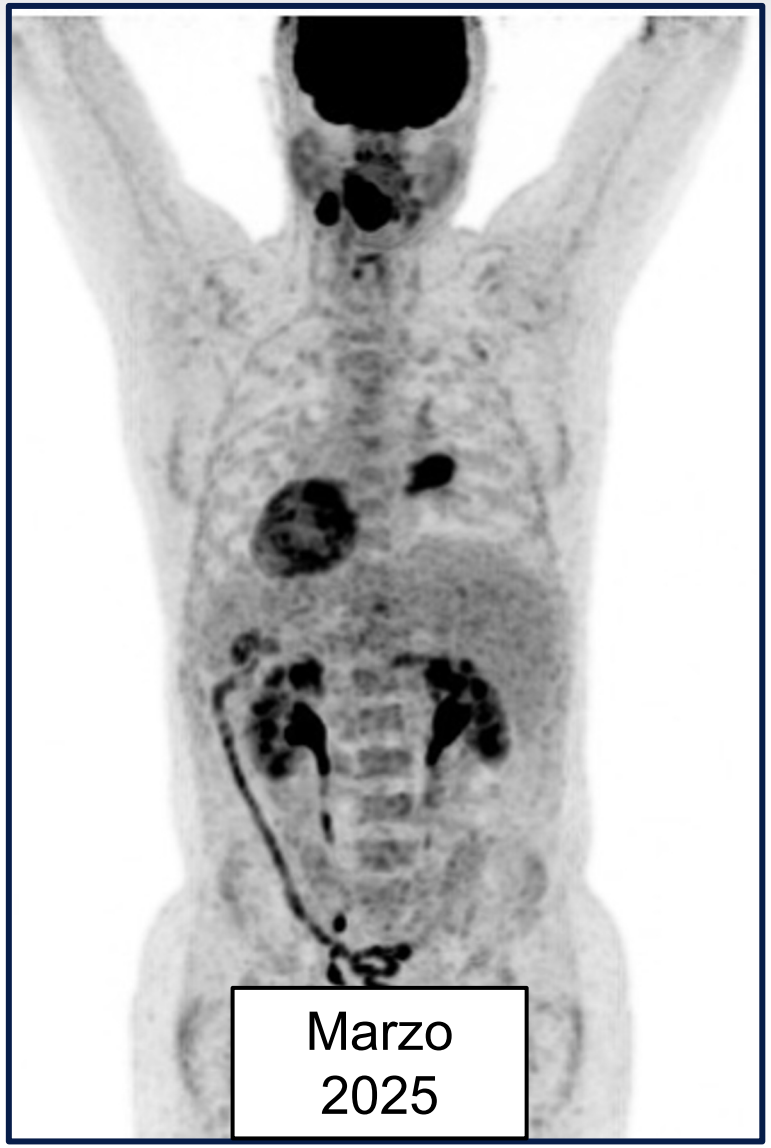

23/01/25 - 20/02/25
Novembre 2024
Recidiva
Ciclo 1
Ciclo 2
Ciclo 3
Epco
Epco
Epco
Epco
48 mg
48 mg
48 mg
48 mg
FUO non CRS


Ottobre
2024
Dicembre
2024
Marzo
2025

14/03/25: In sede dell' ulcera nota, si reperta in data odierna un area depressa di ca. 10x15mm con tessuto di tipo cicatriziale e sul bordo piccola area rilevata eritematosa di 10mm con pattern mucoso sospetto per persistenza di malattia.

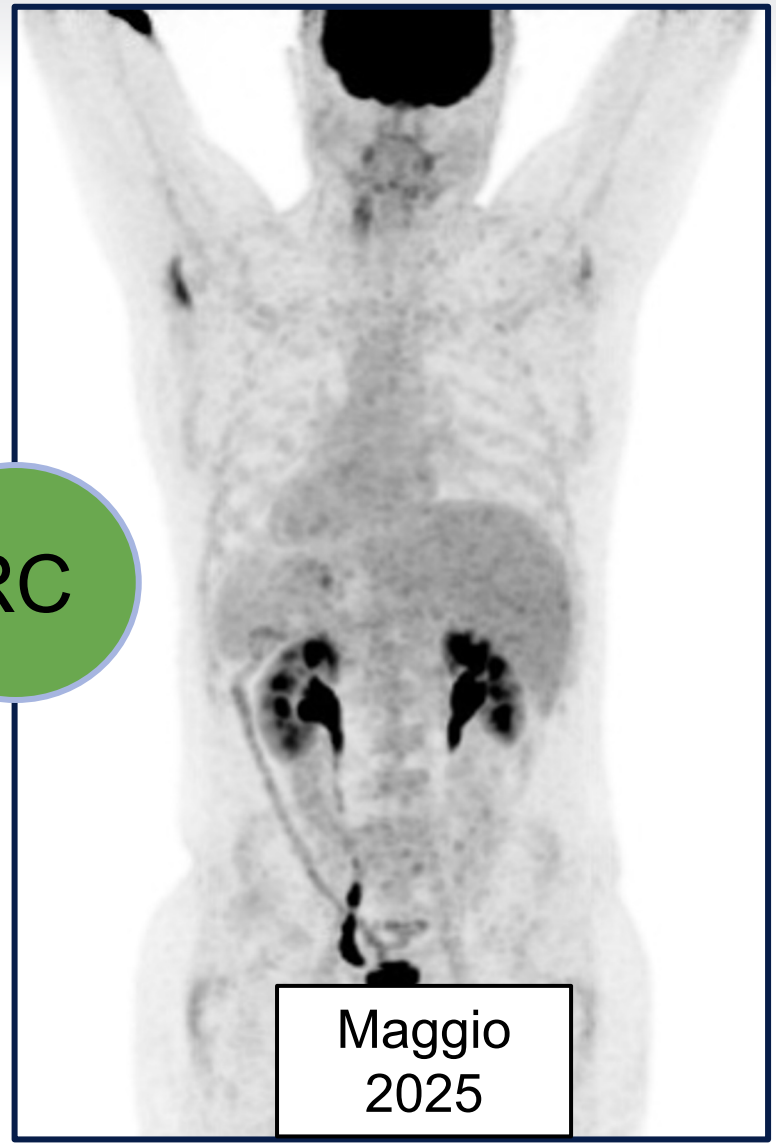
Non evidenza di localizzazione di linfoma nel materiale in esame


27/02/25 - 06/03/25
20/03/25 - 18/04/25
Ciclo 4
Ciclo 5
Epco
48 mg
Epco
48 mg
Epco
48 mg
Epco
48 mg
3600 cGy



Marzo 2025

RC



Maggio 2025

RC post C8

Agosto 2025

# Beyond Anecdotal Evidence

| Treatment | ORR/CRR | Median DOR | Grade 3 (or Higher) CRS | Grade 3 (or Higher) ICANS |
|---|---|---|---|---|
| **Axicabtagene Ciloleucel** | 83%/58% | 11.1 months | 11% | 32% |
| **Lisocabtagene Maraleucel** | 73%/53% | 23.1 months | 2% | 10% |
| **Tisagenlecleucel** | 52%/40% | Not reached | 22% | 12% |
| **Glofitamab** | 52%/39% | 18.4 months | 4% | 3% |
| **Epcoritamab** | 63.1%/40.1% | 17.3 months | 3.2% | 0.6% |

