# Indicaciones del uso de los anticuerpos biespecíficos en los linfomas difusos de células grande

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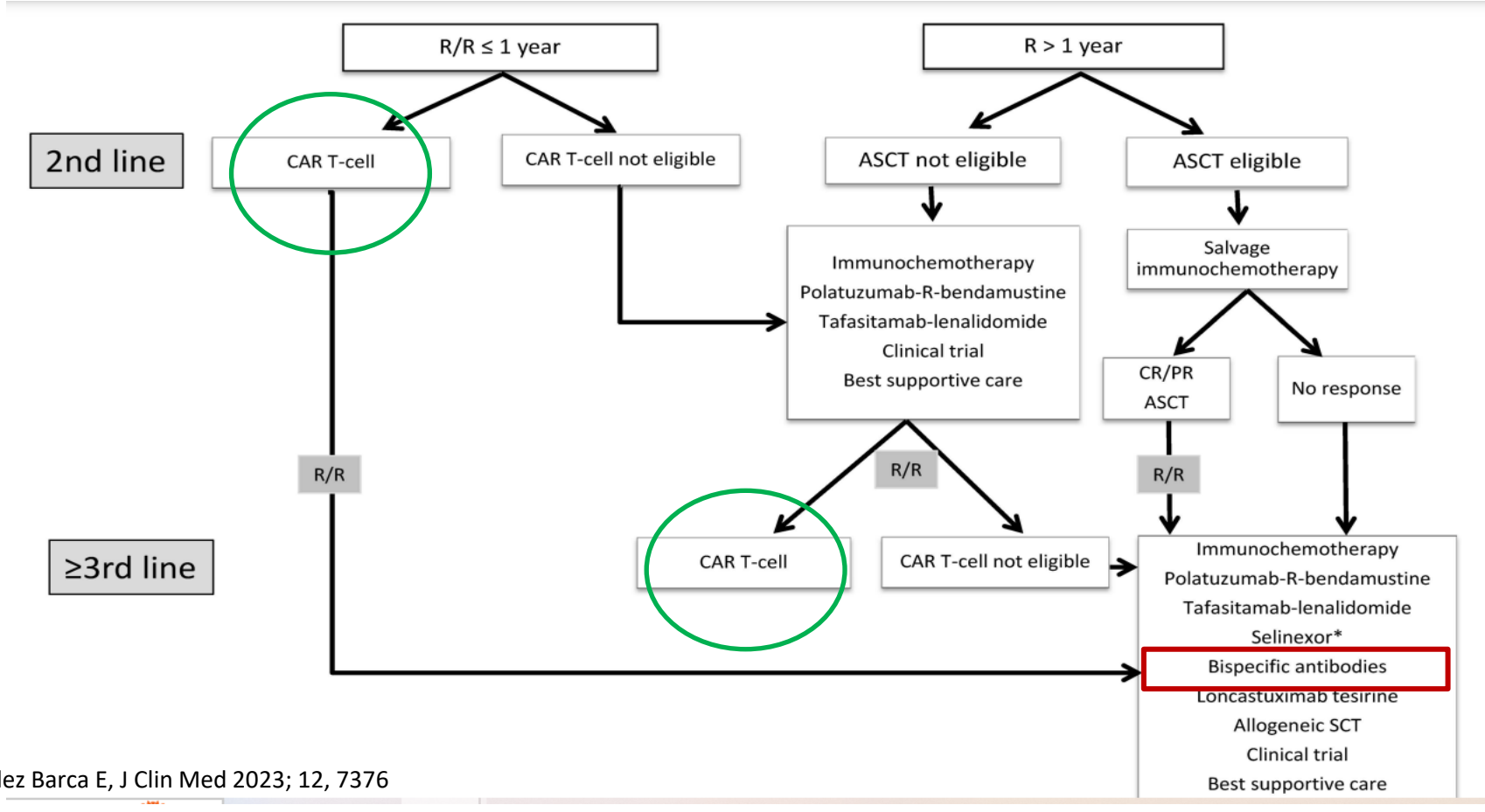
14 noviembre 2024

# Conflictos de Interés

- Consultancy: Janssen, Abbvie, Kiowa, Beigene, SOBI
- Speaker: Janssen, Abbvie, Takeda, Astra-Zeneca, Lilly
- Travel: Janssen, Abbvie, AstraZeneca

