

# La rivoluzione terapeutica nel linfoma e nel mieloma

Napoli, Royal Hotel Continental • 14-15 Maggio 2026

**The big debate: CAR-T vs bispecifici nei LNH B cell aggressivi ed indolenti**

*Martina Di Palma*  
*UOC Oncoematologia*  
*AORN Sant'Anna e San Sebastiano, Caserta*

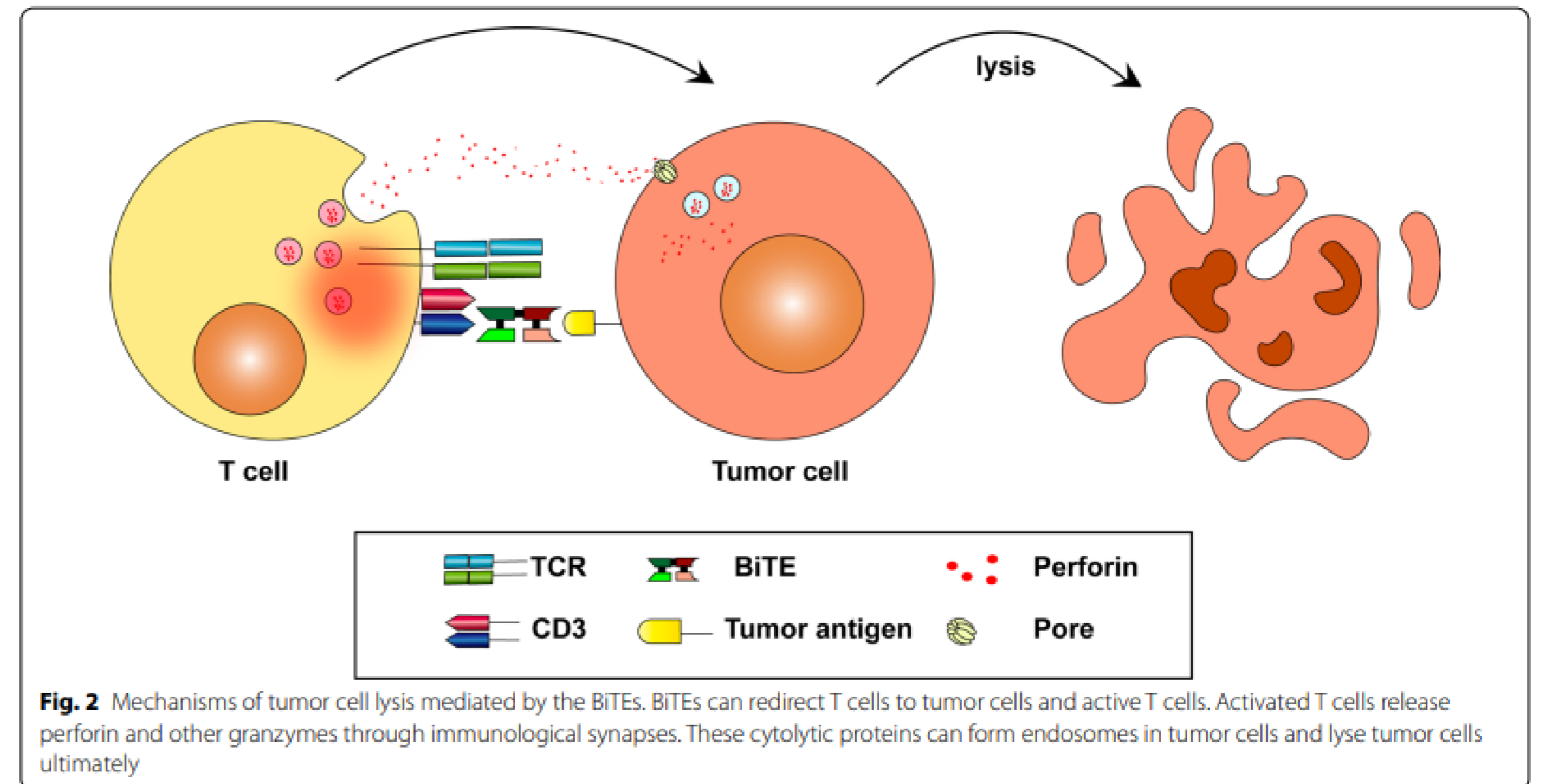
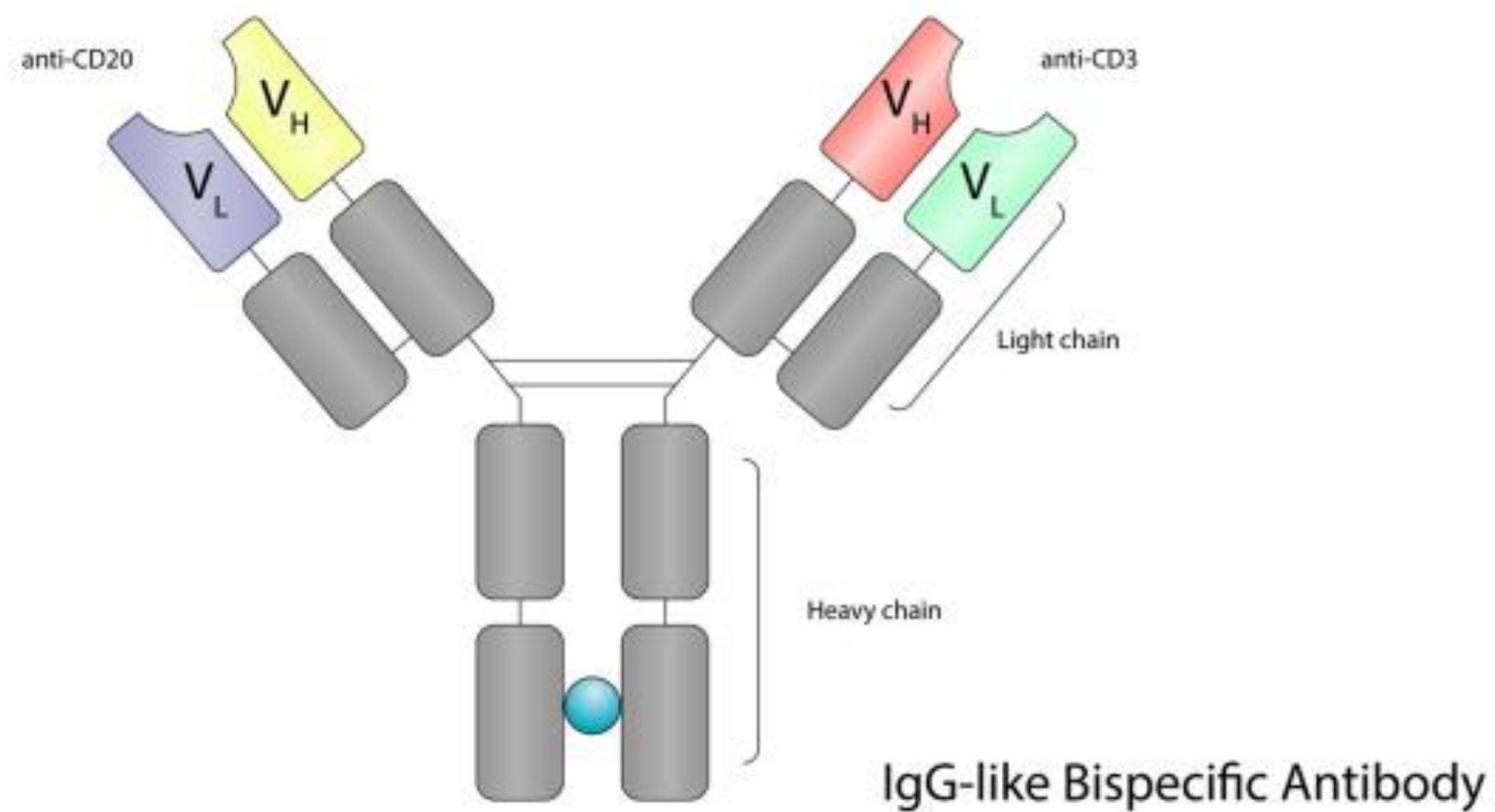


# La rivoluzione terapeutica nel linfoma e nel mieloma


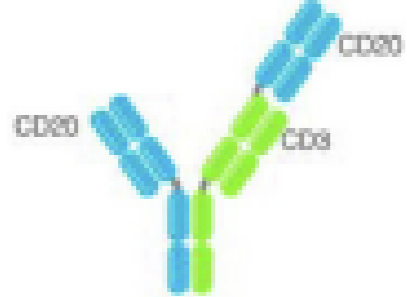
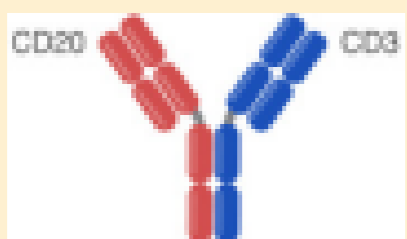
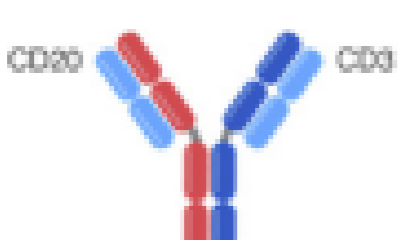
## Disclosures of Martina Di Palma

| Company name  | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
|---------------|------------------|----------|------------|-------------|-----------------|----------------|-------|
| <b>Roche</b>  | x                |          | x          |             |                 |                |       |
| <b>Abbvie</b> | x                |          | x          |             |                 |                |       |
|               |                  |          |            |             |                 |                |       |
|               |                  |          |            |             |                 |                |       |

## BsAbs: structure and mechanism



# Comparative characteristics of CD20XCD3 BsAb in B NHL

| Product name                | Schematic depiction   | Format | Technology                           | CD20:CD3 ratio | CD3 clone                            | CD20 clone  | Fc silencing mutations*                          |
|-----------------------------|---|--------|--------------------------------------|----------------|--------------------------------------|---|--|
| Mosunetuzumab <sup>18</sup> |    | IgG1   | Knobs-into-holes (different Fabs)    | 1:1            | UCHT1v9 (CD3 $\delta\epsilon$ )      | 2H7 (type 1 epitope, identical to rituximab)      | N297G (no Fc $\gamma$ R binding)                 |
| Glofitamab <sup>15</sup>    |   | IgG1   | Head-to-tail fusion                  | 2:1            | SP34-der.(CD3 $\epsilon$ )           | By-L1 (type 2 epitope, identical to obinutuzumab) | IgG1-P329G-LALA (no Fc $\gamma$ R binding)       |
| Epcoritamab <sup>16</sup>   |  | IgG1   | Controlled Fab-arm exchange          | 1:1            | huCACAO (SP34-der.)(CD3 $\epsilon$ ) | 7D8 (type 1 epitope, shared by ofatumomab)        | L234F,L235E,D265A (no Fc $\gamma$ R,C1q binding) |
| Odronexamab <sup>17</sup>   |  | IgG4   | Heavy chains with different affinity | 1:1            | REG1250 (CD3 $\delta\epsilon$ )      | 3B9-10 (type 1 epitope, shared by ofatumomab)     | Modified IgG4 (no Fc $\gamma$ RIII binding)      |

## BsAbs in B cell lymphomas

DLBCL

| III LINE                | II LINE                                | I LINE   |
|-------------------------|--|--|
| GLOFITAMAB ✓            | STARGLO<br>Glofit + R-GemOx vs GemOx ⌚ | Skyglo<br>Glofit + Pola-R-CHP vs PolaR-CHP<br>NCT04980222<br>Glofit + R-CHOP (high-risk) |
| EPCORITAMAB ✓           | EPCORE DLBCL-1<br>Epcor monotherapy    | EPCORE-DLBCL2<br>Epcor + R-CHOP vs R-CHOP<br>NCT05660967<br>Epcor +/- Len (frail/unfit)  |
| ODRONEXAMAB<br>(no EMA) | OLYMPIA-4<br>Odro monotherapy          | OLYMPIA-3<br>Odro + CHOP vs R-CHOP   |

FL

| III LINE                | II LINE  | I LINE  |
|-------------------------|--|---|
| MOSUNETUZUMAB ✓         | CELESTIMO<br>Mosun (IV) + Len vs R-Len   | MorningSun<br>Mosu untreated FL<br>NCT05410418<br>Mosu+Pola |
| EPCORITAMAB ✓           | EPCORE FL-1<br>fixed Epcoritamab (SC) + R-Len vs R-Len<br>inMIND<br>Epcor+Tafa+Len | NCT06112847<br>Epcoritamab+Len                              |
| GLOFITAMAB              |  | GLOBIN<br>Glofi+Obinu                                       |
| ODRONEXAMAB<br>(no EMA) | OLYMPIA-5<br>Odro + Len  | OLYMPIA-1 e 2<br>Odro±chemo                                 |

✓ APPROVED ≥ 3L

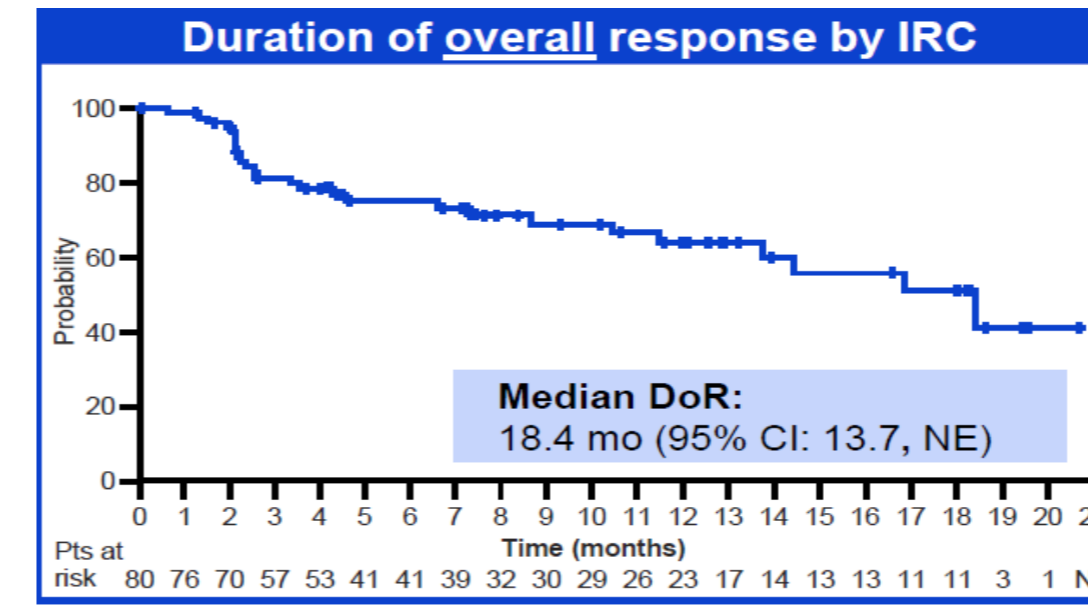
⌚ NEXT APPROVAL 2L

## BsAbs in DLBCL: currently status 3 L

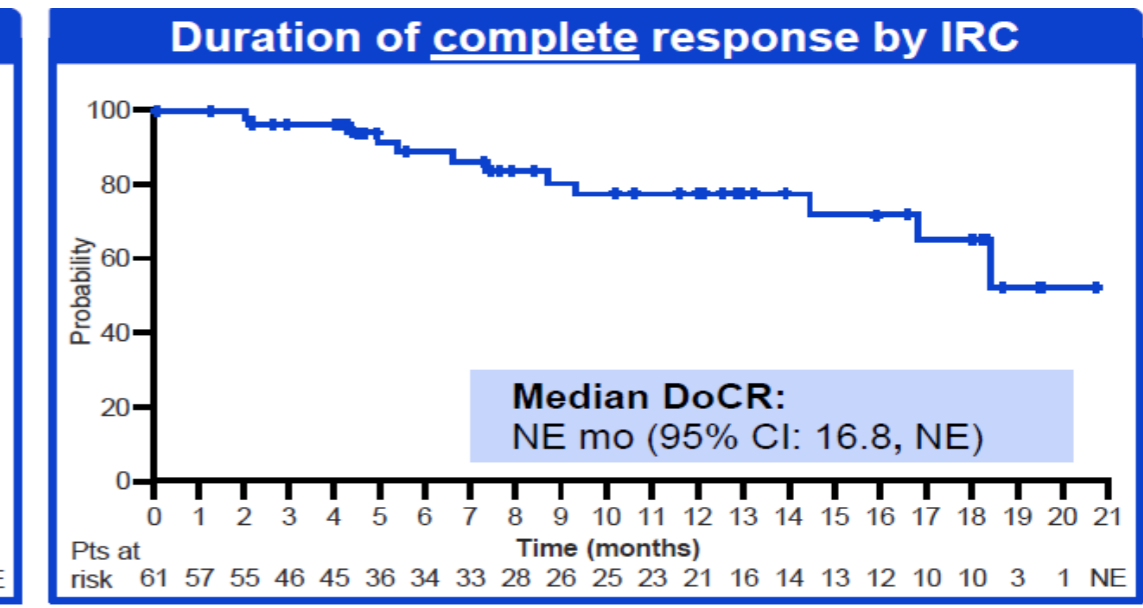
### NP30179: Glofitamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