# Beyond Anecdotal Evidence

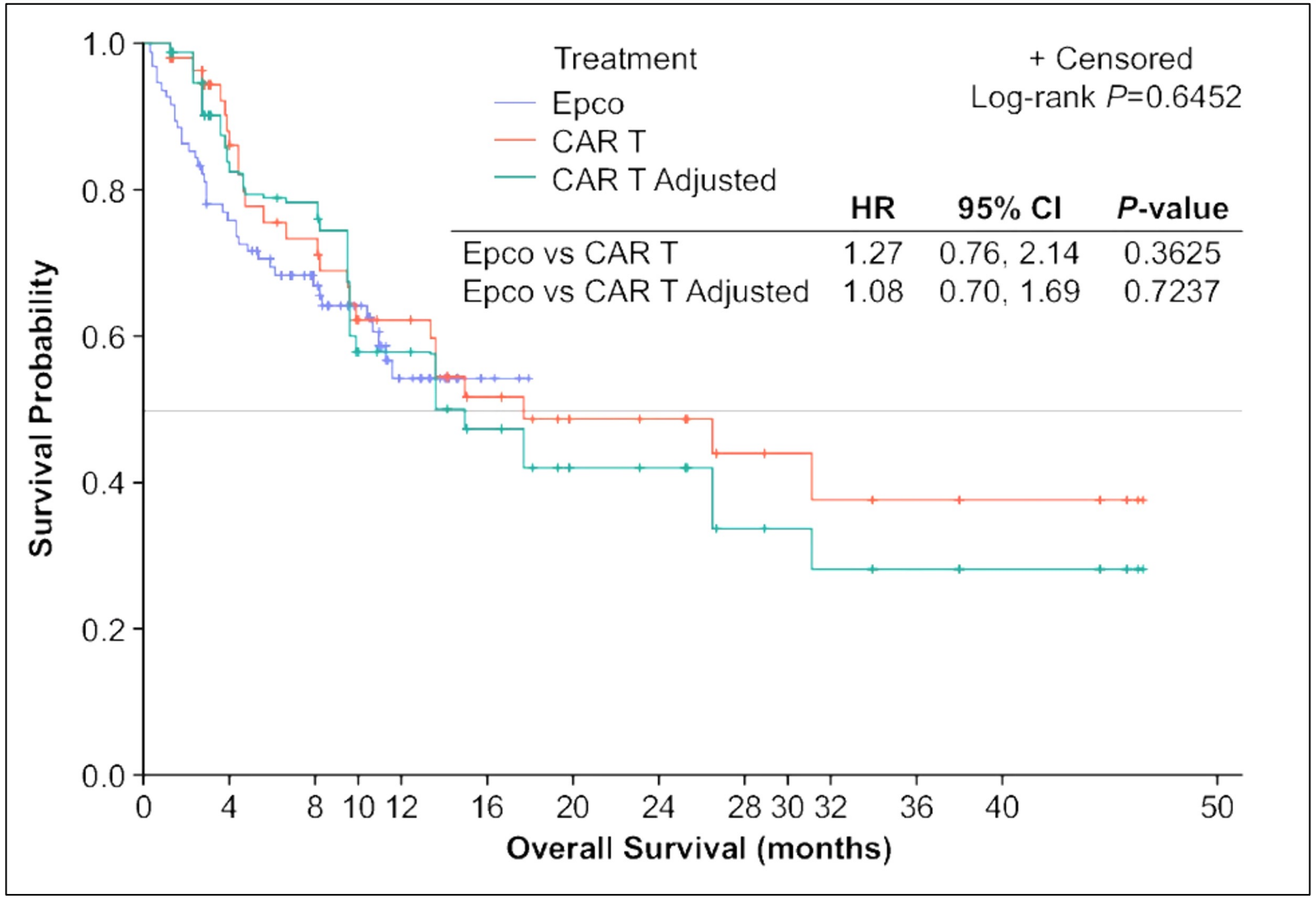
| Demographics | LBCL, N=157 |
|---|---|
| Median age (range), y | 64 (20–83) |
| <65 y, n (%) | 80 (51.0) |
| 65 to <75 y, n (%) | 48 (30.6) |
| ≥75 y, n (%) | 29 (18.5) |
| ECOG PS[a], n (%) | |
| 0 | 74 (47.1) |
| 1 | 78 (49.7) |
| 2 | 5 (3.2) |
| **Disease Characteristics[b]** | **LBCL, N=157** |
| Disease type, n (%) | |
| DLBCL[c] | 139 (88.5) |
| De novo | 97/139 (69.8) |
| Transformed | 40/139 (28.8) |
| DLBCL with DH/TH by central FISH[d] | 13/99 (13.1) |
| HGBCL | 9 (5.7) |
| PMBCL | 4 (2.5) |
| FL G3B | 5 (3.2) |

| Prior Treatments | LBCL, N=157 |
|---|---|
| Median time from initial diagnosis to first dose[e], y | 1.6 (0.0–28.4) |
| Median time from end of last therapy to first dose, mo | 2.4 (0.0–153.0) |
| Median prior lines of therapy (range) | 3 (2–11) |
| ≥3 Lines of therapy, n (%) | 111 (70.7) |
| Primary refractory[f] disease, n (%) | 96 (61.1) |
| Refractory[f] to last systemic therapy, n (%) | 130 (82.8) |
| Refractory[f] to ≥2 consecutive lines of therapy, n (%) | 119 (75.8) |
| Prior ASCT, n (%) | 31 (19.7) |
| Prior CAR T therapy, n (%) | 61 (38.9) |
| Refractory[f] to CAR T therapy | 46/61 (75.4) |

Thieblemont C, et al. J Clin Oncol. 2023;41:2238-47.