# Algorithm for the treatment of relapsed/refractory diffuse large B-cell lymphoma patients

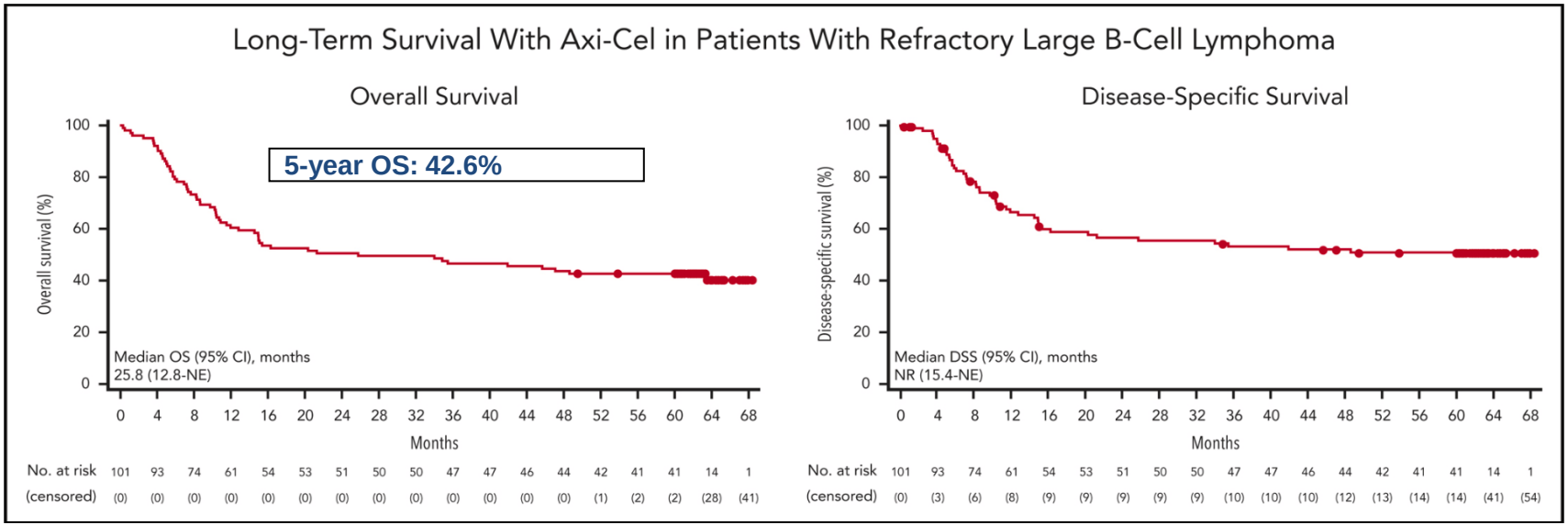



Gonzalez Barca E, J Clin Med 2023; 12, 7376

# Datos de CART en 3ra linea o posteriores y de CARTs en segunda linea

# Zuma-1. **Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma**

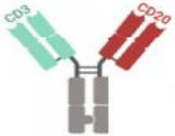
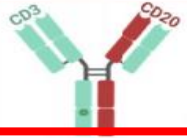
Overall survival at 5 years: long-lasting responses.




Neelapu et al, Blood 2023 May 11;141(19):2307-2315.

# Nuevas opciones:
# el futuro parece la inmunoterapia!

# Anticuerpos biespecíficos

| Bi-Specific Antibody | Targets | Design | Ig Fragment Formats |
|---|---|---|---|
| blinatumomab | CD19 x CD3 |   | • two murine scFv joined by a glycine-serine linker<br>• monovalent CD19 and monovalent CD3 binding<br>• cloned from anti-CD19 (clone HD37) and anti-CD3 (clone L2K-07) murine mAbs |
| mosunetuzumab | CD20 x CD3 |   | • humanized mouse heterodimeric IgG1-based antibody<br>• monovalent CD20 and monovalent CD3ε binding<br>• modified Fc devoid of FcγR and complement binding |
| glofitamab | $(CD20)_2$ x CD3 |   | • humanized mouse IgG1-based antibody<br>• bivalent CD20 and monovalent CD3ε binding<br>• modified Fc devoid of FcγR and complement binding |
| odronextamab | CD20 x CD3 |   | • fully human IgG4-based heterodimeric antibody<br>• monovalent CD20 and monovalent CD3ε binding<br>• Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding<br>• common κ light chain from anti-CD3ε mAb |
| epcoritamab | CD20 x CD3 |   | • humanized mouse IgG1-based heterodimeric antibody<br>• monovalent CD20 and monovalent CD3 binding<br>• IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield |

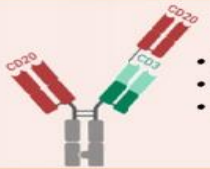
Schuster SJ. Hematological Oncology. 2021;39(S1):113–116.

# Glofitamab, a Novel, Bivalent CD20-Targeting T-Cell–Engaging Bispecific Antibody, Induces Durable Complete Remissions in Relapsed or Refractory B-Cell Lymphoma: A Phase I Trial

Martin Hutchings, PhD[1]; Franck Morschhauser, MD, PhD[2]; Gloria Iacoboni, MD[3,4]; Carmelo Carlo-Stella, MD[5]; Fritz C. Offner, MD, PhD[6]; Anna Sureda, MD, PhD[7]; Gilles Salles, MD[8]; Joaquín Martínez-Lopez, MD, PhD, MBA[9]; Michael Crump, MD[10]; Denise N. Thomas, MSc[11]; Peter N. Morcos, PharmD[11]; Cristiano Ferlini, MD[11]; Ann-Marie E. Bröske, PhD[12]; Anton Belousov, PhD[13]; Marina Bacac, PhD[13]; Natalie Dimier, PhD[14]; David J. Carlile, PhD[14]; Linda Lundberg, PhD[15]; David Perez-Callejo, MD, PhD[15]; Pablo Umaña, PhD[13]; Tom Moore, MD[12]; Martin Weisser, MD[12]; and Michael J. Dickinson, MBBS, DMedSci[16]