#### Results

|                               |     |
|-------------------------------|-----|
| ORR %                         | 52% |
| CR%                           | 39% |
| DoCR months                   | NE  |
| Median time to first CR, days | 42  |
| Median PFS, months            | 4,9 |



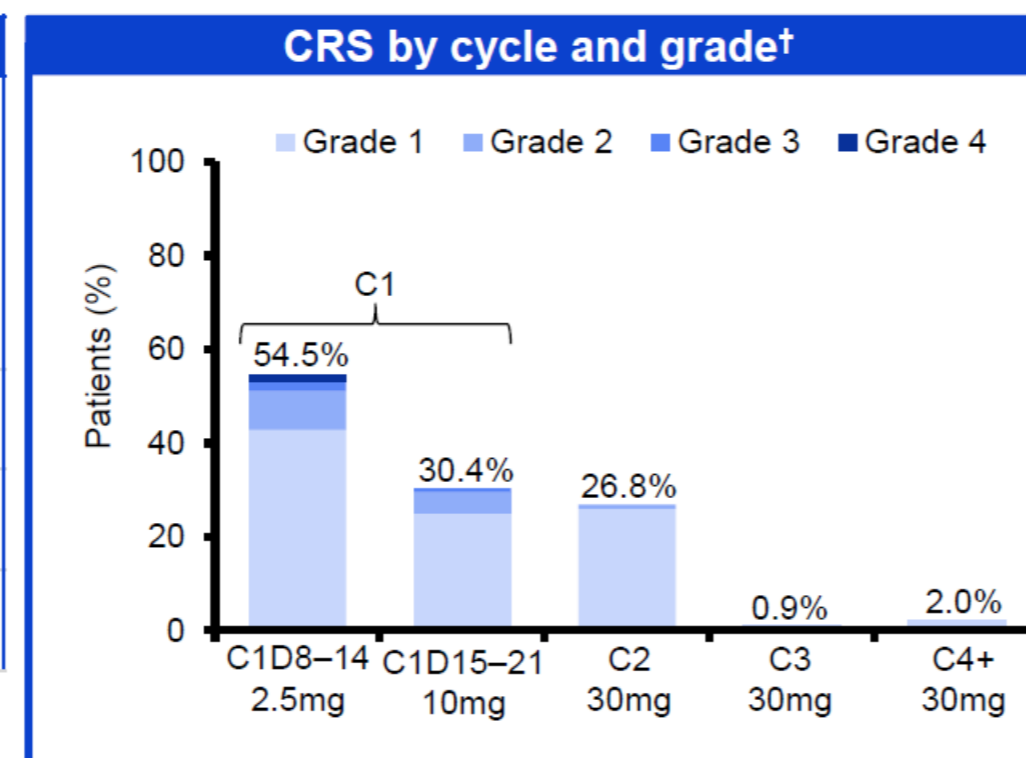
| N=80                             |                          |
|----------------------------------|--------------------------|
| Median DoR follow-up, mo (range) | 10.6 (0–21)              |
| <b>12-months DoR, % (95% CI)</b> | <b>63.6 (51.1, 76.2)</b> |
| ORs ongoing at CCOD, n (%)       | 53 (66.3)                |



| N=61                              |                          |
|-----------------------------------|--------------------------|
| Median DoCR follow-up, mo (range) | 10.6 (0–21)              |
| <b>12-months DoCR, % (95% CI)</b> | <b>77.6 (64.3, 90.8)</b> |
| CRs ongoing at CCOD, n (%)        | 49 (80.3)                |

#### Safety

| n (%)  | N=154           |
|--|-----------------|
| CRS (any grade)*                                       | 97 (63.0)       |
| Grade 1 (fever)  | 73 (47.4)       |
| Grade 2  | 18 (11.7)       |
| Grade 3  | 4 (2.6)         |
| Grade 4  | 2 (1.3)         |
| Median time to CRS onset from C1D8 dose, hours (range) | 13.6 (6.2–51.8) |
| Corticosteroids for CRS management                     | 27/97 (27.8)    |
| Tocilizumab for CRS management                         | 31/97 (32.0)    |



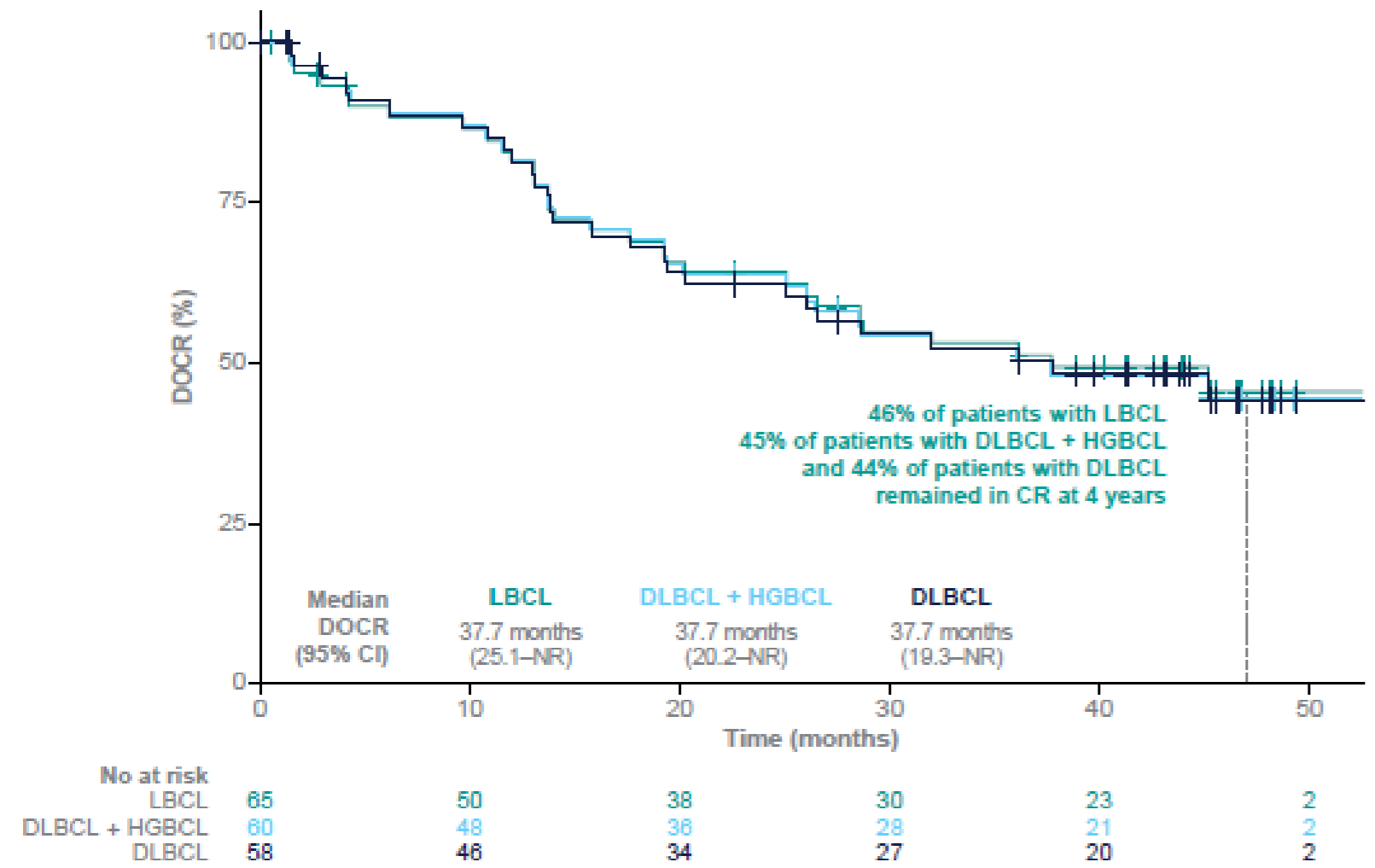
| n (%)                            | N=154     |
|----------------------------------|-----------|
| Infections (all grades)          | 59 (38.3) |
| Grade ≥3                         | 23 (14.9) |
| Neutropenia* (all grades)        | 58 (37.7) |
| Grade ≥3                         | 41 (26.6) |
| Febrile neutropenia (all grades) | 4 (2.6)   |
| Grade ≥3                         | 4 (2.6)   |
| Tumor flare events (all grades)  | 17 (11.0) |
| Grade ≥3                         | 4 (2.6)   |
| Neurologic AEs† (all grades)     | 59 (38.3) |
| Grade ≥3                         | 5 (3.2)   |
| ICANS‡ (derived)                 |           |
| All grades (CTCAE)               | 12 (7.8)  |
| Grade ≥3 (CTCAE)                 | 4 (2.6)§  |

| n (%)                                   | N=154    |
|---|----------|
| AE leading to treatment discontinuation | 14 (9.1) |
| Infections and infestations¶            | 6 (3.9)  |
| Delirium                                | 2 (1.3)  |
| Neutropenia**                           | 2 (1.3)  |
| Hepatobiliary disorders#                | 1 (0.6)  |
| Gastrointestinal hemorrhage**           | 1 (0.6)  |
| CRS**                                   | 1 (0.6)  |
| Melanoma recurrent                      | 1 (0.6)  |

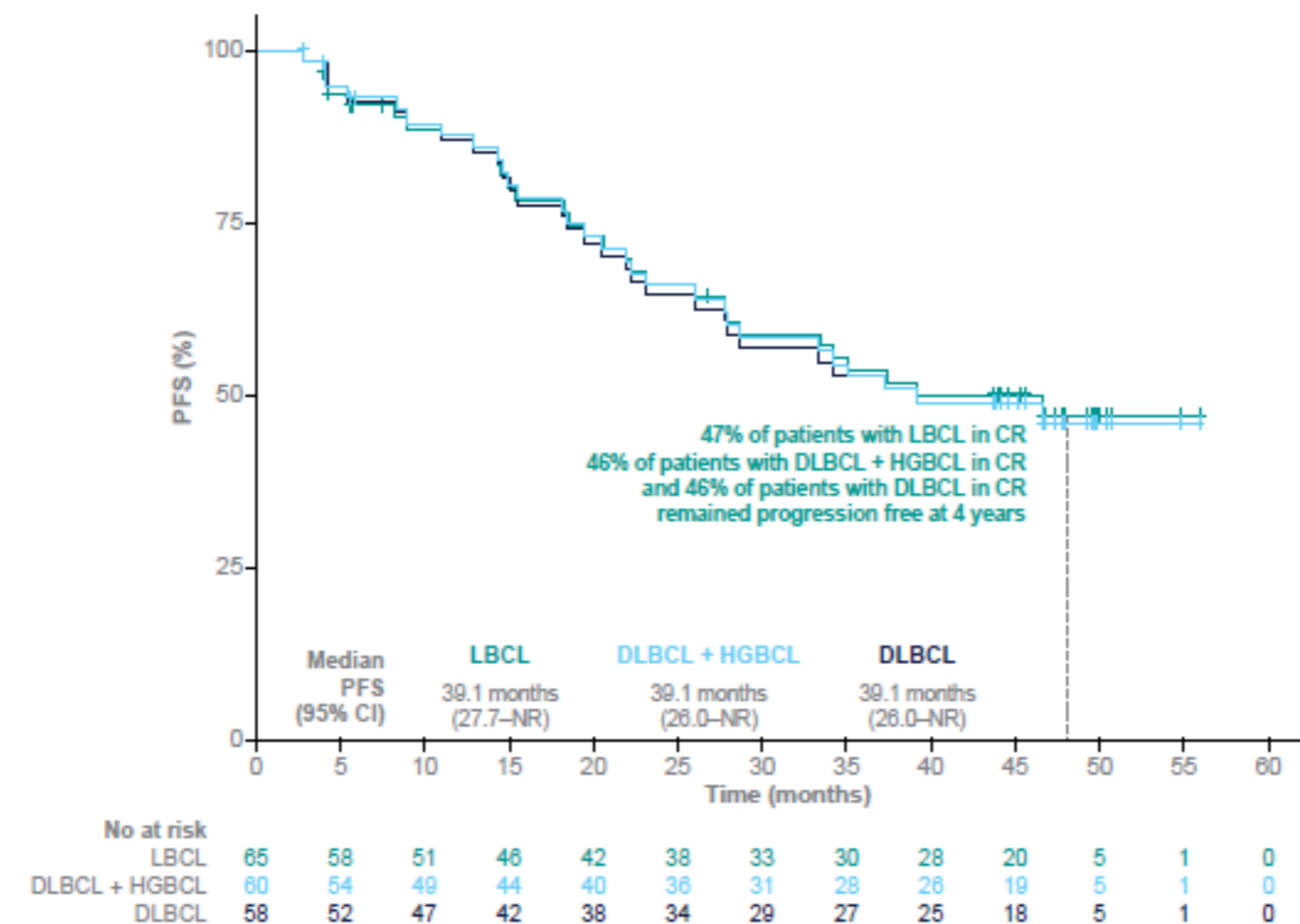
## BsAbs in DLBCL: currently status 3 L

### EPCORE NHL-1 trial: Epcoritamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

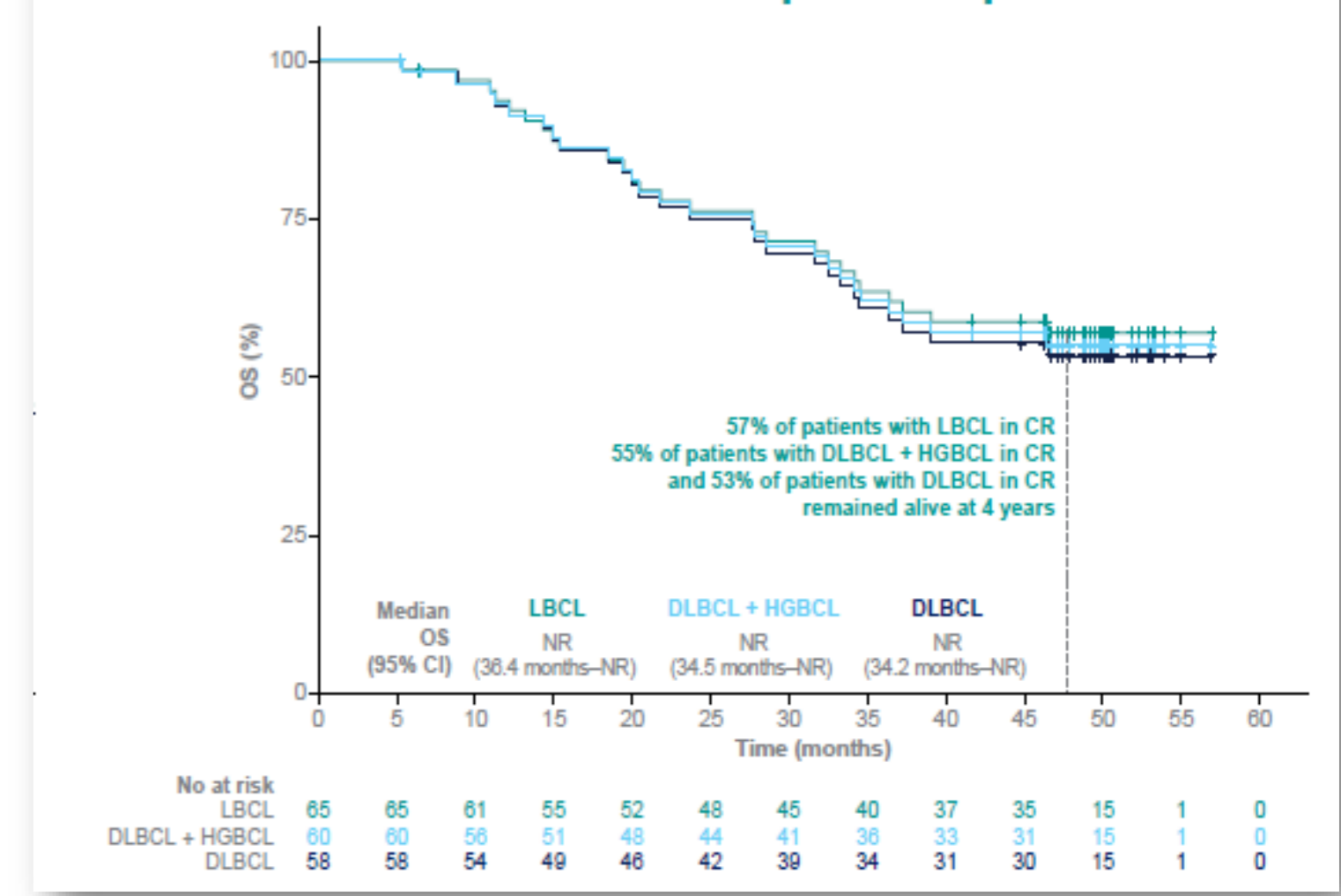
**Durable CRs > 4 Years**



**Sustained PFS > 4 Years in Complete Responders**



**Sustained OS > 4 Years in Complete Responders**



- Median DOCR 37.7 months
- Median treatment duration in patients with CR 18 months
- At data cut off, 42% of patients in CR were ongoing