# Beyond Anecdotal Evidence

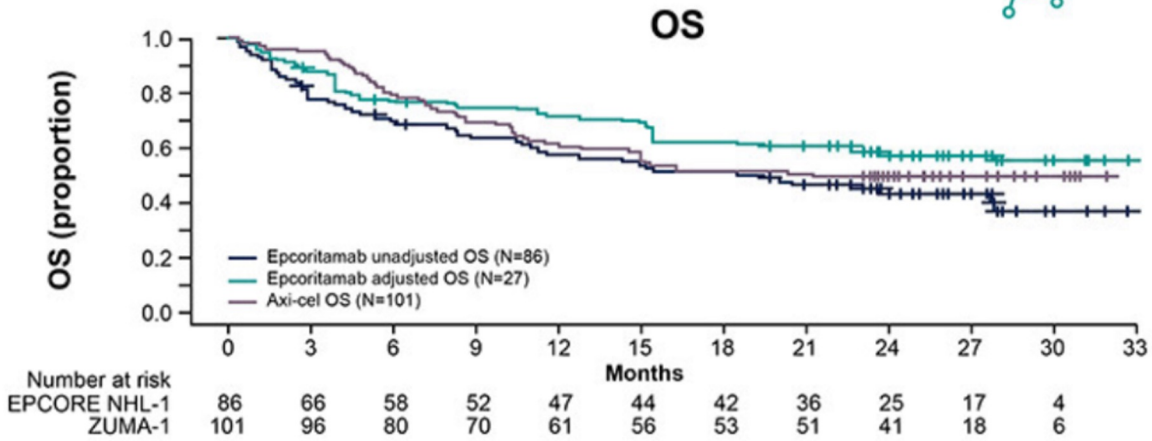
| Outcome | Epcoritamab (N = 139) | CAR T (Adjusted N = 53) |
|---|---|---|
| ORR | 61.9% | 72.0% |
| OR (95% CI) for ORR for epcoritamab vs | | 0.95 (0.79, 1.15)<br>*P* = 0.626 |
| CR | 38.9% | 36.5% |
| OR (95% CI) for CR for epcoritamab vs | | 1.1 (0.8, 1.6)<br>*P* = 0.472 |
| mPFS (mo) | 4.4 | 5.6 |
| HR (95% CI) for PFS for epcoritamab vs | | 0.8 (0.6, 1.1)<br>*P* = 0.169 |
| mOS (mo) | NR | 15.0 |
| HR (95% CI) for OS for epcoritamab vs | | 1.1 (0.7, 1.7)<br>*P* = 0.724 |

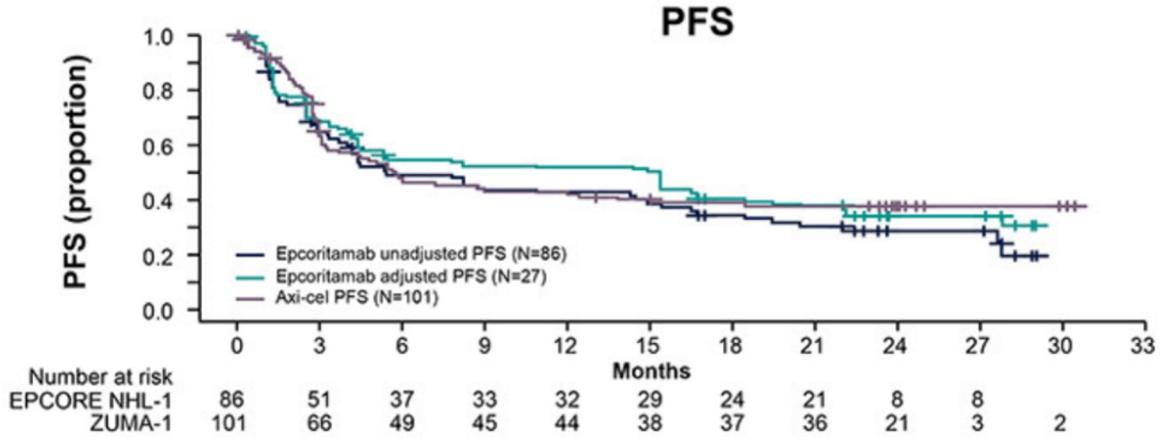



Rosenthal A, Munoz J, Jun M, et al. Comparisons of treatment outcomes of epcoritamab versus chemoimmunotherapy, polatuzumab-based regimens, tafasitamab-based regimens, or chimeric antigen receptor T-cell therapy, in third-line or later relapsed/refractory large B-cell lymphoma. *J Hematol Oncol*. 2024;17(1):69. Published 2024 Aug 16. doi:10.1186/s13045-024-01594-x