**J Clin Oncol 2021;39:1959-1970**

**glofitamab** $(CD20)_2 \times CD3$

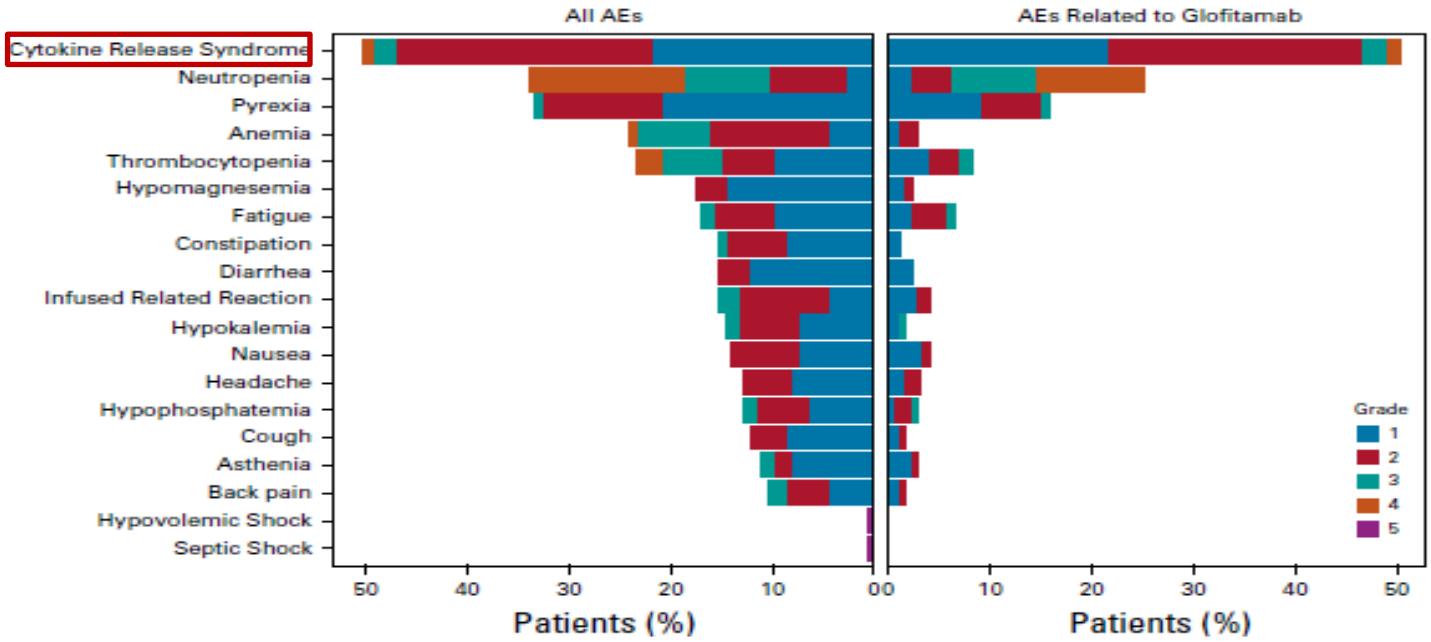


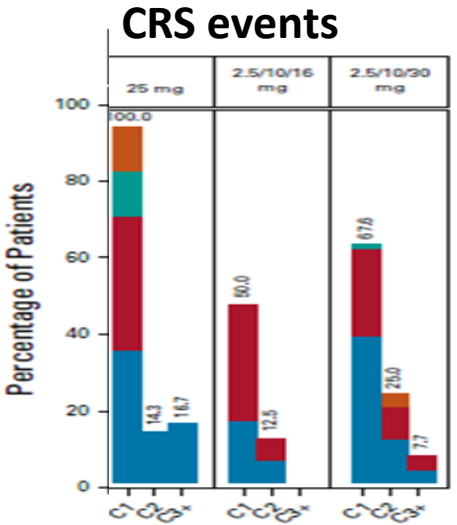

- humanized mouse IgG1-based antibody
- bivalent CD20 and monovalent CD3ε binding
- modified Fc devoid of FcγR and complement binding

## Glofitamab was given 21-day cycles up to 12 cycles.

- Dose escalation was guided by a Bayesian-modified continuous reassessment method with overdose control
- 2.5 mg (C1D1), 10 mg (C1D8), and 16/30 mg (C2D1)
- Seven days before 1,000 mg obinutuzumab to deplete peripheral and tissue based B cells and mitigate serious AE.