- Median PFS 39.1 months
- PFS at 39.1 months was 47% in patient with LBCL in CR

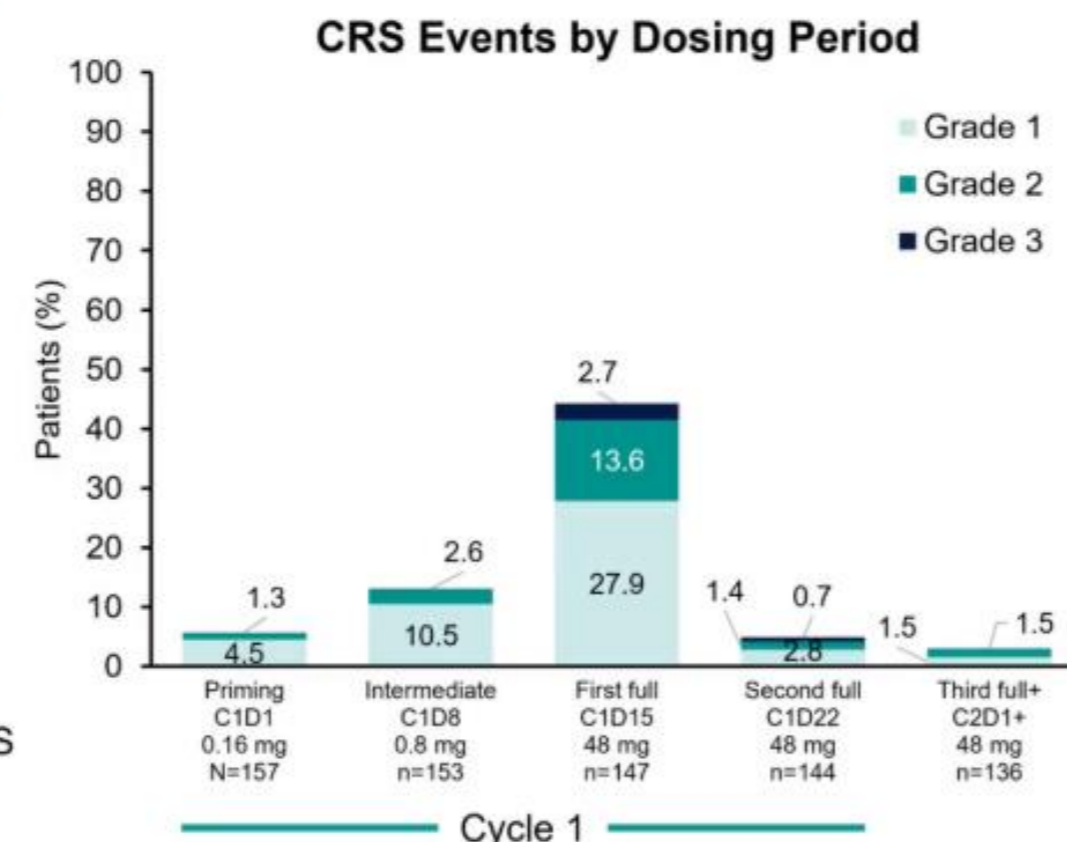
- Median OS NR
- A 4 years 57% of patients in CR remained alive

## BsAbs in DLBCL: currently status 3 L

### EPCORE NHL-1 trial: Epcoritamab for Relapsed or Refractory Diffuse Large B-Cell Lymphoma

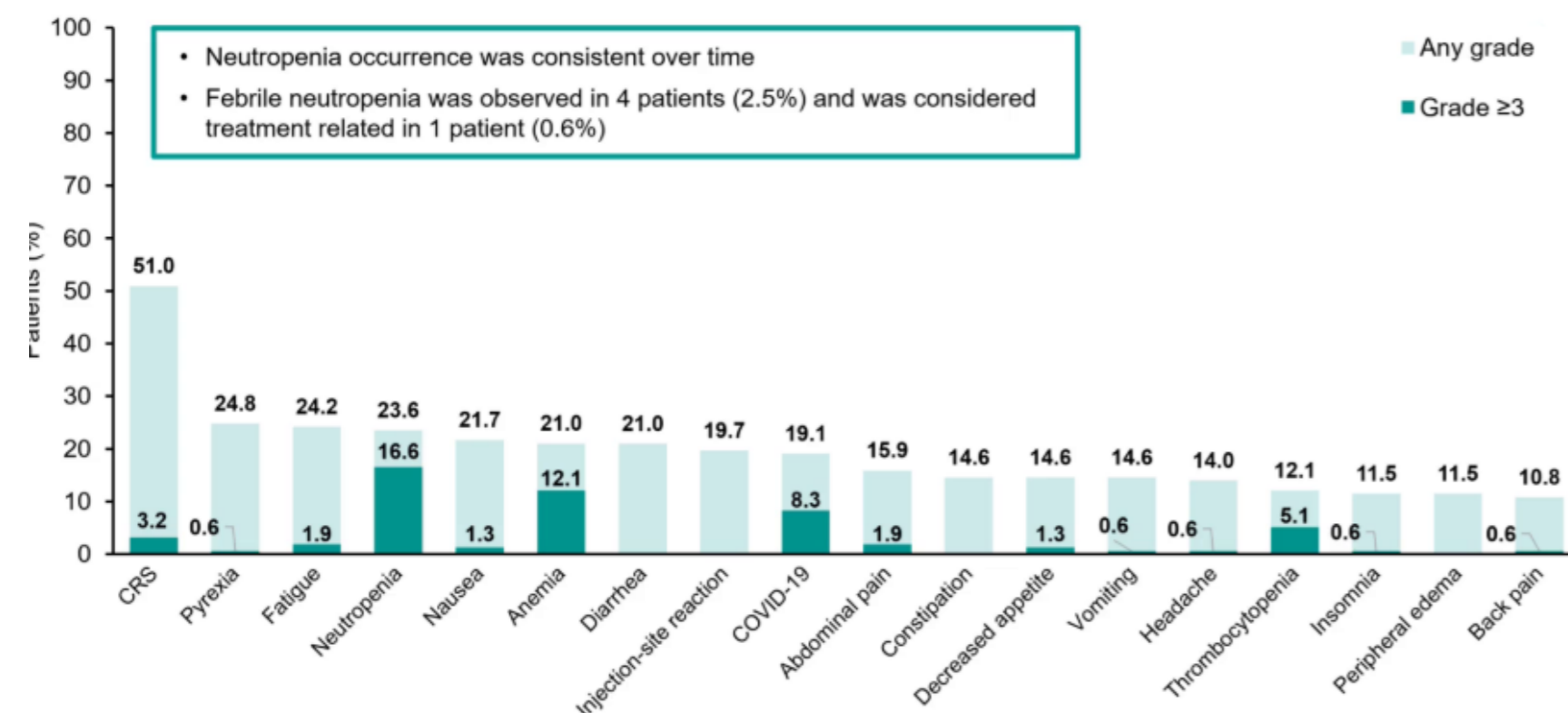
|  | LBCL<br>N=157    |
|--|------------------|
| CRS events, n (%) <sup>a</sup>                           | 80 (51.0)        |
| <b>Grade 1</b>   | <b>50 (31.8)</b> |
| Grade 2  | 25 (15.9)        |
| Grade 3  | 5 (3.2)          |
| CRS resolution, n/n (%)                                  | 78/80 (97.5)     |
| <b>Median time to resolution from first full dose, d</b> | <b>2</b>         |
| Treated with tocilizumab, n (%)                          | 23 (14.6)        |
| Treated with corticosteroids, n (%)                      | 17 (10.8)        |

- Results from the optimization part of the trial suggest that prophylactic dexamethasone and hydration in cycle 1 further reduce the frequency and severity of CRS



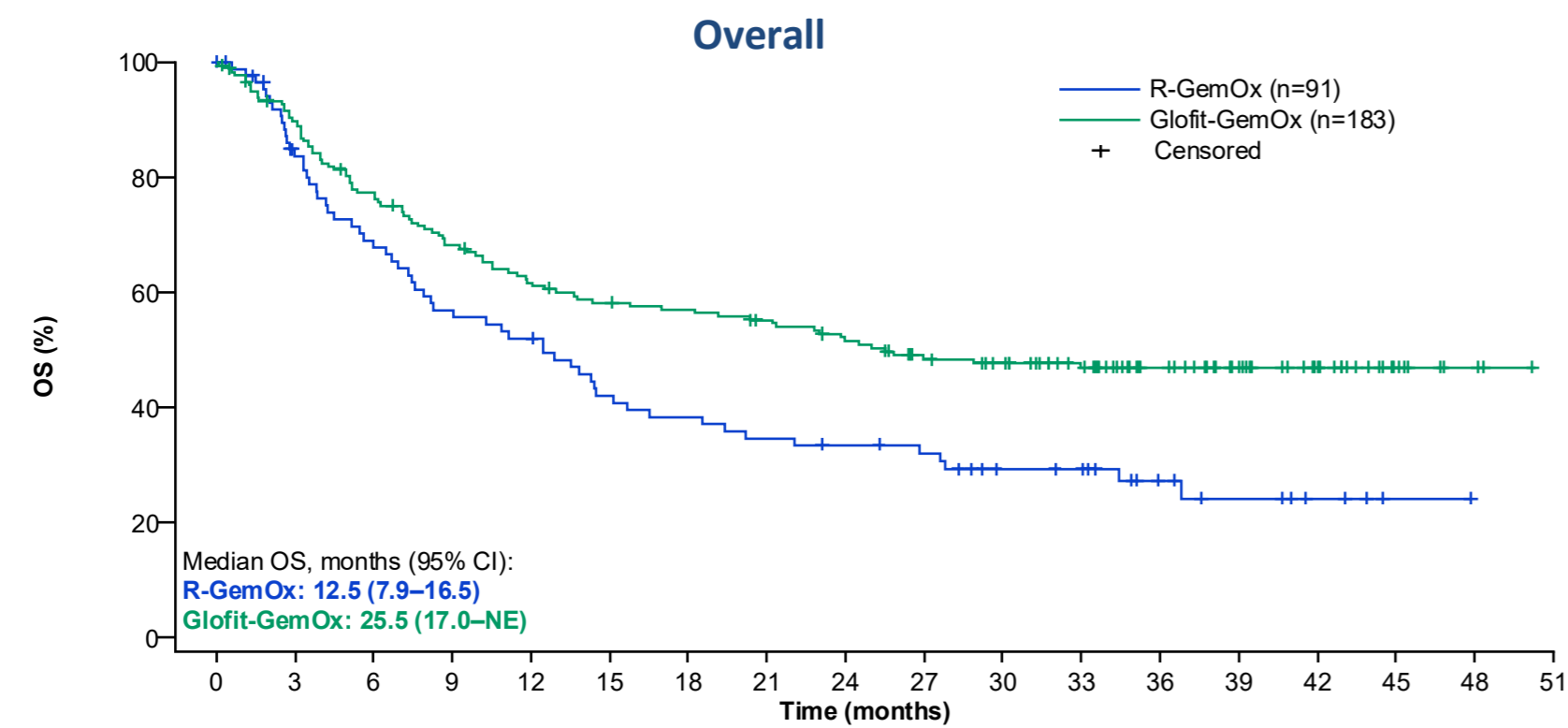
### Consistent Long-Term Safety

- Between years 3–4, 18 patients were on treatment; the longest duration of therapy at data cutoff was 54.8 months
  - Five discontinued treatment between years 3–4
    - Four discontinued as a result of patient and/or physician preference
    - One discontinued due to an AE (n = 1; grade 2 bronchitis)
- Most patients did not experience new grade  $\geq 3$  TEAEs since the previous report (May 2024–May 2025)
  - Four new grade  $\geq 3$  infections were reported in 3 patients: urosepsis (grade 3) and urinary tract infection (grade 3); pneumonia (grade 3); COVID-19 (grade 5)
  - One new fatal TEAE was reported: COVID-19 (grade 5; listed above)



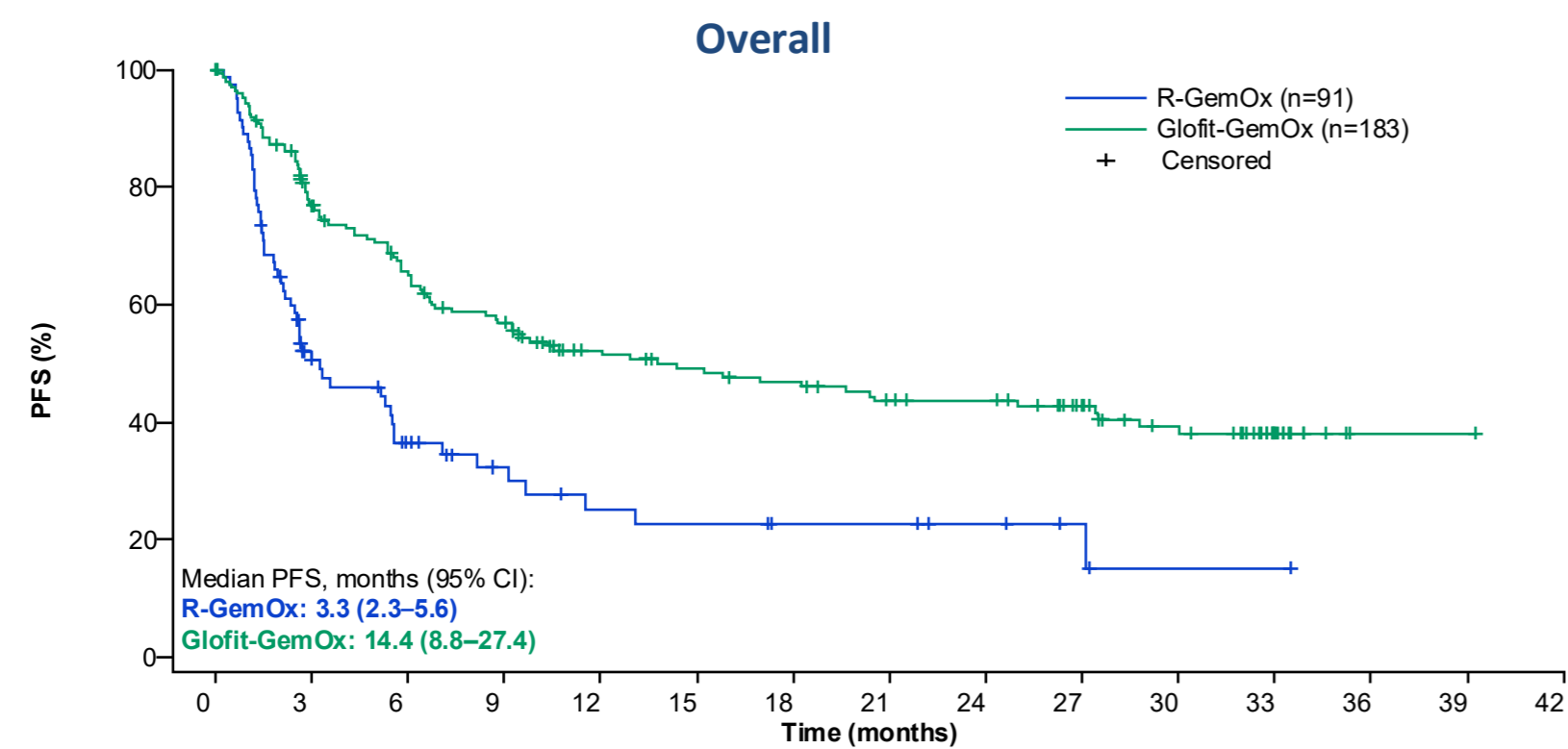
## BsAb in DLBCL: near future 2 L

### STARGLO: Glofitamab plus R-Gemox vs R-Gemox



n at risk:

| Time (months)        | 0   | 3   | 6   | 9   | 12  | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 | 45 | 48 | 51 |
|----------------------|-----|-----|-----|-----|-----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| R-GemOx (n=91)       | 91  | 69  | 56  | 47  | 43  | 34 | 31 | 28 | 26 | 24 | 18 | 17 | 10 | 7  | 4  | 1  | NE | NE |
| Glofit-GemOx (n=183) | 183 | 159 | 136 | 119 | 106 | 99 | 96 | 91 | 84 | 74 | 69 | 56 | 41 | 30 | 20 | 8  | 3  | NE |



n at risk:

| Time (months)        | 0   | 3   | 6   | 9  | 12 | 15 | 18 | 21 | 24 | 27 | 30 | 33 | 36 | 39 | 42 |
|----------------------|-----|-----|-----|----|----|----|----|----|----|----|----|----|----|----|----|
| R-GemOx (n=91)       | 91  | 34  | 21  | 14 | 10 | 9  | 7  | 7  | 5  | 3  | 1  | 1  | NE | NE | NE |
| Glofit-GemOx (n=183) | 183 | 129 | 106 | 90 | 70 | 64 | 60 | 53 | 51 | 42 | 30 | 13 | 1  | 1  | NE |

| Outcome   | R-GemOx (n=91)           | Glofit-GemOx (n=183) |
|---|--------------------------|----------------------|
| <b>~3-year follow up analysis</b> (median follow up: 35.1 [0-50]) |                          |                      |
| OS, median (95% CI); months                                       | 12.5 (7.9, 16.5)         | 25.5 (17.0, NE)      |
| HR (95% CI)   | <b>0.60</b> (0.43, 0.83) |                      |
| p-value*  | 0.0018                   |                      |
| 36-month OS, % (95% CI)   | 27.4 (17.3, 37.5)        | 47.1 (39.5, 54.6)    |

| Outcome                       | R-GemOx (n=91)           | Glofit-GemOx (n=183)     |
|-------------------------------|--------------------------|--------------------------|
| PFS, median (95% CI); months  | <b>3.3</b> (2.3, 5.6)    | <b>14.4</b> (8.8, 27.4)  |
| 30-month PFS, % (95% CI)      | <b>15.2</b> (0.9, 30)    | <b>38.1</b> (30, 46)     |
| ORR, % (95% CI)               | <b>40.7</b> (30.5, 51.5) | <b>68.3</b> (61.0, 75.0) |
| CR rate, % (95% CI)           | <b>25.3</b> (16.8, 35.5) | <b>58.5</b> (51.0, 65.7) |
| DoCR, median (95% CI); months | 24.2 (6.9, NE)           | NE (27.2, NE)            |
| Ongoing CR, % (n)             | <b>69.6</b> (16/23)      | <b>71.8</b> (74/107)     |

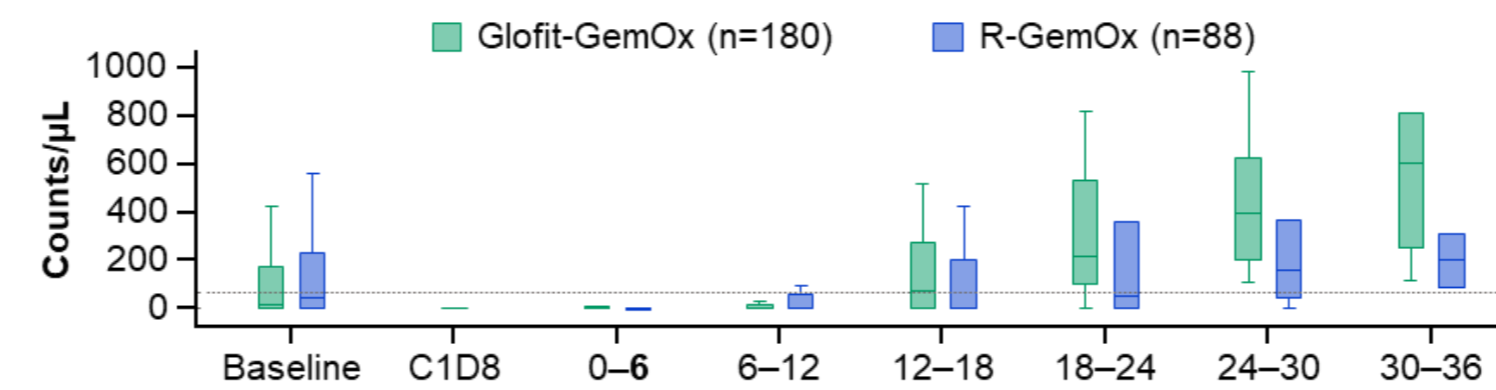
## BsAbs in DLBCL: near future 2 L

### STARGLO: Glofitamab plus R-Gemox vs R-Gemox

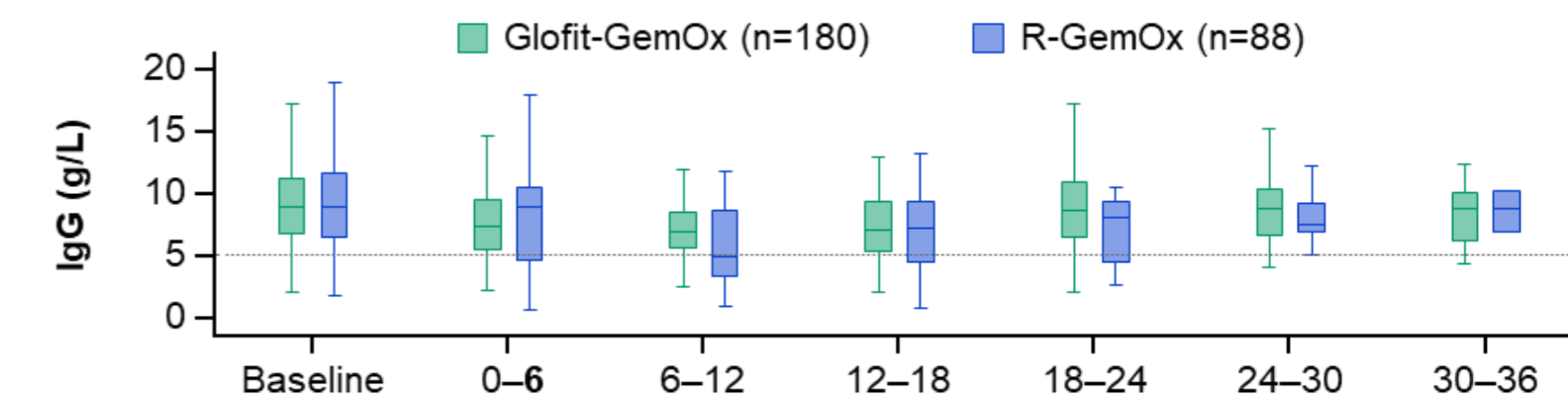
| n (%), unless otherwise stated          | R-GemOx (n=88) | Glofit-GemOx (Glofit-exposed) (n=172) |
|---|----------------|---------------------------------------|
| <b>Any grade AE</b>                     | 85 (96.6)      | 172 (100)                             |
| Grade 3–4 AE                            | 36 (40.9)      | 119 (69.2)                            |
| Grade 5 (fatal) AE                      | 4 (4.5)        | 13 (7.6)                              |
| Serious AE                              | 15 (17.0)      | 90 (52.3)                             |
| AE leading to discontinuation*          | 3 (3.4)        | 13 (7.6)                              |
| <b>CRS<sup>†</sup></b>                  | 0              | 77 (44.8)                             |
| Grade 1                                 | 0              | 55 (32.0)                             |
| Grade 2                                 | 0              | 18 (10.5)                             |
| Grade 3                                 | 0              | 4 (2.3)                               |
| <b>Infections Grade 3–5<sup>‡</sup></b> | 11 (12.5)      | 34 (19.8)                             |

\*COVID-19 was the most common infection in both treatment arms, occurring during the COVID-19 pandemic

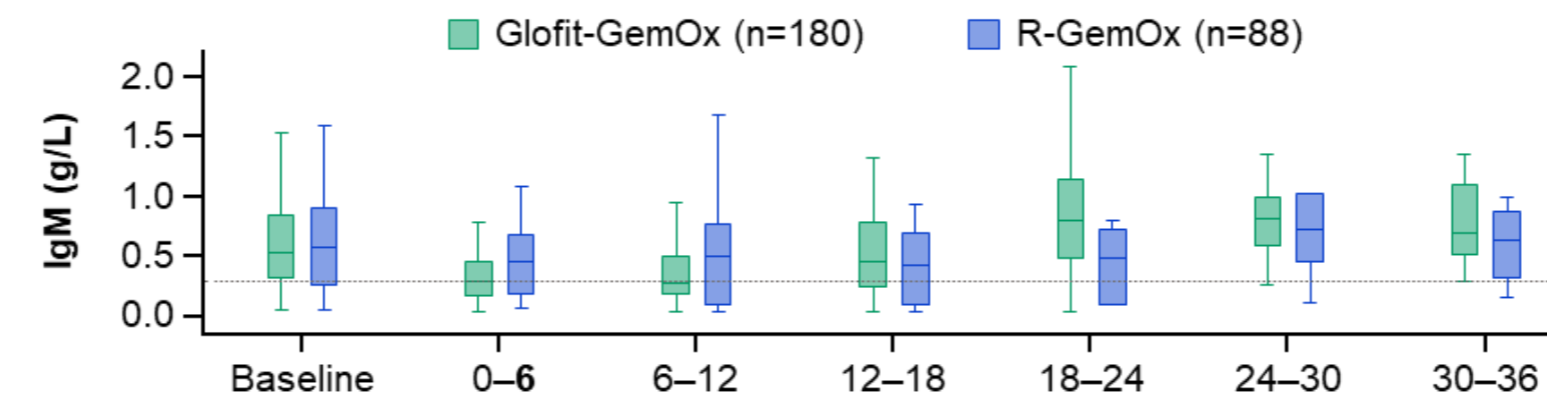
ICANS occurred in four patients (all concurrent with CRS; most Grade 1–2 [n=3])



|                     | Visit |      |      |      |       |        |        |        |
|---------------------|-------|------|------|------|-------|--------|--------|--------|
| <b>Glofit-GemOx</b> |       |      |      |      |       |        |        |        |
| n                   | 122   | 120  | 89   | 46   | 46    | 36     | 26     | 11     |
| Median              | 19.00 | 0.00 | 0.00 | 0.00 | 73.50 | 218.50 | 395.50 | 602.00 |
| <b>R-GemOx</b>      |       |      |      |      |       |        |        |        |
| n                   | 43    | 0    | 30   | 14   | 10    | 7      | 7      | 2      |
| Median              | 44.00 | NE   | 0.00 | 0.87 | 6.24  | 54.00  | 160.00 | 199.00 |



|                     | Visit |      |      |      |      |      |      |  |
|---------------------|-------|------|------|------|------|------|------|--|
| <b>Glofit-GemOx</b> |       |      |      |      |      |      |      |  |
| n                   | 138   | 92   | 60   | 59   | 51   | 38   | 11   |  |
| Median              | 8.88  | 7.36 | 6.85 | 7.10 | 8.68 | 8.83 | 8.79 |  |
| <b>R-GemOx</b>      |       |      |      |      |      |      |      |  |
| n                   | 48    | 31   | 17   | 14   | 9    | 6    | 3    |  |
| Median              | 8.89  | 8.91 | 4.97 | 7.28 | 8.03 | 7.55 | 8.75 |  |



|                     | Visit |      |      |      |      |      |      |  |
|---------------------|-------|------|------|------|------|------|------|--|
| <b>Glofit-GemOx</b> |       |      |      |      |      |      |      |  |
| n                   | 141   | 95   | 62   | 59   | 52   | 38   | 11   |  |
| Median              | 0.53  | 0.29 | 0.29 | 0.46 | 0.80 | 0.81 | 0.70 |  |
| <b>R-GemOx</b>      |       |      |      |      |      |      |      |  |
| n                   | 50    | 33   | 17   | 14   | 9    | 6    | 4    |  |
| Median              | 0.58  | 0.46 | 0.50 | 0.42 | 0.48 | 0.73 | 0.63 |  |

- B-cell depletion on treatment was rapid recovery was observed within 18–24 months after EOT
- Median B-cell and immunoglobulin (Ig) counts were above the lower limit of normal 18–24 months after EOT;

## BsAbs in DLBCL: future 1 L

### EPCORE NHL-2 Arm 1: subcutaneous Epcoritamab + R-CHOP vs R-CHOP

#### KEY INCLUSION CRITERIA

- Newly diagnosed CD20 DLBCL
- IPI score  $\geq 3$
- ECOG PS 0-2
- Adequate organ function
- Misurable disease

Step-up dosing

Epcoritamab (SC)  
48 mg  
QW C1-4,  
Q3W C5-6,  
Q4W C7+  
+ R-CHOP  
C1-6

Epcoritamab monotherapy for 1 year treatment

Received Epcoritamab + R-CHOP (n) 47

|                       |            |
|-----------------------|------------|
| Median age (years)    | 64 (19-82) |
| Bulky disease (%)     | 34         |
| Double/triple hit (n) | 6/31       |
| IPI score 3 (%)       | 57%        |
| IPI score 4-5 (%)     | 38%        |

|                                      |                 |
|--------------------------------------|-----------------|
| Median Follow-up (months)            | 38.8 (0.8-44.4) |
| ORR (%)                              | 98              |
| - CR (%)                             | - 85            |
| CR rates (%)                         |                 |
| - IPI 3                              | - 86            |
| - IPI 4-5                            | - 83            |
| 33 months PFS (%)                    | 80              |
| Median duration Epcoritamab (months) | 11.5 (0.6-13.2) |

|  |           |
|--|-----------|
| Pts completed treatment (n; %)                     | 32/47; 68 |
| Reasons to failure to complete treatment (%)       |           |
| - AEs  | - 11      |
| - Progressive disease                              | - 9       |
| - Withdrawal by patient                            | - 6       |
| - COVID 19   | - 2       |
| - Others (physician decision, incomplete response) | - 4       |
| CR at EOT (n)                                      | 30/32     |
| Median follow-up for DOR (months)                  | 25.3      |
| CR during follow-up (%)                            | 27        |