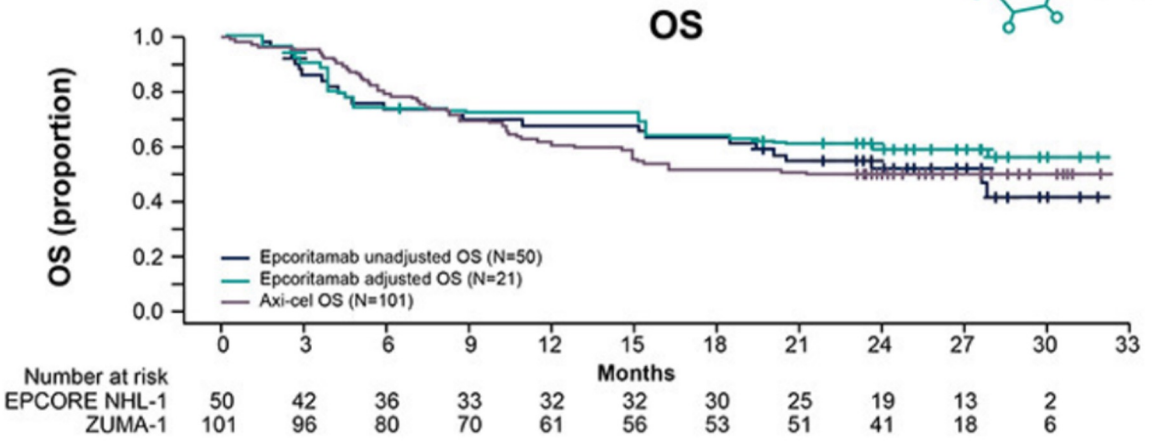
# Beyond Anecdotal Evidence

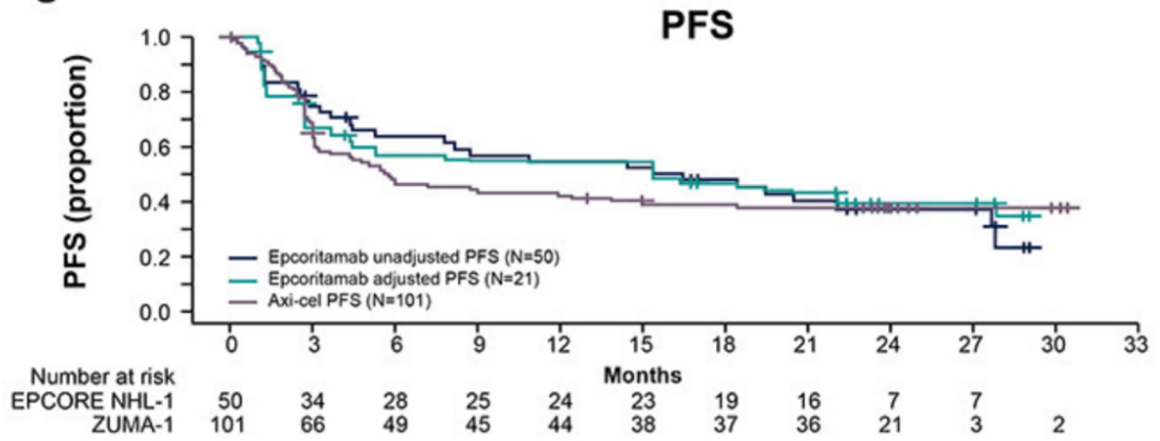
## CAR T-naive




## CAR T-eligible

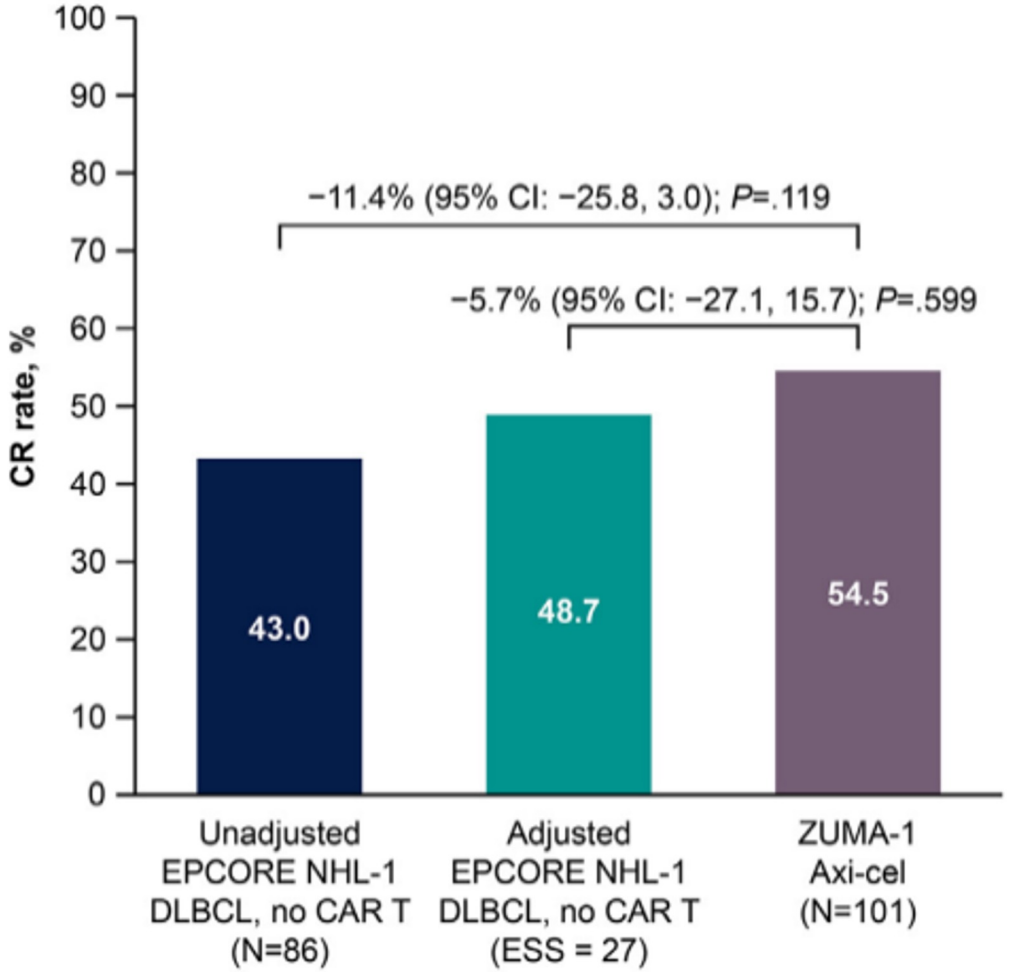


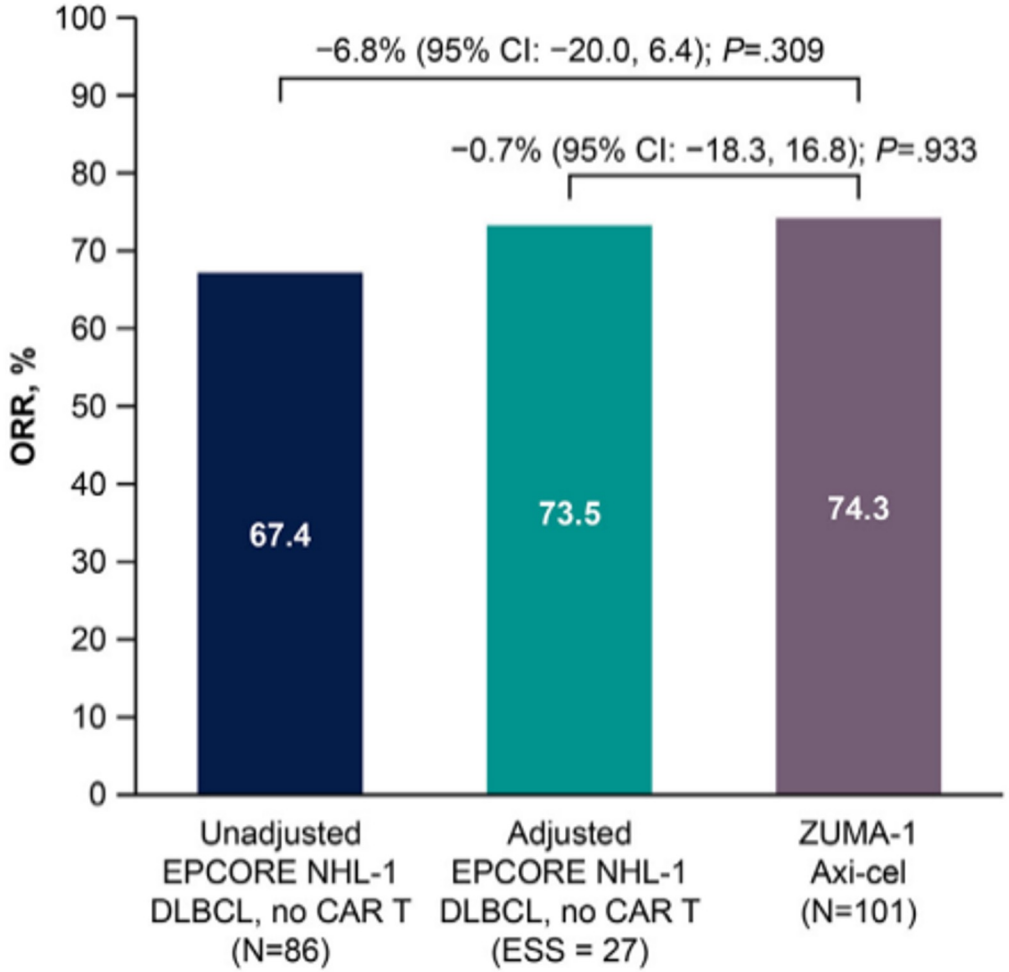




Salles G, Fox CP, Hamadani M, et al. Indirect Comparison of Epcoritamab Versus Axicabtagene Ciloleucel in Chimeric Antigen Receptor T-Cell-Eligible and -Naive Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma. *Clin Lymphoma Myeloma Leuk*. Published online July 31, 2025. doi:10.1016/j.clml.2025.07.015