# PRIMARY OBJECTIVE: MTD and SAFETY

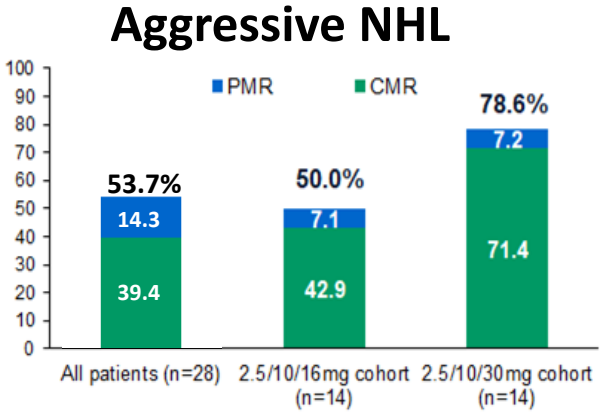



**ICAN:**

- **8 / 171 (4.8%), grade 3: 2 (1.8%); no grade 4-5**
- **All transient 3-72h**

# Response and survival



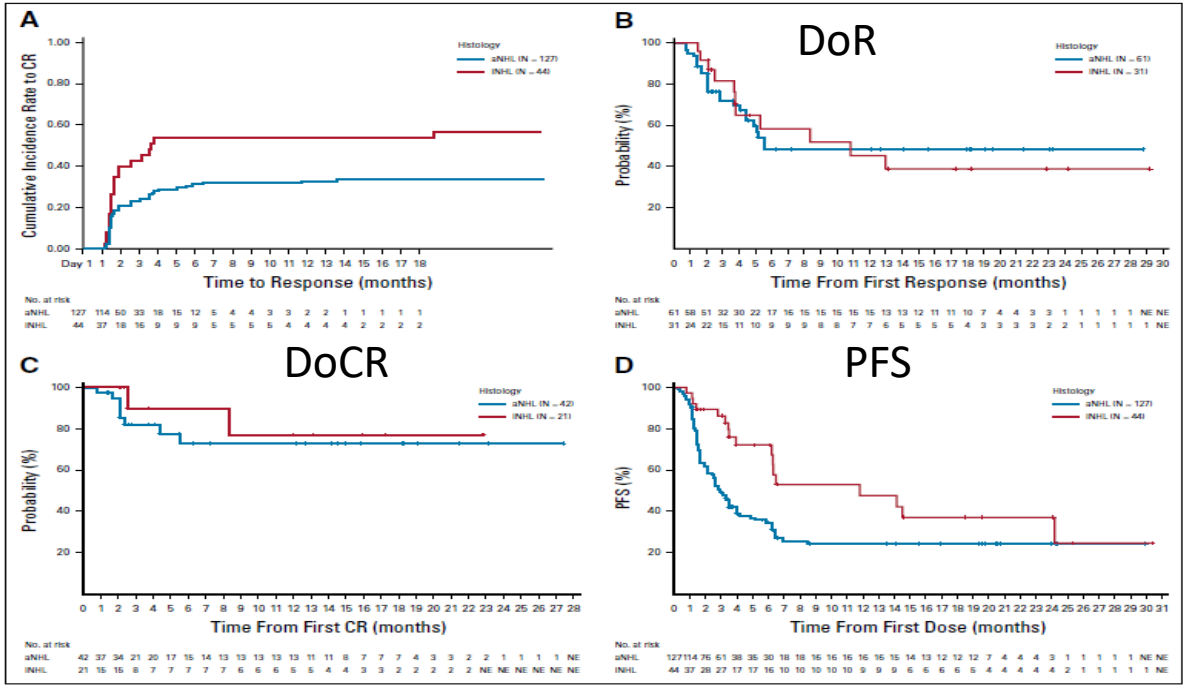




**FIG 3.** (A) Represents the cumulative incidence of time to CR. Kaplan-Meier curves for (B) DOR (PR and CR), (C) duration of CR, and (D) PFS. aNHL, aggressive non-Hodgkin lymphoma; CR, complete response; DOR, duration of response; iNHL, indolent non-Hodgkin lymphoma; NE, not estimable; PFS, progression-free survival; PR, partial response.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Michael J. Dickinson, M.B., B.S., D.Med.Sc., Carmelo Carlo-Stella, M.D., Franck Morschhauser, M.D., Ph.D., Emmanuel Bachy, M.D., Ph.D., Paolo Corradini, M.D., Gloria Iacoboni, M.D., Cyrus Khan, M.D., Tomasz Wróbel, M.D., Fritz Offner, M.D., Ph.D., Marek Trněný, M.D., Shang-Ju Wu, M.D., Ph.D., Guillaume Cartron, M.D., Ph.D., Mark Hertzberg, M.B., B.S., Ph.D., Anna Sureda, M.D., Ph.D., David Perez-Callejo, Ph.D., Linda Lundberg, Ph.D., James Relf, M.D., Mark Dixon, M.Sc., Emma Clark, M.Sc., Kathryn Humphrey, B.Sc., and Martin Hutchings, M.D., Ph.D.