# Treatment of DLBCL: past, present and future

|          | DLBCL 2020  | DLBCL 2021-2026  | DLBCL 2026-  |
|----------|---|--|--|
| I line   | <ul style="list-style-type: none"> <li>• Chemo-Immunotherapy</li> </ul>   | <ul style="list-style-type: none"> <li>• Chemo-Immunotherapy</li> </ul>  | <ul style="list-style-type: none"> <li>• BsABs or CART+/- chemoimmunotherapy</li> </ul>  |
| II line  | <ul style="list-style-type: none"> <li>• Chemo-immunotherapy</li> <li>• ASCT</li> </ul>   | <ul style="list-style-type: none"> <li>• CART</li> <li>• BsABs+chemo-immunotherapy</li> <li>• Chemo-immunotherapy</li> <li>• ASCT</li> <li>• ADCs, Tafa-Len</li> </ul> | <ul style="list-style-type: none"> <li>• CART</li> <li>• BsABs +/- X</li> <li>• BsABs combo</li> <li>• ASCT?</li> </ul>          |
| III line | <ul style="list-style-type: none"> <li>• CART</li> <li>• Chemo-immunotherapy</li> <li>• ASCT</li> <li>• ADCs, Tafa-Len</li> </ul> | <ul style="list-style-type: none"> <li>• BsABs (CD20)</li> <li>• CAR-T (CD19)</li> <li>• ADCs, Tafa-Len</li> </ul>   | <ul style="list-style-type: none"> <li>• BsABs+/- X</li> <li>• CAR-T</li> <li>• BsABs combo</li> <li>• ADCs, Tafa-Len</li> </ul> |

## BsAbs in FL: currently status 3 L

### GO29781: Mosunetuzumab for patients with R/R FL and $\geq 2$ prior therapies

| Efficacy endpoints                       | Overall population   | Non-POD24 <sup>1</sup><br>(n=43) | POD24 <sup>1</sup><br>(n=47)  |
|--|----------------------|----------------------------------|-------------------------------|
| ORR, n (%) [95% CI] <sup>1</sup>         | 70 (78%) [67.8–85.9] | 32 (74%) [58.8–86.5]             | 38 (81%) [66.7–90.9]          |
| CR rate, n (%) [95% CI] <sup>1</sup>     | 54 (60%) [49.1–70.2] | 26 (61%) [44.4–75.0]             | 28 (60%) [44.3–73.6]          |
| <b>DOR</b>                               |                      |                                  |                               |
| Median, months (95% CI)                  | 46 (34-59)           | 35.9 (20.7–NE)                   | NR (10.6–NE)                  |
| 30-month DOR, % (95% CI)                 | 55% (43.3–67.8)      | 61% (43.9–78.5)                  | 50% (33.2–67.4)               |
| 54-month DOR, % (95% CI)                 | 46% (33.8-59.1)      | -                                | -                             |
| <b>DOCR</b>                              |                      |                                  |                               |
| Median, months (95% CI)                  | NR (44.1–NE)         | NR (31.5–NE)                     | 50.1 (18.7–NE) <sup>2</sup>   |
| 30-month DOCR, % (95% CI)                | 71% (58.2–84.0)      | 75% (56.5–92.6)                  | 67% (48.8–86.1)               |
| 54-month DOCR, % (95% CI)                | 52% (36.2-67.9)      | -                                | 48% (24.9-71.5) <sup>2</sup>  |
| <b>PFS</b>                               |                      |                                  |                               |
| Median, months (95% CI)                  | 24 (12–53,2)         | 26 (11,8–NE)                     | 22 (11.6–61) <sup>2</sup>     |
| 5-years PFS, % (95% CI)                  | 36.5% (25.3-47.7)    | 36 (20.4-51.5)                   | 36.9 (20.7-53.1) <sup>2</sup> |
| Median OS <sup>2</sup> , months (95% CI) | NR (NE)              | NR (NE)                          | NR (NE)                       |

- At a median follow-up of 60.2 months (5 years) over half of patients with a CR are in remission
- OS remained high after 5 years of follow up
- High and durable response rates were achieved, irrespective of POD24 status
- Similar PFS and OS benefit were observed in patients with non-POD24 and POD24

1. Shadman M, et al. ASH 2024; abstract #4407.

2. Budde LE, et al. ASH 2025; abstract #5352.

## BsAbs in FL: currently status 3 L

### *EPCORE NHL-1 FL e NHL3 FL : Epcoritamab for patients with R/R FL and ≥2 prior therapies*

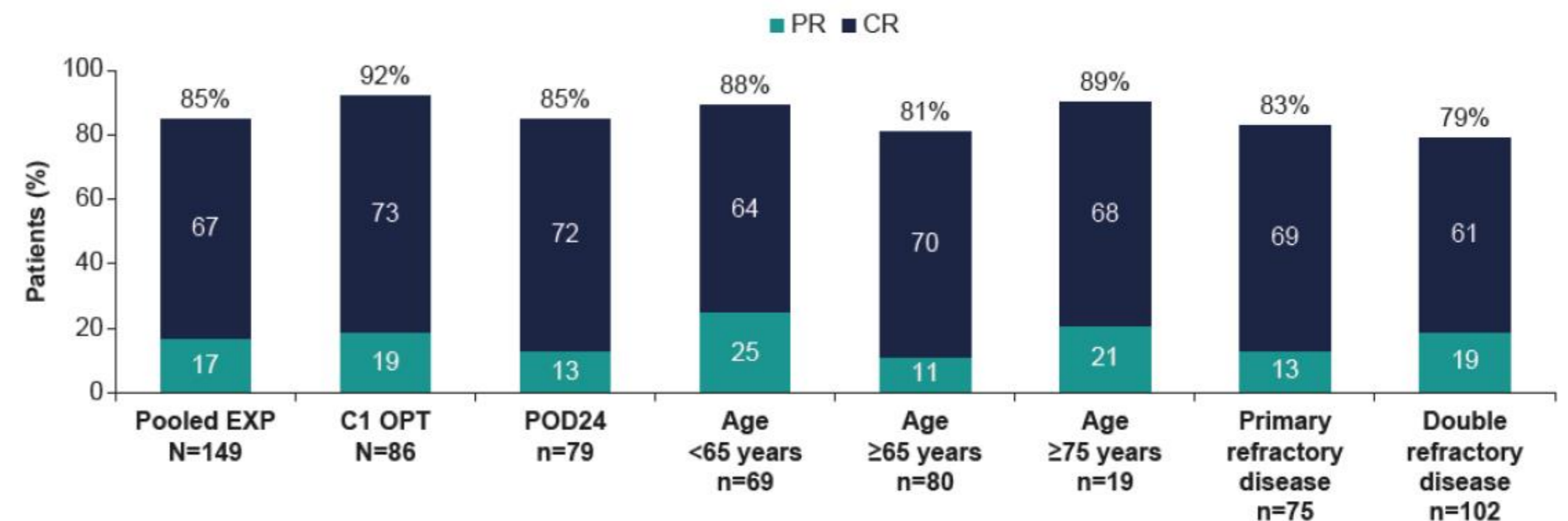
- Last update 2025
- To increase diversity and expand patients population, the EXP cohort of NHL-1 and NHL-3 were pooled → pooled EXP n=149 (NHL-1 n= 128; NHL-2 n= 21)
- In the pooled cohort, the sensitivity analysis for PFS and OS were performed based on adjusted population excluding deaths related to COVID19

| Efficacy endpoints              | Without covid19 adjustment | With covid19 adjustment |
|---------------------------------|----------------------------|-------------------------|
| DOCR<br>Median, months (95% CI) | NR (31.1–NR)               | NR (NR–NR)              |
| PFS<br>Median, months (95% CI)  | 15.4 (9.5-34)              | 34.2 (13.2-NR)          |
| 30 months OS, months (95% CI)   |                            | 79%                     |

TTNT (95% CI)

45.4 (22.7-NR)

EPCORITAMAB TREATMENT RESULTED IN DEEP RESPONSES ACROSS SUBGROUP



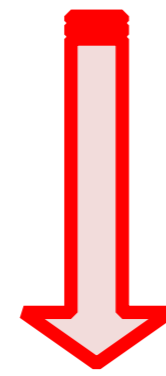
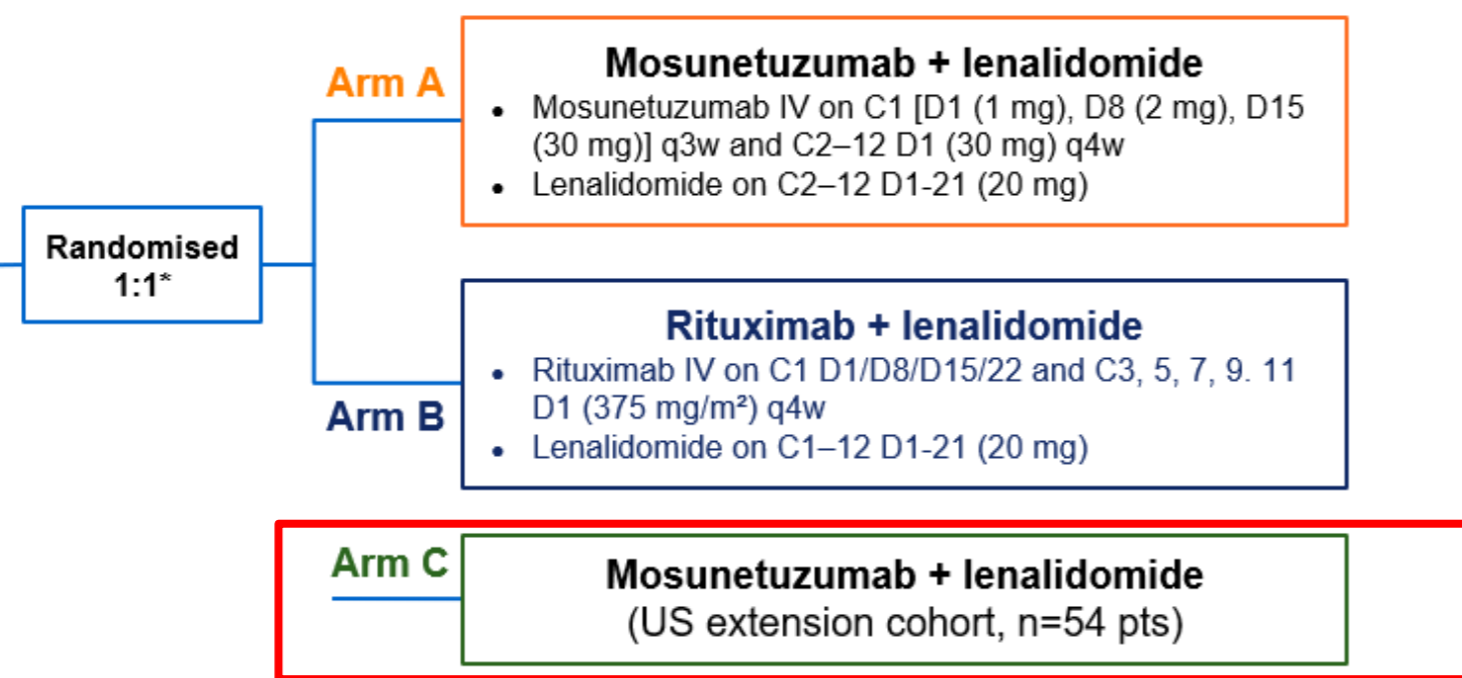
Vitolo et al, PF881, EHA 2025

## BsAbs in FL: near future 2 L

**CELESTIMO: Mosun (IV) + Len vs R-Len for patients with R/R FL and ≥1 prior therapies**

| Eligibility   |
|---|
| <ul style="list-style-type: none"> <li>Age ≥18 years</li> <li>Grade 1–3a CD20+ FL</li> <li>ECOG PS 0–2</li> <li>≥1 prior systemic anti-lymphoma therapy</li> <li>Target enrolment (Randomised cohort): 400</li> </ul> |

| Stratification factors   |
|--|
| <ul style="list-style-type: none"> <li>POD 24 status</li> <li>Prior lines of therapy (1 vs ≥2)</li> <li>Refractoriness to anti-CD20 therapy</li> </ul> |



| Key inclusion criteria   |
|--|
| <ul style="list-style-type: none"> <li>CD20+ FL Grade 1–3a</li> <li>≥1 prior systemic therapy for FL</li> <li>ECOG PS 0–2</li> </ul> |

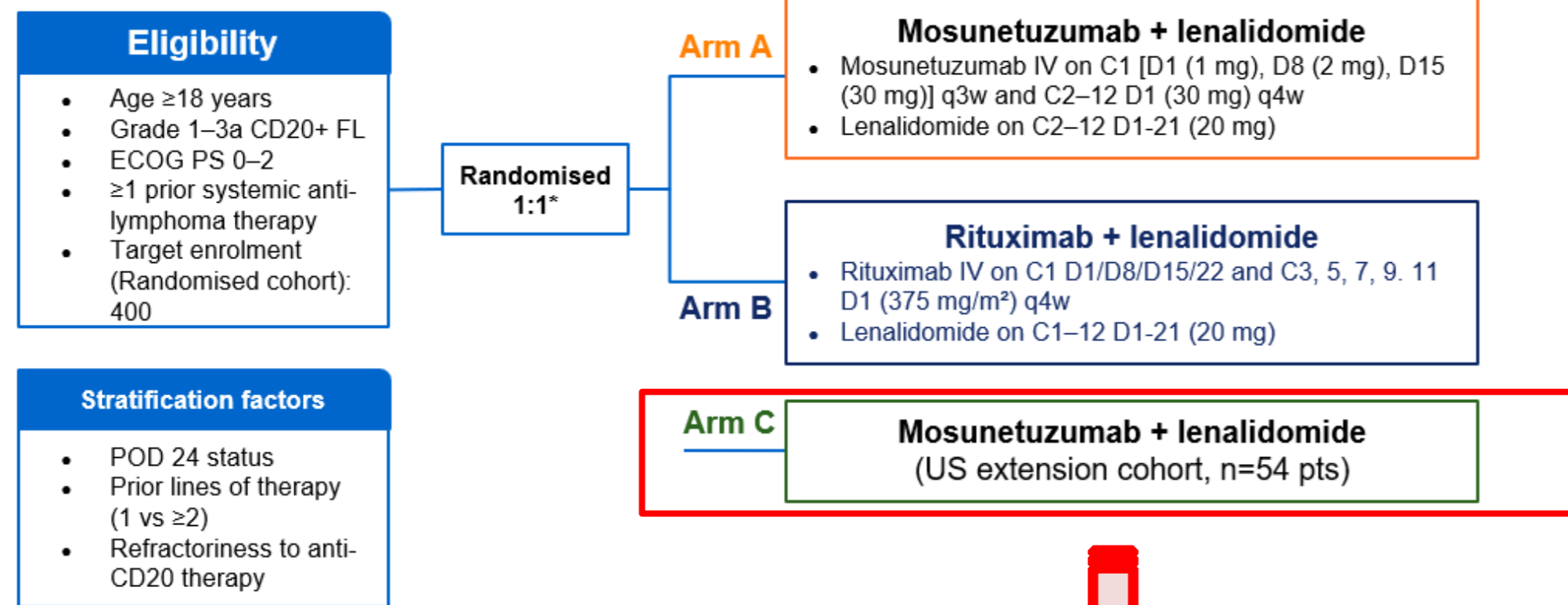
| Endpoints  |
|--|
| <ul style="list-style-type: none"> <li>Preliminary efficacy of Mosun-Len: INV-assessed ORR and CR (Lugano criteria<sup>1</sup>)</li> <li>Safety: incidence and severity of AEs and CRS according to CTCAE v5.0 and ASTCT<sup>2</sup> criteria, respectively</li> </ul> |

| Efficacy overview          | US cohort (N=54) |
|----------------------------|------------------|
| ORR, n (%)                 | 52 (96.3)        |
| CR rate, n (%)             | 47 (87.0)        |
| PR rate, n (%)             | 5 (9.3)          |
| Stable disease, n (%)      | 0                |
| Progressive disease, n (%) | 2 (3.7)          |
| 12-month DOR, % (95% CI)   | 88.4 (78.7-98.0) |

- median follow-up of 12.7 months (range: 5-20)
- ORR was 96.3%, and 87.0% of patients achieved a CR