# Beyond Anecdotal Evidence

## CAR-T Naive

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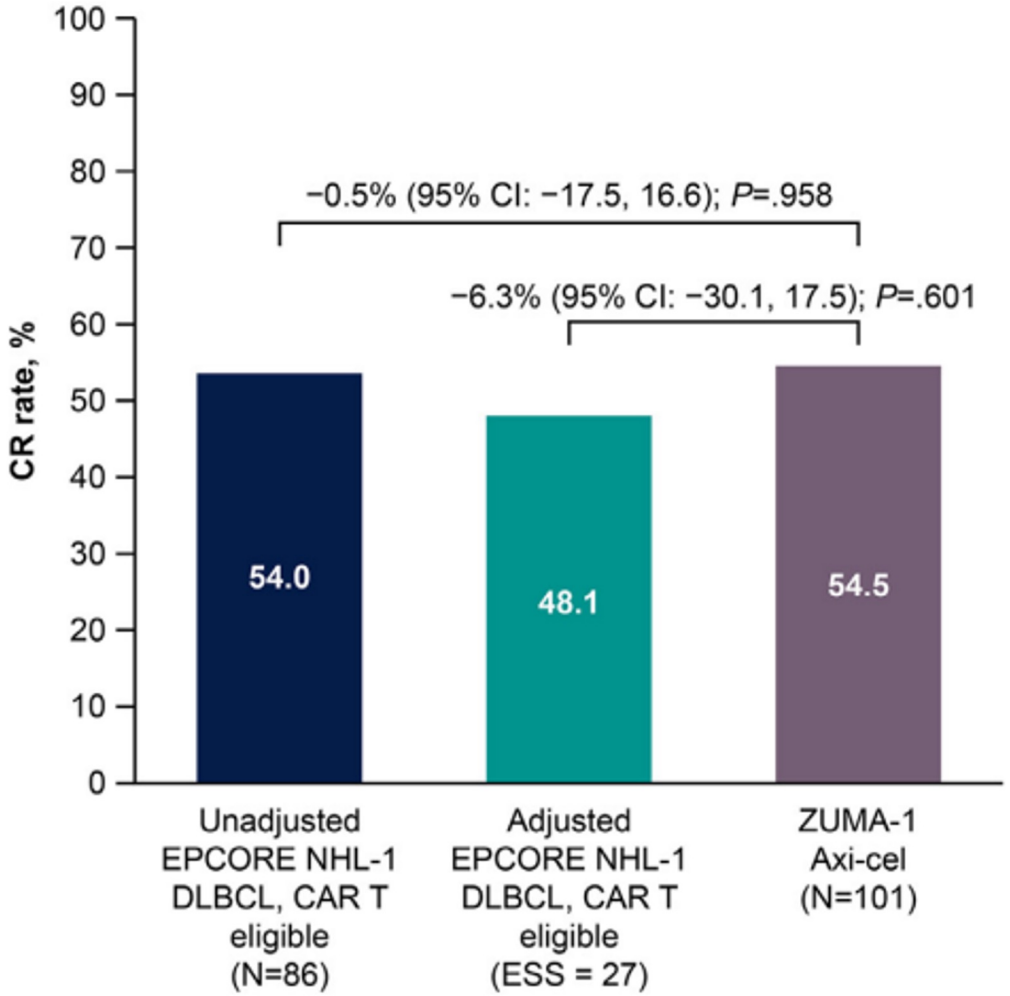
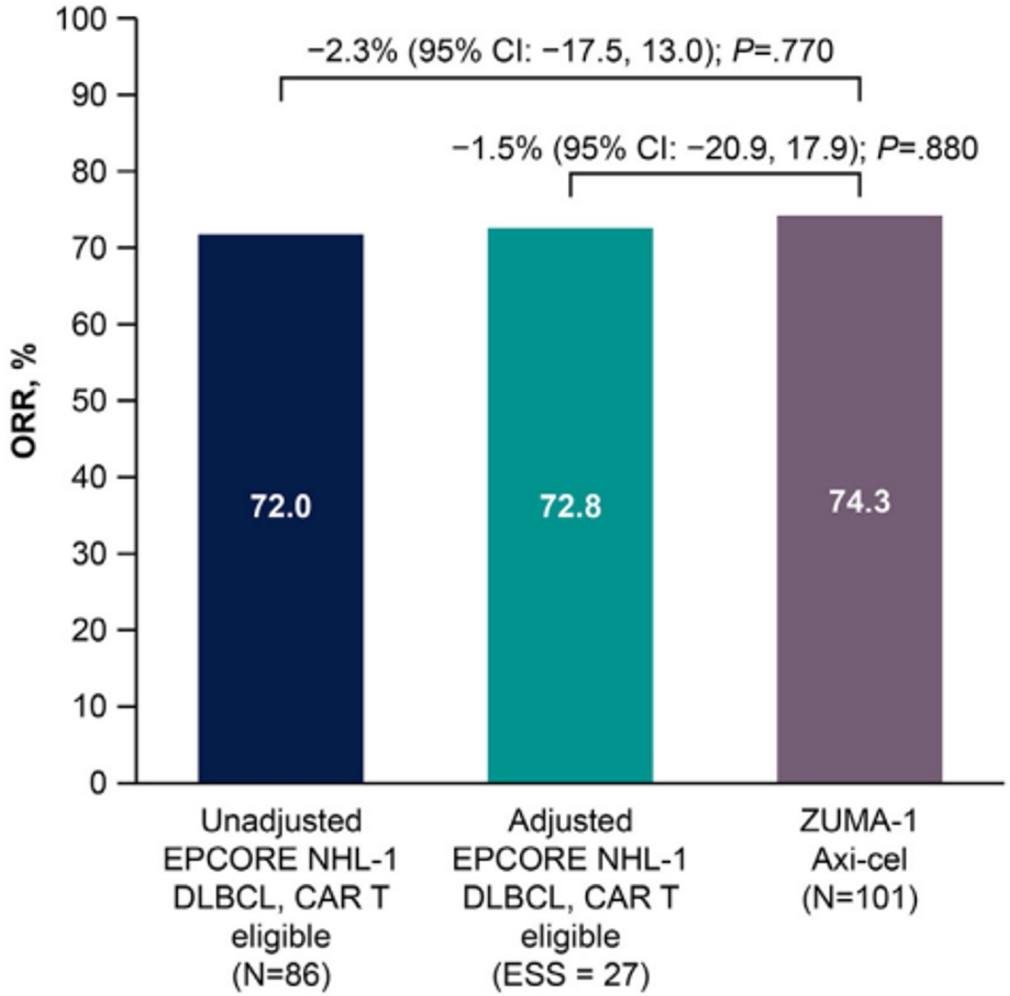
# Beyond Anecdotal Evidence