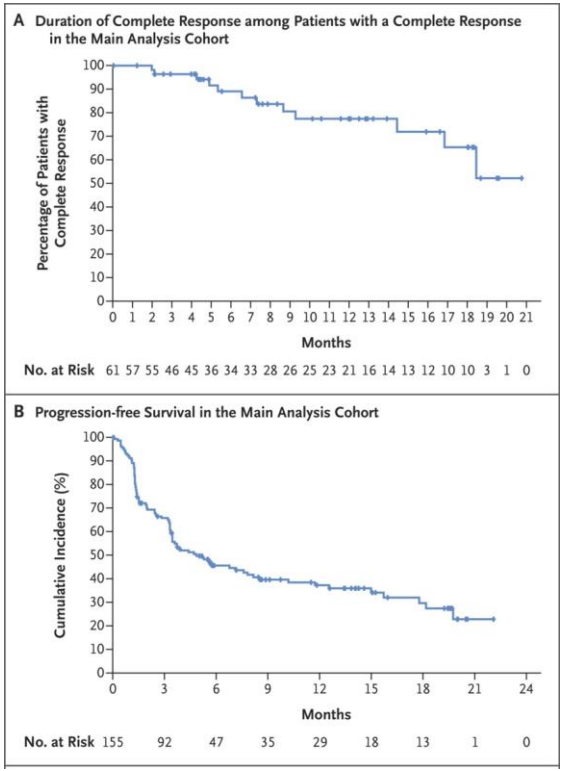
Dickinson MJ et al. N Engl J Med 2022;387:2220-2231

**Demographic and clinical characteristics at baseline of all 155 patients treated at the Phase 2**

| Characteristic | Value |
|---|---|
| Median age (range) — yr | 66 (21–90) |
| Male sex — no. (%) | 100 (65) |
| ECOG performance-status score — no. (%)† | |
| 0 | 69 (45) |
| 1 | 84 (55) |
| Previous lines of therapy | |
| Median no. of lines (range) | 3 (2–7) |
| Only 2 previous lines — no. (%) | 62 (40) |
| ≥3 previous lines — no. (%) | 92 (60) |
| Previous therapy for lymphoma — no. (%) | |
| Anti-CD20 antibody | 154 (100) |
| Anthracycline | 149 (97) |
| CAR T-cell therapy | 51 (33) |
| Autologous stem-cell transplantation — no. (%) | 28 (18) |
| Relapsed or refractory status — no. (%)‡ | |
| Refractory to any previous therapy | 139 (90) |
| Refractory to last previous therapy | 132 (86) |
| Primary refractory | 90 (58) |
| Refractory to any previous anti-CD20 therapy | 128 (83) |
| Refractory to previous CAR T-cell therapy | 46 (30) |

# Response and survival

| Outcome | Assessment According to Independent Review Committee (N=155) |
|---|---|
| Complete response | |
| No. of patients with response | 61 |
| Percentage of patients (95% CI) | 39 (32–48) |
| Objective response | |
| No. of patients with response | 80 |
| Percentage of patients (95% CI) | 52 (43–60) |
| Duration of complete response† | |
| Median (95% CI) — mo | NR (16.8–NR) |
| Complete response at 12 mo (95% CI) — % | 78 (64–91) |
| Duration of objective response‡ | |
| Median (95% CI) — mo | 18.4 (13.7–NR) |
| Objective response at 12 mo (95% CI) — % | 64 (51–76) |
| Median time to first complete response (range) — days† | 42 (31–308) |
| Progression-free survival | |
| Median (95% CI) — mo | 4.9 (3.4–8.1) |
| Alive without progression at 12 mo (95% CI) — % | 37 (29–46) |
| Overall survival | |
| Median (95% CI) — mo | — |
| Alive at 12 mo (95% CI) — % | — |




Indicado para el tratamiento de pacientes adultos con linfoma B de célula grande en recaída o refractario después de dos o más líneas de tratamiento sistémico

# Dose escalation of subcutaneous epcoritamab in patients with relapsed or refractory B-cell non-Hodgkin lymphoma: an open-label, phase 1/2 study

*Martin Hutchings, Rogier Mous, Michael Roost Clausen, Peter Johnson, Kim M Linton, Martine E D Chamuleau, David John Lewis, Anna Sureda Balari, David Cunningham, Roberto S Oliveri, Brian Elliott, Dena DeMarco, Ada Azaryan, Christopher Chiu, Tommy Li, Kuo-mei Chen, Tahamtan Ahmadi, Pieternella J Lugtenburg*

**Lancet 2021; 398: 1157–69**

**epcoritamab** | **CD20 x CD3**


- humanized mouse IgG1-based heterodimeric antibody
- monovalent CD20 and monovalent CD3 binding
- IgG1 Fc modified to minimize Fc-dependent effector functions and to control Fab-arm exchange of mAb half-molecules, resulting in high bispecific product yield

**Subcutaneous epcoritamab (1 mL) was administered in 28-day cycles until disease progression or unacceptable toxicity. Doses escalated.**

Weekly dosing in cycles 1 and 2 (days 1, 8, 15, 22)
Every 2 weeks in cycles 3–6 (days 1, 15)
Every 4 weeks from cycle 7 onward