## BsAb in FL: near future 2 L

### CELESTIMO: Mosun (IV) + Len vs R-Len for patients with R/R FL and ≥1 prior therapies



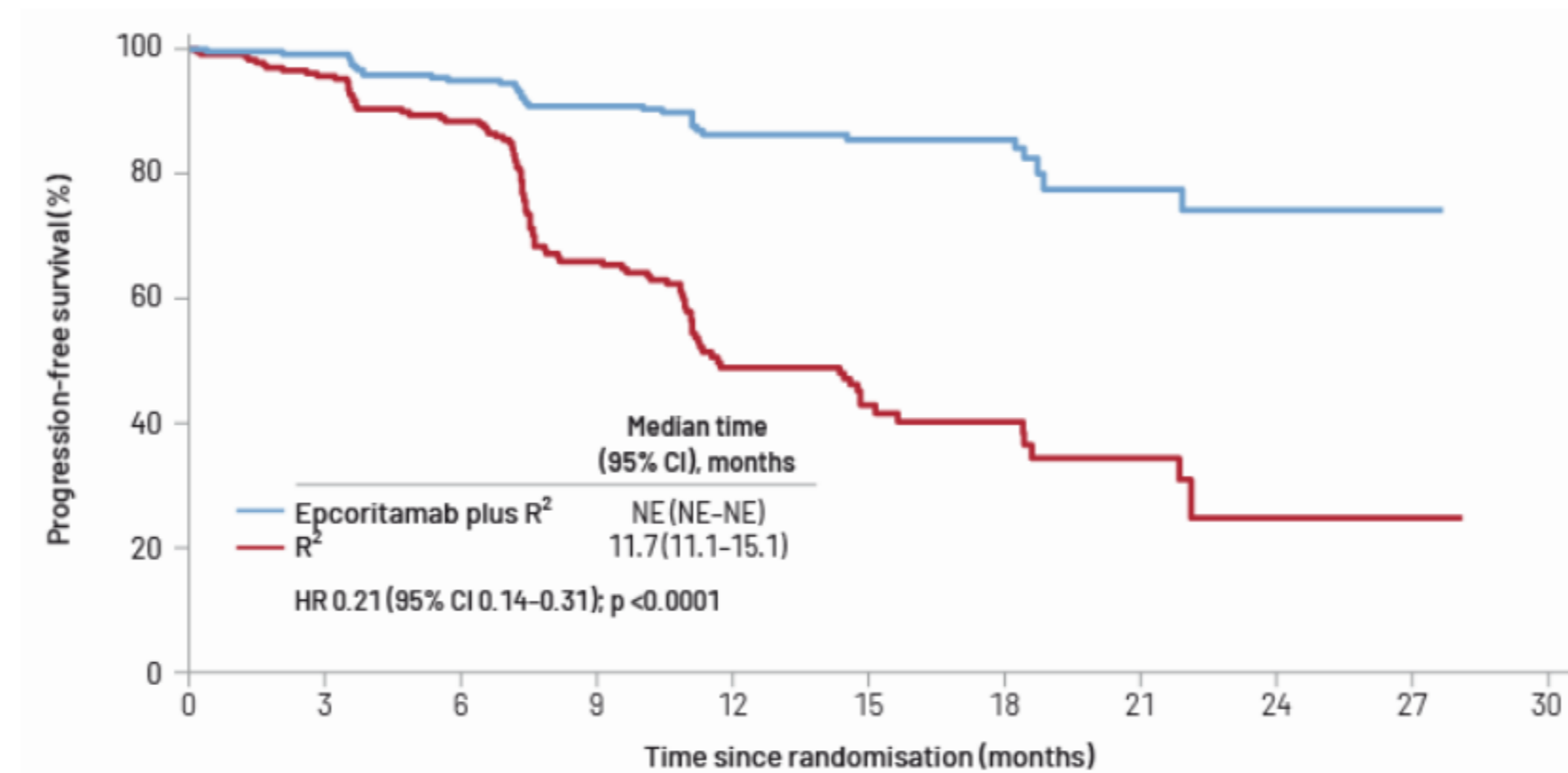
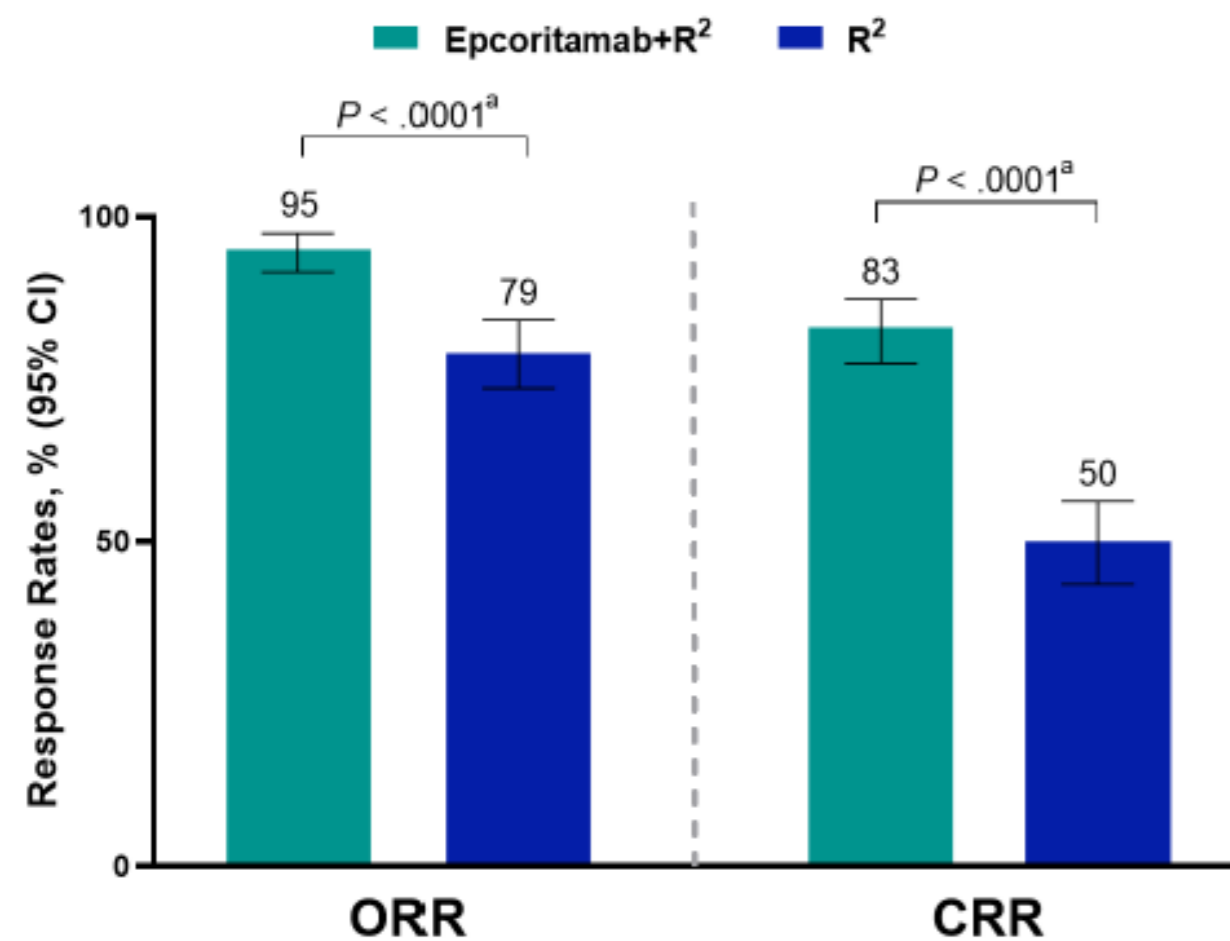
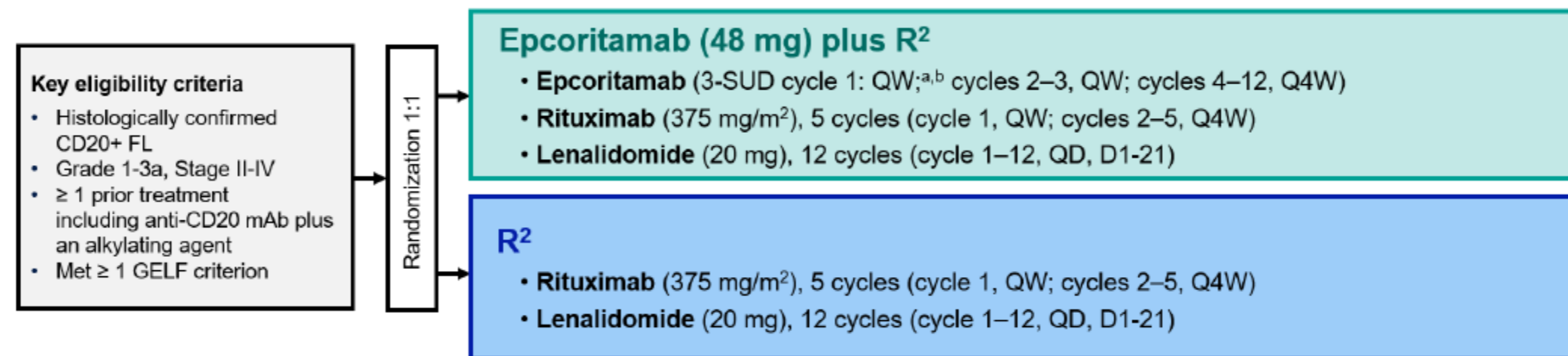
| Key inclusion criteria   | Endpoints  |
|--|--|
| <ul style="list-style-type: none"> <li>CD20+ FL Grade 1–3a</li> <li>≥1 prior systemic therapy for FL</li> <li>ECOG PS 0–2</li> </ul> | <ul style="list-style-type: none"> <li>Preliminary efficacy of Mosun-Len: INV-assessed ORR and CR (Lugano criteria<sup>1</sup>)</li> <li>Safety: incidence and severity of AEs and CRS according to CTCAE v5.0 and ASTCT<sup>2</sup> criteria, respectively</li> </ul> |

| n (%)                                       | US cohort (N=54) | n (%)   | US cohort (N=54) |
|---|------------------|---|------------------|
| <b>Any grade AE</b>                         | <b>54 (100)</b>  | <b>Infections<sup>†</sup></b>                 | <b>31 (57.4)</b> |
| Mosunetuzumab related                       | 48 (88.9)        | Grade 1                                       | 2 (3.7)          |
| Lenalidomide related                        | 50 (92.6)        | Grade 2                                       | 24 (44.4)        |
| AE leading to mosunetuzumab discontinuation | 6 (11.1)         | Grade 3                                       | 3 (5.6)          |
| AE leading to lenalidomide discontinuation  | 10 (18.5)        | Grade 4                                       | 1 (1.9)          |
|   |                  | Grade 5                                       | 1 (1.9)          |
| <b>Grade 3–4 AE</b>                         | <b>31 (57.4)</b> | <b>Neutropenia/neutrophil count decreased</b> | <b>22 (40.7)</b> |
| <b>Grade 5*</b>                             | <b>1 (1.9)</b>   | Grade 3/4                                     | 18 (33.3)        |
| <b>Serious AE</b>                           | <b>15 (27.8)</b> | <b>Febrile neutropenia Grade 3</b>            | <b>2 (3.7)</b>   |
| Mosunetuzumab related                       | 9 (16.7)         |   |                  |
| Lenalidomide related                        | 4 (7.4)          |   |                  |
| <b>CRS by ASTCT grading</b>                 | <b>15 (27.8)</b> |   |                  |
| Grade 1                                     | 12 (22.2)        |   |                  |
| Grade 2                                     | 2 (3.7)          |   |                  |
| Grade 3                                     | 1 (1.9)          |   |                  |

- CRS events were reported in 27.8% of patients. All were resolved and were predominately low grade, with a median duration of 4.0 days (range: 1.0-23.0).
- Infections were reported in 57.4% of patients and were mainly Grade 2 (44.4%) in severity.

## BsAbs in FL: near future 2 L

### EPCORE FL-1 : fixed Epcoritamab (SC) + R-Len vs R-Len



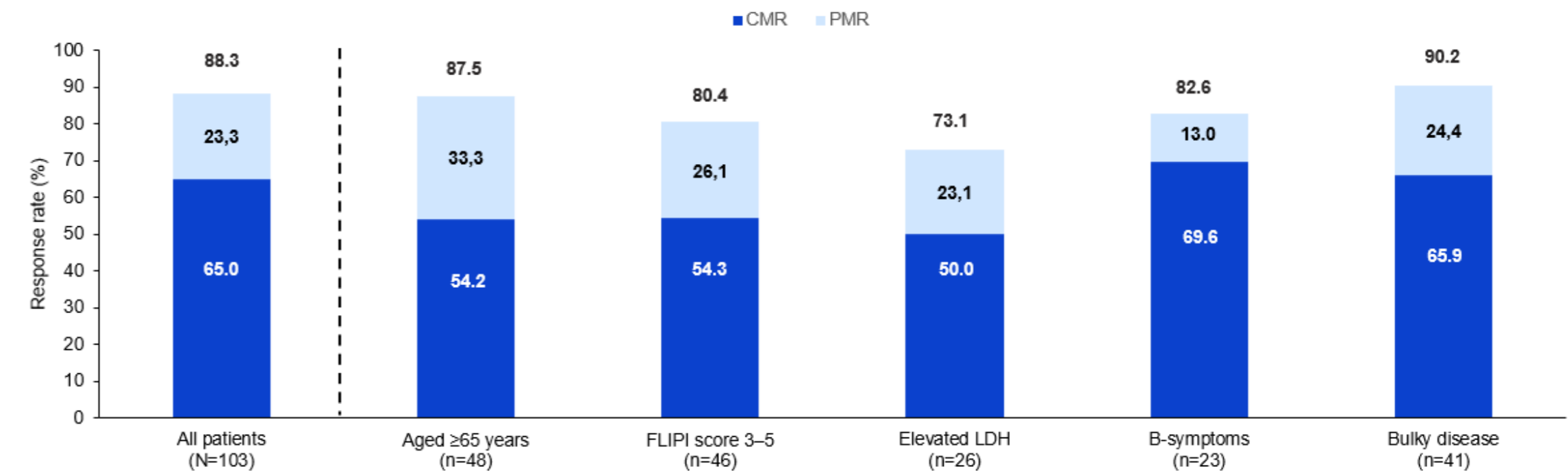
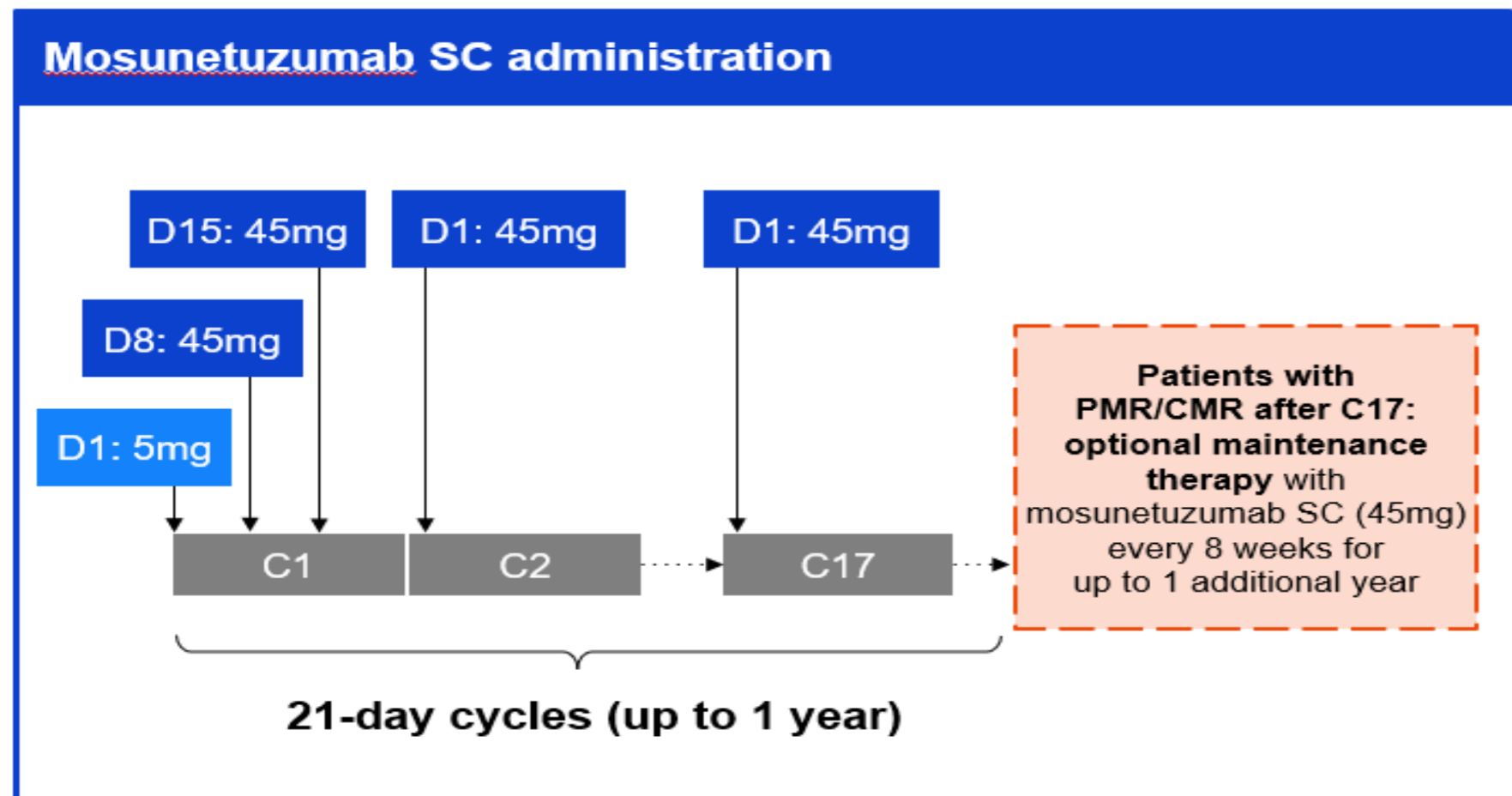
| Adverse Event, n (%)                                    | Epcoritamab+R <sup>2</sup> (N = 243) |           | R <sup>2</sup> (N = 238) |           |
|---|--------------------------------------|-----------|--------------------------|-----------|
|   | Any Grade                            | Grade ≥ 3 | Any Grade                | Grade ≥ 3 |
| Any adverse event                                       | 242 (100)                            | 219 (90)  | 235 (99)                 | 161 (68)  |
| Serious adverse event                                   | 135 (56)                             | -         | 69 (29)                  | -         |
| Adverse event leading to treatment discontinuation      | 46 (19)                              | -         | 29 (12)                  | -         |
| <i>Epcoritamab</i>                                      | 21 (9)                               | -         | -                        | -         |
| <i>Rituximab</i>  | 7 (3)                                | -         | 12 (5)                   | -         |
| <i>Lenalidomide</i>                                     | 45 (19)                              | -         | 29 (12)                  | -         |
| Adverse event of clinical interest > 20% <sup>a,b</sup> |                                      |           |                          |           |
| <i>Infections<sup>c</sup></i>                           | 188 (77)                             | 81 (33)   | 125 (53)                 | 37 (16)   |
| <i>Neutropenia</i>                                      | 180 (74)                             | 167 (69)  | 123 (52)                 | 100 (42)  |
| <i>Cytokine release syndrome</i>                        | 85 (35)                              | -         | 1 (< 1)                  | -         |
| <i>Anemia</i>   | 68 (28)                              | 19 (8)    | 41 (17)                  | 11 (5)    |
| <i>Thrombocytopenia</i>                                 | 67 (28)                              | 23 (9)    | 44 (18)                  | 15 (6)    |
| <i>Pyrexia</i>  | 58 (24)                              | 1 (< 1)   | 33 (14)                  | 3 (1)     |
| <i>Rash</i>   | 58 (24)                              | 19 (8)    | 53 (22)                  | 9 (4)     |
| <i>COVID-19</i>   | 54 (22)                              | 7 (3)     | 32 (13)                  | 4 (2)     |