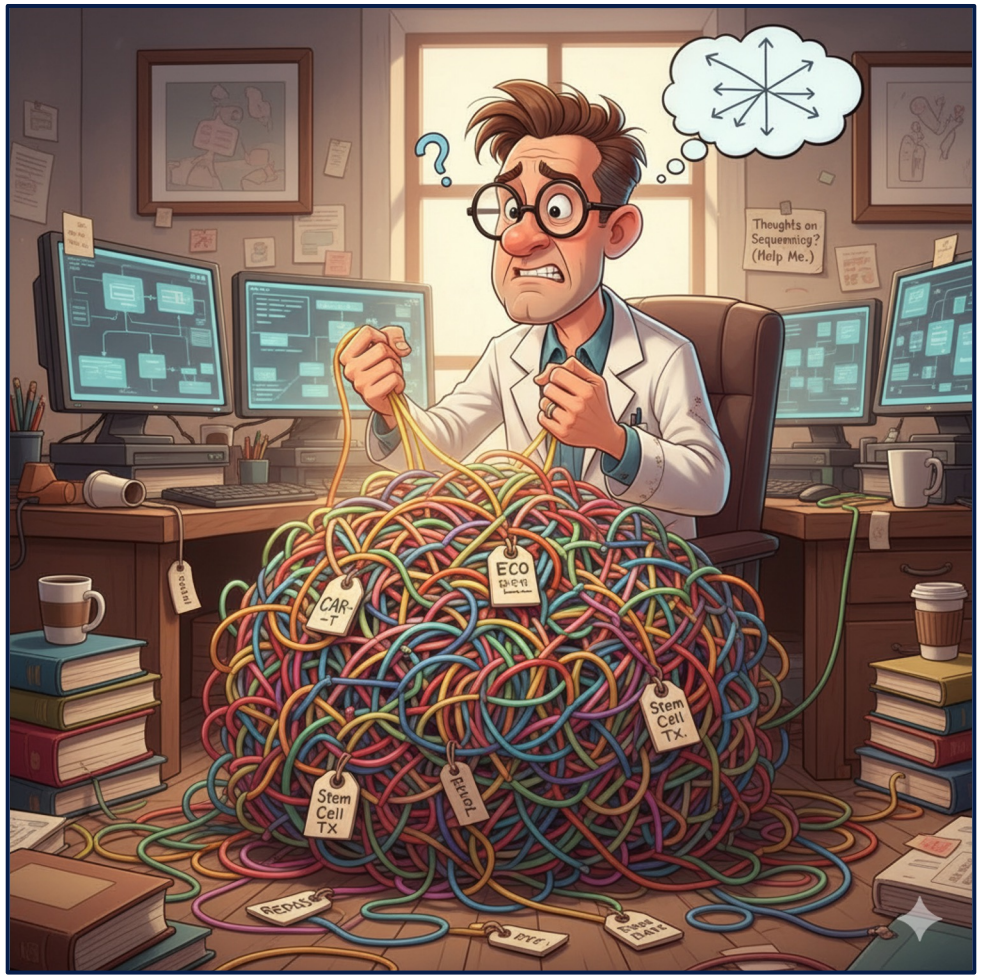
## CAR-T Eligible




Salles G, Fox CP, Hamadani M, et al. Indirect Comparison of Epcoritamab Versus Axicabtagene Ciloleucel in Chimeric Antigen Receptor T-Cell-Eligible and -Naive Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma. *Clin Lymphoma Myeloma Leuk*. Published online July 31, 2025. doi:10.1016/j.clml.2025.07.015

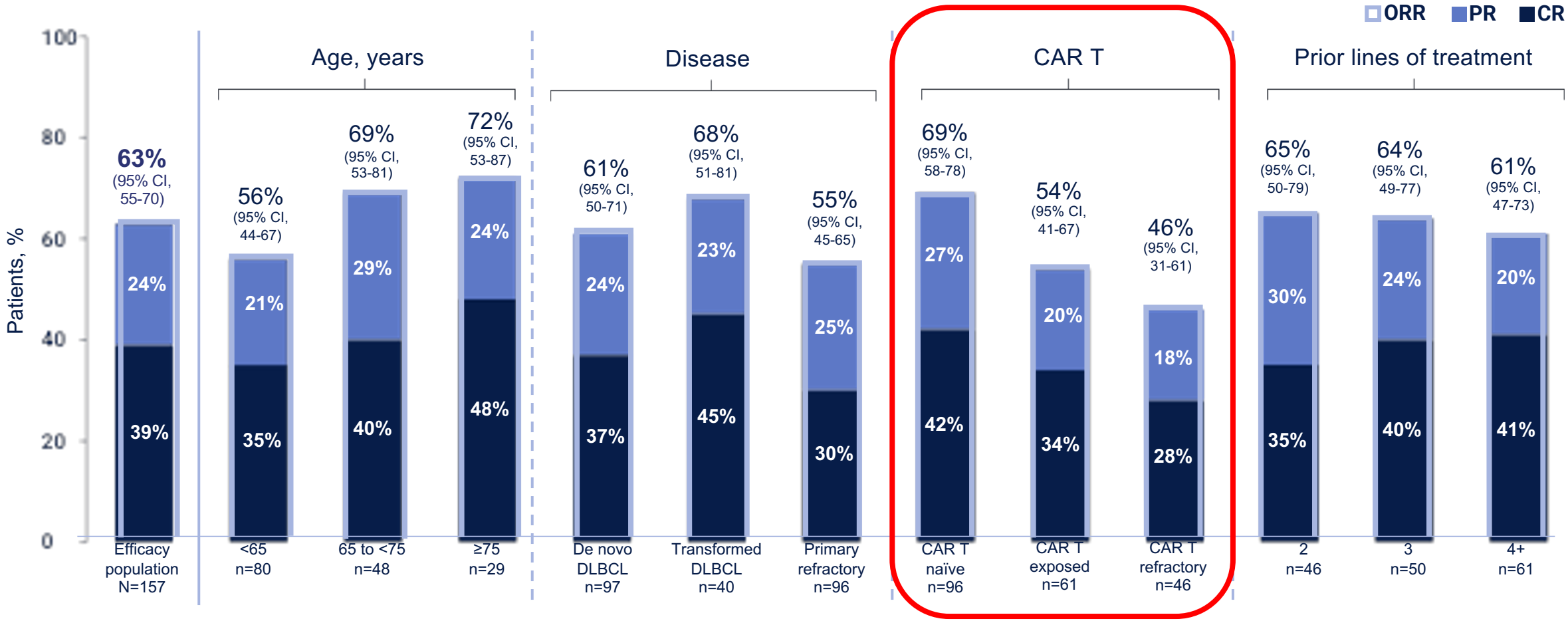
# Thoughts on Sequencing




Salles G, Fox CP, Hamadani M, et al. Indirect Comparison of Epcoritamab Versus Axicabtagene Ciloleucel in Chimeric Antigen Receptor T-Cell-Eligible and -Naive Patients With Relapsed/Refractory Diffuse Large B-Cell Lymphoma. *Clin Lymphoma Myeloma Leuk*. Published online July 31, 2025. doi:10.1016/j.clml.2025.07.015