| | Relapsed or refractory diffuse large B-cell lymphoma (n=46) | Relapsed or refractory follicular lymphoma (n=12) | All patients (n=68)* |
|---|---|---|---|
| Age, years | 68 (55–74) | 73 (63–76) | 68 (57–75) |
| Sex | | | |
| Female | 16 (35%) | 4 (33%) | 23 (34%) |
| Male | 30 (65%) | 8 (67%) | 45 (66%) |
| ECOG performance status | | | |
| 0 | 23 (50%) | 6 (50%) | 35 (51%) |
| 1 | 21 (46%) | 4 (33%) | 29 (43%) |
| 2 | 2 (4%) | 1 (8%) | 3 (4%) |
| 3† | 0 | 1 (8%)† | 1 (1%)† |
| Ann Arbor stage | | | |
| I | 3 (7%) | 0 | 3 (4%) |
| II | 5 (11%) | 4 (33%) | 12 (18%) |
| III | 12 (26%) | 4 (33%) | 16 (24%) |
| IV | 26 (57%) | 4 (33%) | 37 (54%) |
| Extranodal disease | 29 (63%) | 6 (50%) | 42 (62%) |
| Time since diagnosis, months | 25·4 (11·0–54·6) | 61·5 (34·3–153·1) | 29·7 (13·7–66·8) |
| Time since relapse or progression, months | 1·5 (1·1–2·3) | 1·6 (1·2–2·6) | 1·6 (1·1–2·3) |
| Number of lines of previous therapy | 3·0 (2·0–4·0) | 4·5 (2·5–8·0) | 3·0 (2·0–4·5) |
| Previous therapies | | | |
| Anti-CD20 monoclonal antibody | 46 (100%) | 12 (100%) | 68 (100%) |
| Anthracyclines | 46 (100%) | 9 (75%) | 62 (91%) |
| Alkylating agents | 46 (100%) | 12 (100%) | 67 (99%) |
| Autologous stem-cell transplantation | 7 (15%) | 1 (8%) | 10 (15%) |
| CAR-T therapy | 5 (11%) | 0 | 6 (9%) |
| Treatment-refractory patients by therapy | | | |
| Last line of systemic therapy | 41 (89%) | 10 (83%) | 58 (85%) |
| Alkylating agents | 40 (87%) | 9 (75%) | 56 (82%) |
| Last anti-CD20 monoclonal antibody | 41 (89%) | 10 (83%) | 59 (87%) |

# PRIMARY OBJECTIVE: MTD and SAFETY

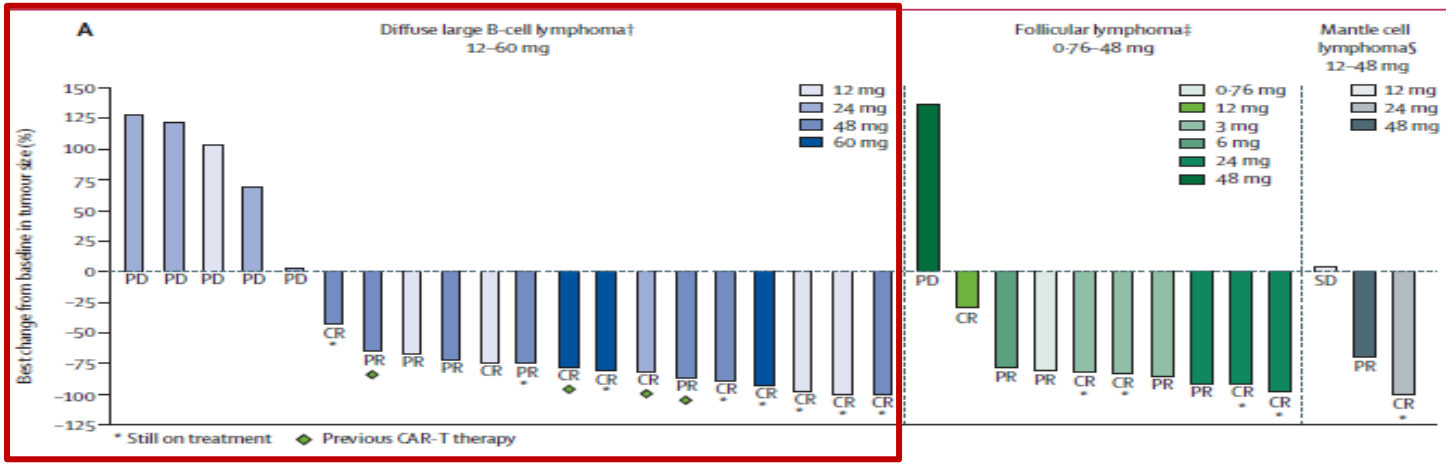
| | Grade 1–2 | Grade 3 | Grade 4 |
|---|---|---|---|
| Pyrexia* | 43 (63%) | 4 (6%) | 0 |
| Cytokine release syndrome | 40 (59%) | 0 | 0 |
| Injection site reaction | 32 (47%) | 0 | 0 |
| Fatigue | 26 (38%) | 4 (6%) | 0 |
| Diarrhoea | 18 (26%) | 0 | 0 |
| Hypotension* | 17 (25%) | 4 (6%) | 0 |
| Dyspnoea | 16 (24%) | 0 | 1 (1%) |
| Tachycardia* | 14 (21%) | 0 | 0 |
| Anaemia | 7 (10%) | 9 (13%) | 0 |

*Most pyrexia, hypotension, and tachycardia events were associated with cytokine release syndrome.