16 months PFS 85,4% vs 40,2%

AEs ≥ 3 grade in Epcoritamab + R<sup>2</sup>  
CRS 1 21% e CRS 2 7%

## BsAbs in FL: future 1 L

### MorningSun: Mosunetuzumab (SC) untreated FL



- Median follow-up was 22.3 months (95% CI: 20.9–24.1)
- 12-month PFS rate of 86.7%,
- 12 month ORR of 88.3% and a CMR rate of 65%,
- 66% patients achieved a PMR/CMR after 17 cycles and were eligible to receive maintenance treatment
  - 44.7% patients received maintenance treatment, with 15 (14.6%) still receiving maintenance at data cut-off
  - one patient died during maintenance treatment (pneumonia)

| AE summary, n (%)                                  | All patients N=103 | Patients who received maintenance treatment n=46 |
|--|--------------------|--|
| <b>Patients with ≥1 AE</b>                         | 103 (100)          | 38 (82.6)  |
| <b>Grade 3/4 AE</b>                                | 48 (46.6)          | 7 (15.2)   |
| <b>Serious AE</b>                                  | 37 (35.9)          | 6 (13.0)   |
| <b>AEs of special interest</b>                     | 29 (28.2)          | 4 (8.7)  |
| Infections*  | 81 (78.6)          | 21 (45.7)  |
| ISR  | 69 (67.0)          | 15 (32.6)  |
| CRS (by ASTCT criteria)                            | 35 (34.0)          | 0  |
| Neutropenia/neutrophil count decreased             | 23 (22.3)          | 2 (4.3)  |
| <b>Grade 5 AEs</b>                                 | 5 (4.9)†           | 1 (2.2)‡   |
| <b>AE leading to mosunetuzumab discontinuation</b> | 11 (10.7)§         | 4 (8.7)¶   |

# Treatment of FL: past, present and future

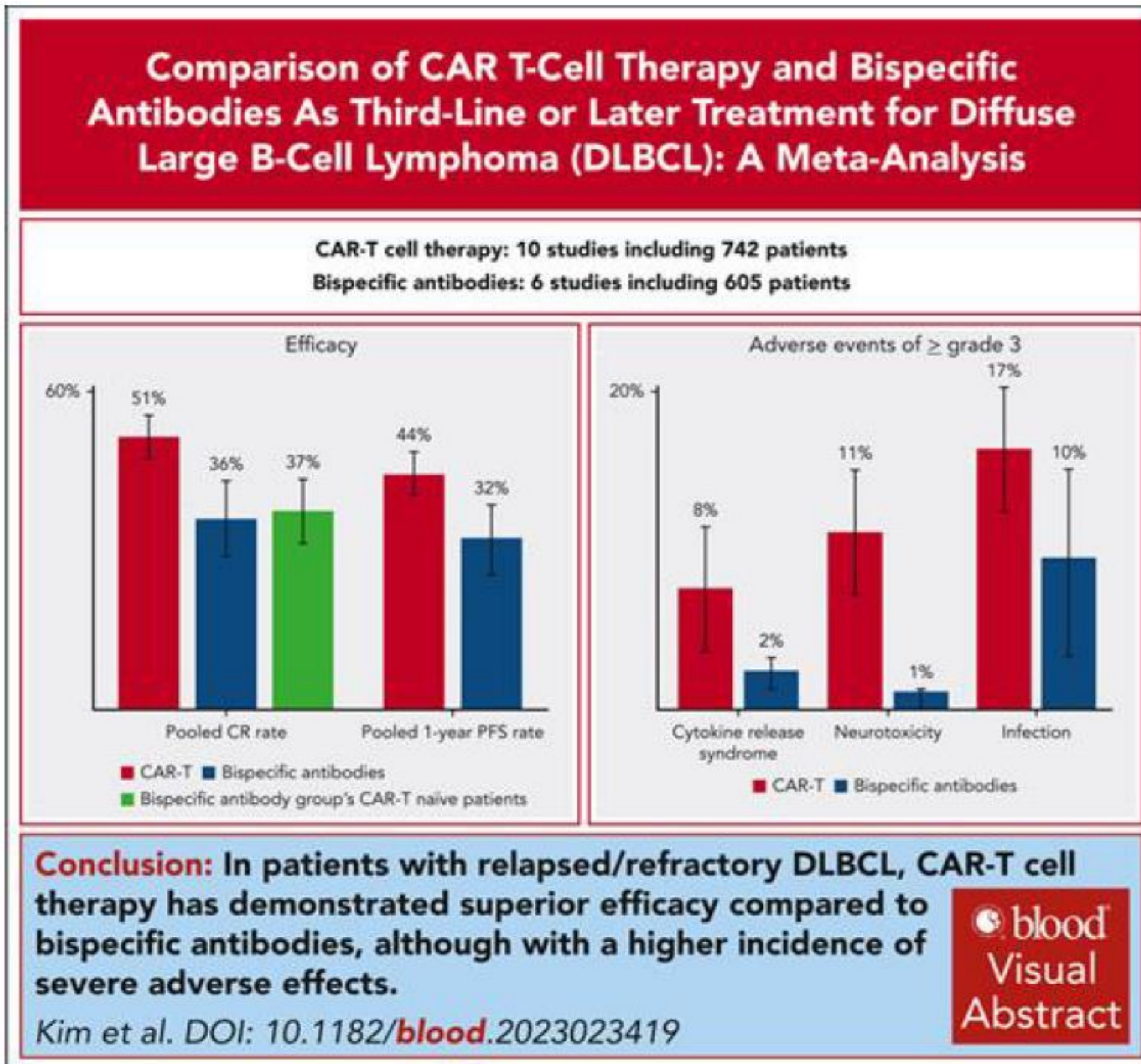
|          | FL 2020   | FL 2021-2026  | FL 2026-  |
|----------|---|---|---|
| I line   | <ul style="list-style-type: none"> <li>• Chemo-Immunotherapy</li> </ul>   | <ul style="list-style-type: none"> <li>• Chemo-Immunotherapy</li> </ul>   | <ul style="list-style-type: none"> <li>• BsABs+/-X (R2,R,Small Mol) (CD20 or CD19-based)</li> </ul>   |
| II line  | <ul style="list-style-type: none"> <li>• Chemo-immunotherapy</li> <li>• ASCT</li> <li>• R2</li> </ul>                 | <ul style="list-style-type: none"> <li>• R2</li> <li>• Chemo-immunotherapy</li> <li>• ASCT</li> <li>• Tafa-R2</li> <li>• Babs-R2</li> </ul> | <ul style="list-style-type: none"> <li>• BsABs+/-R2, X (CD20 or CD19-based)</li> <li>• CAR-T (CD19)</li> <li>• BsABs combo</li> </ul>                                     |
| III line | <ul style="list-style-type: none"> <li>• PI3k</li> <li>• Chemo-immunotherapy</li> <li>• ASCT</li> <li>• R2</li> </ul> | <ul style="list-style-type: none"> <li>• Babs (CD20)</li> <li>• CAR-T (CD19)</li> </ul>   | <ul style="list-style-type: none"> <li>• BsABs+/-R2, X</li> <li>• BsABs combo</li> <li>• CAR-T (CD19)</li> <li>• Alternative Combinations (e.g. ADCs+BsABs+SM)</li> </ul> |

## BsAbs vs CAR-T

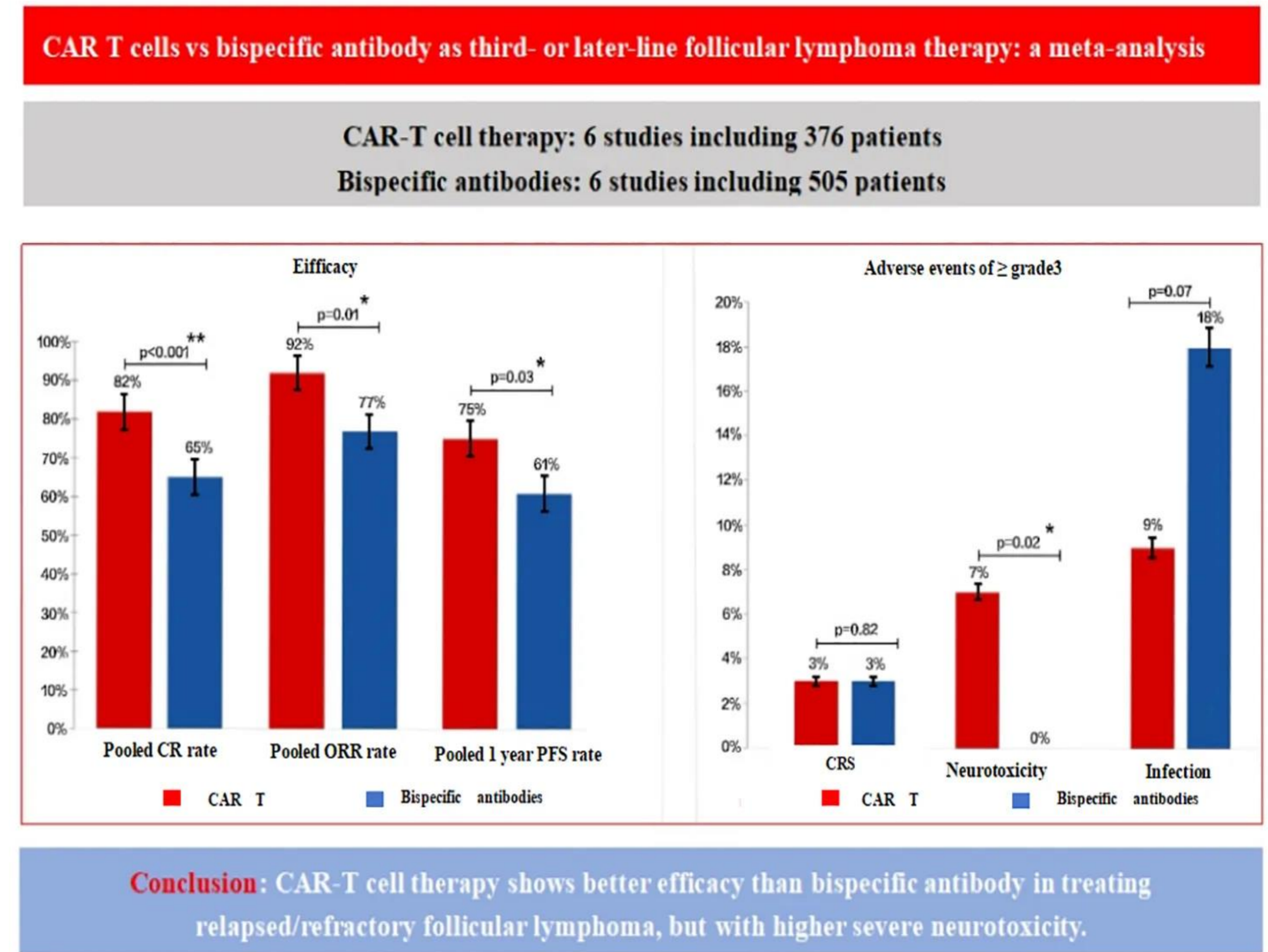
- No comparative studies
- Indirect comparison
- Cross-trial comparisons remain limited by substantial heterogeneity.
- Major limitations: differences in trial design, eligibility, patient characteristics and time of follow-up
- Several studies relied on matching-adjusted indirect comparisons (MAICs) to evaluate CAR T versus BsAbs.

| Features                      | CAR-T   | BsABs   |
|-------------------------------|---|---|
| <b>Therapy type</b>           | Autologous cellular therapy                           | Off-the-shelf recombinant proteins                              |
| <b>Target antigen</b>         | CD19  | CD19 or CD20  |
| <b>T-cell engagement</b>      | Genetically engineered T cells expressing CAR         | Simultaneous binding of CD3 on T cells and CD19/CD20 on B cells |
| <b>Availability</b>           | Several weeks (patient-specific)                      | Immediate use   |
| <b>Bridging therapy</b>       | Often required  | Not required  |
| <b>Administration</b>         | Single infusion, inpatient setting                    | Multiple doses, often outpatient/subcutaneous                   |
| <b>Manufacturing failures</b> | <10% cases  | Not applicable  |
| <b>T-cell persistence</b>     | Long-lived memory T cells                             | Shorter half-life: persistence depends on dosing                |
| <b>Immune activation</b>      | Self-amplifying in vivo                               | Dose-dependent activation                                       |
| <b>Patient population</b>     | Cannot be used in frail/unfit patients                | Can be used in elderly patients                                 |
| <b>Safety profile</b>         | High risk of CRS and ICANS                            | Generally milder CRS and fewer neurotoxic events                |
| <b>B cell aplasia/</b>        | Recovers 12 months after infusion                     | Recovers 6-18 months after last infusion.                       |
| <b>Cytopenia</b>              | Common 15-95%; often persist >90 days (2-45%)         | Persistent cytopenia rare                                       |
| <b>Management</b>             | Requires specialized centers and intensive monitoring | Step-up dosing mitigates CRS risk                               |
| <b>Cost and accessibility</b> | High cost, limited to specialized centers             | Lower cost, more accessible                                     |
| <b>Treatment setting</b>      | Hospital-based  | Potential for outpatient administration                         |