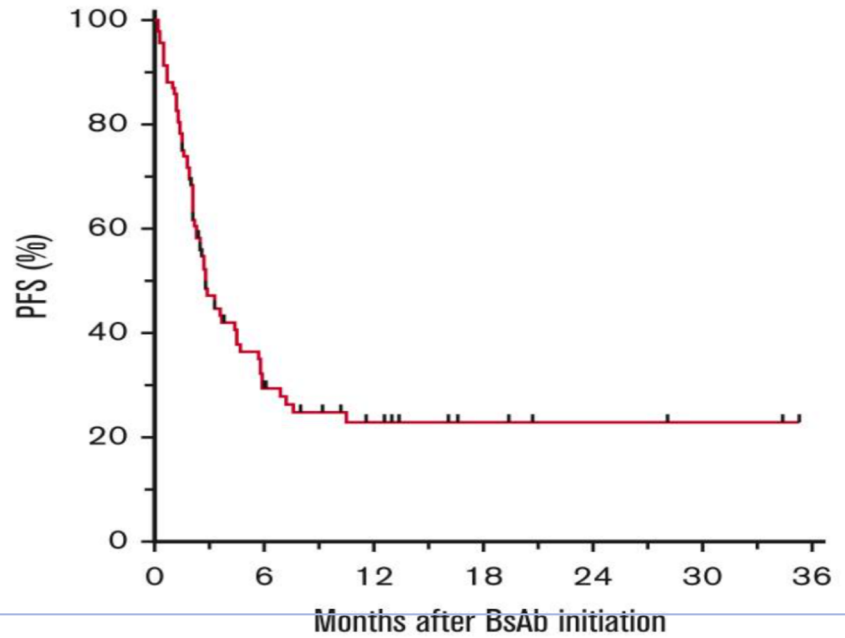
# Thoughts on Sequencing

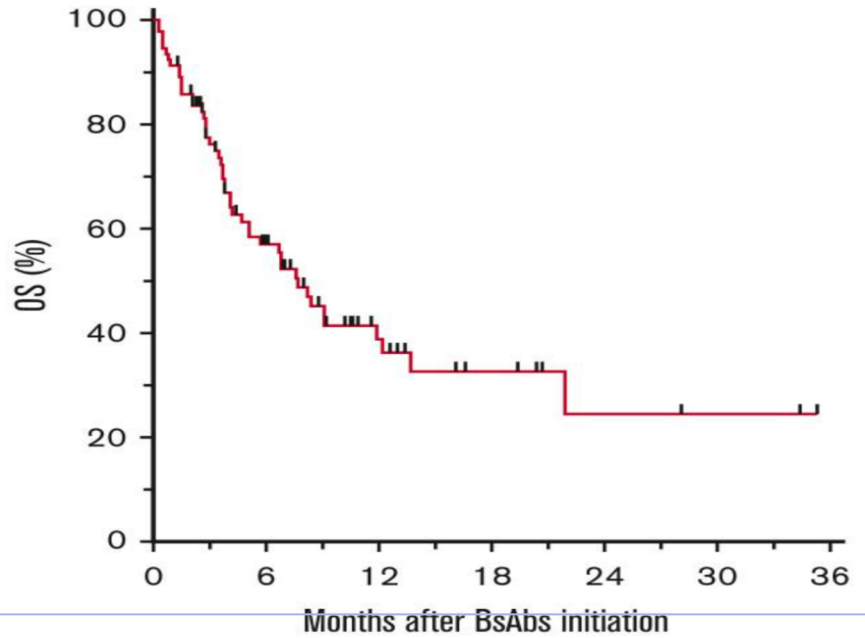
3L+ DLBCL




Thieblemont C, et al. J Clin Oncol. 2023;41:2238-47.

# Thoughts on Sequencing




Shumilov E, Scholz JK, Seib M, et al. Outcomes of bispecific antibody therapy after CAR T-cell failure in relapsed/refractory large B-cell lymphoma. *Blood Adv*. 2025;9(15):3955-3966. doi:10.1182/bloodadvances.2024015719

| Outcomes | All patients |
|---|---|
| Median time to best response (range) - days | 54 (6-337) |
| ORR (CR and PR) | 39 (43) |
| CR | 20 (22) |
| PD | 43 (46) |
| Median time to relapse/PD after first BsAb administration (range) - months | 2.1 (0.2-10.5) |

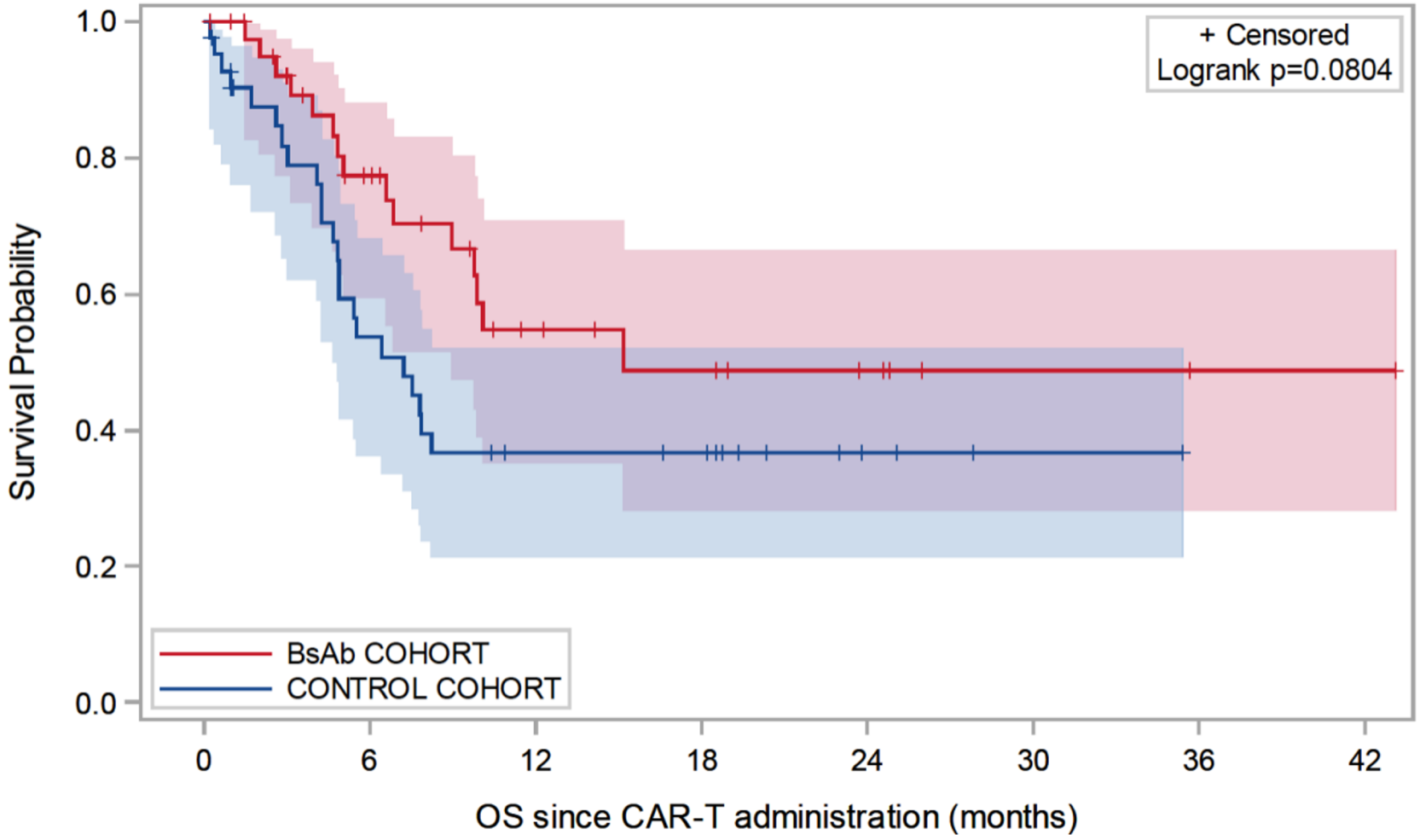
# Thoughts on Sequencing

L'efficacia delle CAR-T non sembra essere influenzata da una precedente terapia con bispecifici