***Table 2:*** **Treatment-emergent adverse events that occurred in at least 20% of the full analysis population (n=68)**

ICAN: 4 (8%), grade 3: 2 (4%), no grade 4-5, all transient, median duratin 3 days

| | Relapsed or refractory diffuse large B-cell lymphoma* | | | Relapsed or refractory follicular lymphoma† | | Relapsed or refractory mantle cell lymphoma‡ | |
|---|---|---|---|---|---|---|---|
| | 12–60 mg (n=22) | 48 mg (n=8) | 60 mg (n=3) | 0·76–48 mg (n=10) | 48 mg (n=1) | 0·76–48 mg (n=4)§ | 48 mg (n=1) |
| Overall response, n (%, 95% CI) | 15 (68%, 45–86) | 7 (88%, 47–100) | 3 (100%, 29–100) | 9 (90%, 55–100) | 0 (0, 0–98) | 2 (50%, 7–93) | 1 (100%, 3–100) |
| Complete response | 10 (45%) | 3 (38%) | 3 (100%) | 5 (50%) | 0 | 1 (25%) | 0 |
| Partial response | 5 (23%) | 4 (50%) | 0 | 4 (40%) | 0 | 1 (25%) | 1 (100%) |
| Stable disease | 1 (5%) | 0 | 0 | 0 | 0 | 1 (25%) | 0 |
| Progressive disease | 5 (23%) | 0 | 0 | 1 (10%) | 1 (100%) | 0 | 0 |
| Time to response, months | 1·4 (1·3–2·6) | 1·4 (1·3–2·6) | 1·3 (1·1–1·4) | 1·9 (1·5–3·5) | NA | 1·4 (1·3–1·5) | 1·3 (1·3–1·3) |
| Follow-up duration, months | 9·3 (8·2–14·8) | 8·2 (7·4–9·9) | 9·2 (9·2–9·3) | 13·6 (10·4–16·5) | 6·6 (6·6–6·6) | 10·2 (7·7–10·5) | 7·7 (7·7–7·7) |



# Epcoritamab, a Novel, Subcutaneous CD3xCD20 Bispecific T-Cell–Engaging Antibody, in Relapsed or Refractory Large B-Cell Lymphoma: Dose Expansion in a Phase I/II Trial

| Characteristic | Patients (N = 157) |
|---|---|
| Age, years, median (range) | 64 (20-83) |
| Central laboratory FISH analysis: Double-hit/ triple-hit lymphoma (*MYC* and *BCL2* and/or *BCL6* rearrangement), No./n (%) | 13/99 (13.1) |
| Ann Arbor stage, No. (%) | |
| I/II | 39 (24.8) |
| III | 21 (13.4) |
| IV | 97 (61.8) |
| International Prognostic Index, No. (%) | |
| 0-2 | 55 (35.0) |
| ≥ 3 | 82 (52.2) |
| Unknown | 2 (1.3) |

| Characteristic | Patients (N = 157) |
|---|---|
| Prior lines of antilymphoma therapy, No. (%) | |
| 2 | 46 (29.3) |
| 3 | 50 (31.8) |
| ≥ 4 | 61 (38.9) |
| Primary refractory disease,[c] No. (%) | 96 (61.1) |
| Refractory to last systemic therapy,[c] No. (%) | 130 (82.8) |
| Refractory to ≥ 2 consecutive lines of therapy,[c] No. (%) | 119 (75.8) |
| Prior autologous stem-cell transplant, No. (%) | 31 (19.7) |
| Relapsed within 12 months after prior autologous stem-cell transplant, No./n (%) | 18/31 (58.1) |
| Prior CAR T-cell therapy, No. (%) | 61 (38.9) |
| Progressed within 6 months of CAR T-cell therapy, No./n (%) | 46/61 (75.4) |
| Prior anthracycline therapy, No. (%) | 154 (98.1) |
| First line | 139 (88.5) |
| Second line | 16 (10.2) |

Thieblemont C et al, J Clin Oncol 2023 Apr 20;41(12):2238-2247

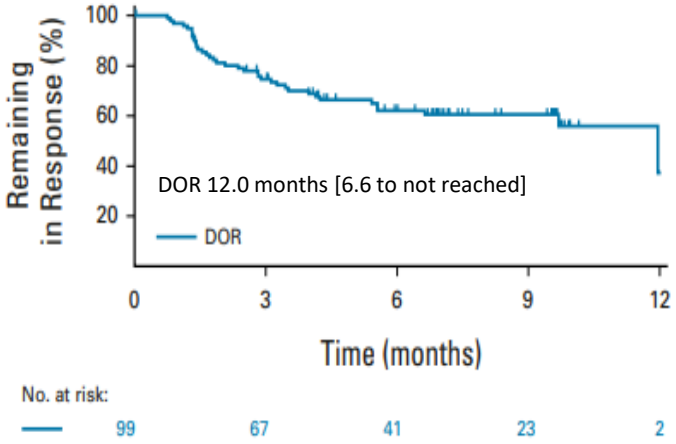
# Response and survival

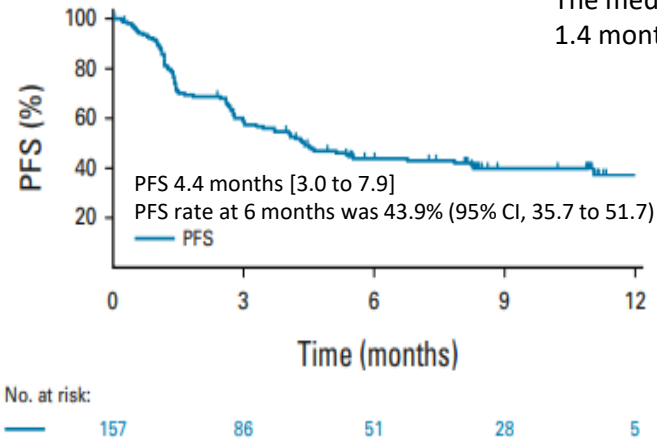
0.16-mg on day 1, 0.8-mg day 8, and subsequent full 48-mg doses on day 15