## BsAbs vs CAR-T



Kim et al. Blood (2024)



Zhang et al. Journal of Translational Medicine (2026)

## BsAbs vs CAR-T

**Comparison of real-world survival outcomes and time toxicity of CAR T-cell versus bispecific antibody therapies in relapsed/refractory follicular lymphoma: A multicenter cohort from 15 US academic institutions**

|                                     |         |
|-------------------------------------|---------|
| Patients from 15 US academic centre | 209     |
| Median age                          | 64      |
| Female %                            | 37%     |
| CAR T                               | 61%     |
| - Axi-cel                           | - 80%   |
| - Liso-cel                          | - 7%    |
| - Tisa-cel                          | - 13%   |
| BsAbs                               | 39%     |
| - Mosu                              | - 93%   |
| - Epcor                             | - 7%    |
| FL 1-2 grade                        | 72%     |
| FL III-IV stage                     | 84%     |
| Extranodal disease                  | 51%     |
| Median prior LOT                    | 3(2-15) |
| POD24                               | 52%     |

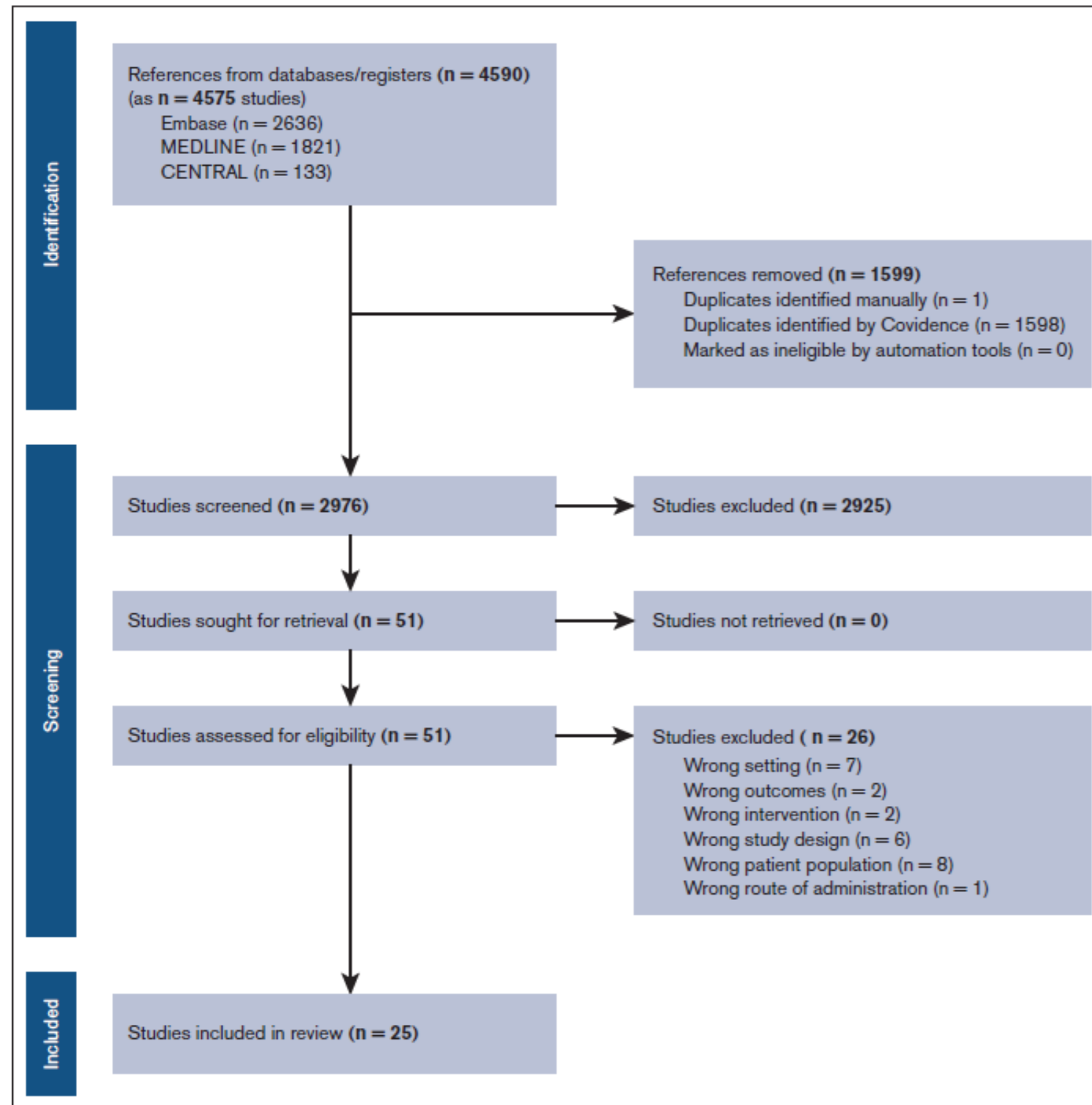
|                    |                                    |
|--------------------|------------------------------------|
| 2 prior LOT cohort | 60% CART<br>40% BsAbs              |
| Median follow-up   | 1.5 years                          |
| Median PFS         | NR for CART<br>1.6 years for BsAbs |
| Median OS          | No differences                     |

|                    |                                     |
|--------------------|-------------------------------------|
| 3 prior LOT cohort | 62% CART<br>38% BsAbs               |
| Median follow-up   | 2 years                             |
| Median PFS         | 3.6 for CART<br>1.6 years for BsAbs |
| Median OS          | No differences                      |

- CAR-T therapy resulted in better PFS but more time toxicity over the first year as compared to BsAb therapy
- Bias selection: older population with CIRS > 2 in BsAbs group

Major et al. ASH 2025; Poster presentation #623

## BsAbs vs CAR-T: risk infection



| Study                                     | Total patients | All-grade infection | Grade 3+ infections | Infection-related mortality |
|---|----------------|---------------------|---------------------|-----------------------------|
| <b>CAR T</b>                              |                |                     |                     |                             |
| Locke et al <sup>13-15</sup>              | 108            | 49                  | 30                  | 6                           |
| Wang et al <sup>16,17</sup>               | 68             | 45                  | 26                  | 3                           |
| Neelapu et al (2024) <sup>18,19</sup>     | 152            | 100                 | 34                  | 14                          |
| Westin et al <sup>20,21</sup>             | 170            | 76                  | 28                  | 14                          |
| Neelapu et al (2022) <sup>22</sup>        | 40             | 13                  | 5                   | 1                           |
| Houot et al <sup>23</sup>                 | 62             | 33                  | 11                  | 6                           |
| Schuster et al <sup>24,25</sup>           | 115            | 43                  | 22                  | 0                           |
| Bishop et al <sup>26</sup>                | 155            | NR                  | NR                  | 5                           |
| Dreyling et al <sup>27,28</sup>           | 97             | 16                  | 9                   | 1                           |
| Abramson et al (2024) <sup>29,30</sup>    | 270            | 135                 | 45                  | 8                           |
| Morschhauser et al <sup>31</sup>          | 130            | NR                  | 10                  | 3                           |
| Wang et al <sup>32</sup>                  | 88             | NR                  | 13                  | 8                           |
| Abramson et al (2023) <sup>33,34</sup>    | 92             | NR                  | 14                  | 4                           |
| Linhares et al <sup>35</sup>              | 82             | 27                  | 9                   | 3                           |
| Sehgal et al <sup>36</sup>                | 61             | NR                  | 4                   | 3                           |
| <b>BsAbs</b>                              |                |                     |                     |                             |
| Dickinson et al <sup>37</sup>             | 154            | 59                  | 23                  | 7                           |
| Phillips et al <sup>38</sup>              | 60             | 44                  | 13                  | 9                           |
| Hutchings et al <sup>39</sup>             | 171            | 88                  | 30                  | 1                           |
| Izutsu et al <sup>40</sup>                | 36             | 16                  | 7                   | 0                           |
| Thieblemont et al <sup>41,42</sup>        | 157            | 71                  | 46                  | 6                           |
| Linton et al (optimization) <sup>43</sup> | 86             | NR                  | NR                  | 0                           |
| Linton et al (pivotal) <sup>43</sup>      | 128            | NR                  | NR                  | 8                           |
| Budde et al <sup>48,49</sup>              | 229            | NR                  | NR                  | 3                           |
| Kim et al <sup>50</sup>                   | 128            | 102                 | 54                  | 14                          |
| Bannerji et al <sup>51</sup>              | 145            | 71                  | 33                  | 3                           |
| Matasar et al <sup>44-47</sup>            | 218            | 102                 | 33                  | 3                           |

CAR T=15

BsAbs=10

## BsAbs vs CAR-T

| Infection type              | Product     | Pooled infection rate per patient | P value      | Pooled infection rate per patient-month | P value       |
|-----------------------------|-------------|-----------------------------------|--------------|---|---------------|
| All-grade infections        | CAR T       | 0.44                              | .18          | 0.0167                                  | <b>.0012*</b> |
|                             | CD28 CAR T  | 0.52                              | .77          | 0.0182                                  | <b>.006*</b>  |
|                             | 4-1BB CAR T | 0.34                              | <b>.02*</b>  | 0.0144                                  | <b>.02*</b>   |
|                             | BsAbs       | 0.54                              | –            | 0.0397                                  | –             |
| Grade 3+ infections         | CAR T       | 0.16                              | .08          | 0.0069                                  | <b>.0003*</b> |
|                             | CD28 CAR T  | 0.22                              | .98          | 0.0076                                  | <b>.01*</b>   |
|                             | 4-1BB CAR T | 0.13                              | <b>.003*</b> | 0.0064                                  | <b>.0002*</b> |
|                             | BsAbs       | 0.22                              | –            | 0.0165                                  | –             |
| Infection-related mortality | CAR T       | 0.04                              | .26          | 0.0023                                  | .89           |
|                             | CD28 CAR T  | 0.07                              | <b>.01*</b>  | 0.0024                                  | .89           |
|                             | 4-1BB CAR T | 0.03                              | .76          | 0.0023                                  | .96           |
|                             | BsAbs       | 0.03                              | –            | 0.0022                                  | –             |

### All grade infections

- 044 CAR T vs 0.54 BsAbs
- Subgroup analyses showed no significant difference between all CAR T studies and BsAb studies
- No significant difference CD28-based CAR T studies vs BsAb studies; higher incidence between 41BB-based CAR T studies vs BsAbs studies
- No significant difference between fixed-duration CAR T studies vs fixed duration BsAbs studies and fixed-duration CAR T studies vs continuous therapy BsAbs studies

### Grade 3+ infection

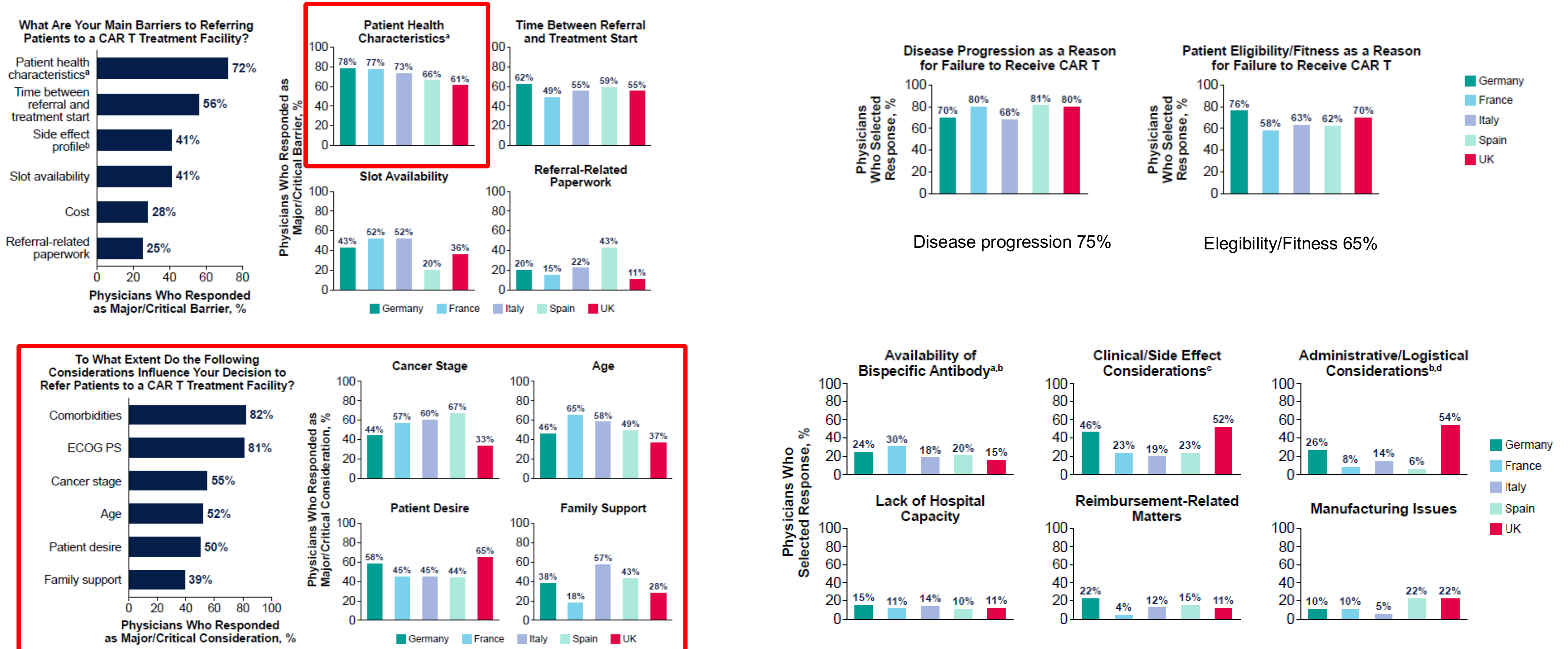
- 016 CAR T vs 0.22 BsAbs
- Subgroup analyses showed no significant difference between all CAR T studies and BsAb studies
- No significant difference CD28 and 41BB -based CAR T studies vs BsAb studies; higher incidence between 41BB-based CAR T studies vs BsAbs studies
- No significant difference between fixed-duration CAR T studies vs fixed duration BsAbs studies, higher incidence between fixed-duration CAR T studies vs continuous therapy BsAbs studies

### Infection-related mortality

- No significant difference between all CAR T studies and BsAb studies

Van Besien et al, Blood Adv (2025)

## BsAbs vs CAR-T: barriers to receive CAR T treatment



## Take home messages

- The development of cellular therapy and immunotherapy is changing the treatment of B-cell lymphomas;
- In relapsed/refractory DLBCL, CAR-T cell therapy remains the standard treatment in second line for fit patients;
- In follicular lymphoma, both CAR-T cells and bispecific antibodies are currently used in third line, but there is still no clear evidence that one treatment is better than the other;
- Many studies show the advantage of anticipating treatment with bispecifics in early therapeutic lines and in the near future BsAbs will be available alone or in combination also in 2L and 3L;
- To date, all comparisons between car t and BsAbs are indirect but BsAbs are an important new option, especially because they are readily available and easier to administer compared with CAR-T therapy.
- In the future, the use of bispecific antibodies in earlier treatment lines may allow a more direct comparison with CAR-T therapies, particularly in DLBCL.
- CAR-T cells and bispecific antibodies will likely become complementary tools in the personalized treatment of B-cell lymphomas



## **U.O.C. Ematologia**

Dott. Ferdinando Frigeri  
Dott. Davide Pio Abagnale  
Dott.ssa Giusy Cetani  
Dott. Alessandro D'Ambrosio  
Dott.ssa Adele Delli Paoli  
Dott.ssa Martina Di Palma  
Dott.ssa Giuliana Farina  
Dott. Salvatore Iaccarino  
Dott.ssa Maria Iovine  
Dott. Giuseppe Monaco  
Dott. Mario Troiano

## **Patologie Linfoproliferative**

Dott. Ferdinando Frigeri  
Dott. Davide Pio Abagnale  
Dott.ssa Martina Di Palma  
Dott.ssa Giuliana Farina



# Thank you!