| Variables | BsAb cohort † n=42 | Control cohort n=42 | p-value |
|---|---|---|---|
| ***Efficacy*** | | | |
| Follow-up from CAR T-cell infusion– median months (95% CI) | 11.5 (6.4-19.0) | 18.8 (10.9-23.0) | |
| Response to CAR T-cell therapy - no (%) | | | |
| - ORR | 36 (86) | 22 (55)[a] | 0.02 |
| - CRR | 18 (43) | 15 (38) | 0.5 |
| 1-year PFS (95% CI) | 43% (26-60) | 29% (15-46) | 0.1 |
| 1-year OS (95% CI) | 55% (35-71) | 37% (21-52) | 0.08 |
| ***Toxicity*** | | | |
| CRS – no (%) | 36 (86) | 32 (78)[b] | 0.41 |
| - Grade ≥2 | 16 (38) | 17 (40) | |
| ICANS – no (%) | 11 (26) | 11 (27)[c] | 1.0 |
| - Grade ≥2 | 7 (17) | 8 (19) | |

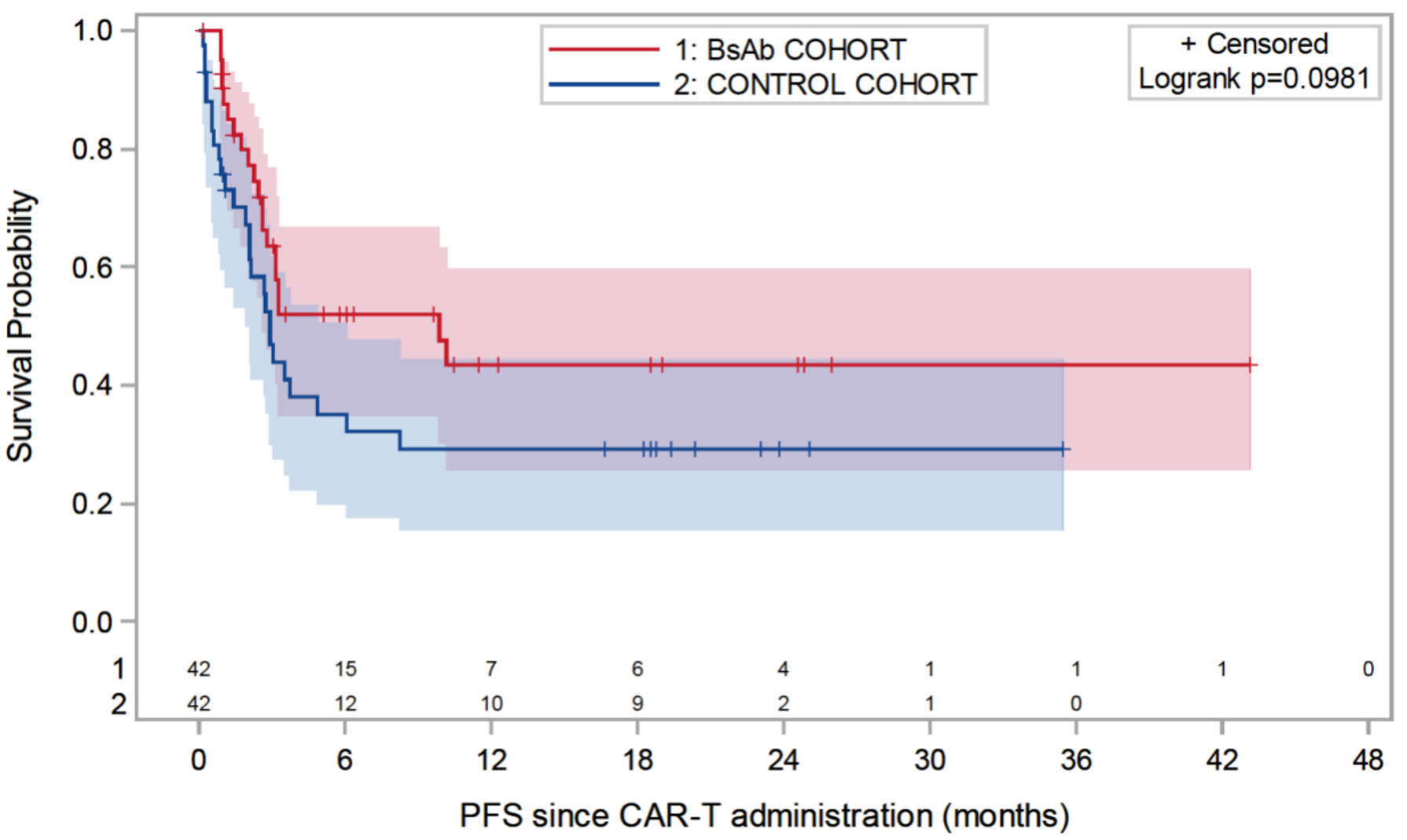
Crochet G, Iacoboni G, Couturier A, et al. Efficacy of CAR T-cell therapy is not impaired by previous bispecific antibody treatment in large B-cell lymphoma. *Blood*. 2024;144(3):334-338. doi:10.1182/blood.2024024526

# Thoughts on Sequencing




Crochet G, Iacoboni G, Couturier A, et al. Efficacy of CAR T-cell therapy is not impaired by previous bispecific antibody treatment in large B-cell lymphoma. *Blood*. 2024;144(3):334-338. doi:10.1182/blood.2024024526

# Thoughts on Sequencing




Crochet G, Iacoboni G, Couturier A, et al. Efficacy of CAR T-cell therapy is not impaired by previous bispecific antibody treatment in large B-cell lymphoma. *Blood*. 2024;144(3):334-338. doi:10.1182/blood.2024024526

# 3L+ DLBCL Treatments

Patient's Characteristics

Disease Characteristics


Head to Head Trials

New Predictive Models

- Axi-Cel
- Liso-Cel
- Tisa-Cel
- Tafa-Len
- Lonca
- R-Pola-Benda
- Glofitamab
- Epcoritamab
- CIT (R-Gemox, R-ICE, R-Benda, etc…)
- ASCT and HSCT
- Clinical Trials

# Thank You!

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