**Response rate**

**ORR 99 (63.1%)**
**CR 61 (38.9%)**
**PR 38 (24.2%)**
SD 5 ( 3.2%)
PD 37 (23.6%)
NE 16 (10.2%)

The median time to response was 1.4 months (range, 1.0-8.4).

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Indicado para el tratamiento de pacientes adultos con linfoma B de célula grande en recaída o refractario después de dos o más líneas de tratamiento sistémico

Thieblemont C et al, J Clin Oncol 2023 Apr 20;41(12):2238-2247

# Single-Agent Mosunetuzumab Shows Durable Complete Responses in Patients With Relapsed or Refractory B-Cell Lymphomas: Phase I Dose-Escalation Study

Lihua E. Budde, MD[1]; Sarit Assouline, MD[2]; Laurie H. Sehn, MD[3]; Stephen J. Schuster, MD[4]; Sung-Soo Yoon, MD, PhD[5]; Dok Hyun Yoon, MD, PhD[6]; Matthew J. Matasar, MD[7]; Francesc Bosch, MD, PhD[8]; Won Seog Kim, MD, PhD[9]; Loretta J. Nastoupil, MD[10]; Ian W. Flinn, MD, PhD[11]; Mazyar Shadman, MD, MPH[12]; Catherine Diefenbach, MD[13]; Carol O'Hear, MD, PhD[14]; Huang Huang, MSc[15]; Antonia Kwan, MBBS, PhD[14]; Chi-Chung Li, PhD[14]; Emily C. Piccione, PhD[14]; Michael C. Wei, MD, PhD[14]; Shen Yin, PhD[14]; and Nancy L. Bartlett, MD[16]

J Clin Oncol 2021;40:481-491

**mosunetuzumab** CD20 x CD3

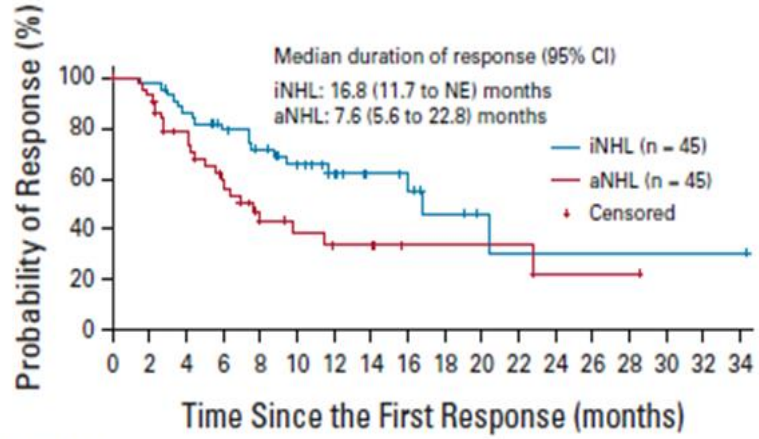

- humanized mouse heterodimeric IgG1-based antibody
- monovalent CD20 and monovalent CD3ε binding
- modified Fc devoid of FcγR and complement binding

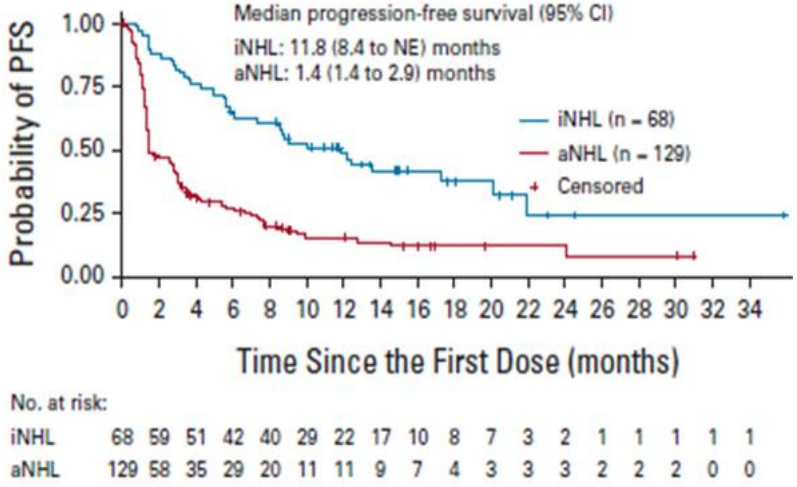
**Mosunetuzumab was given 21-day cycles up to 8 cycles for patients with a CR and 17 cycles for hose with PR or SD.**

- In group A, mosunetuzumab was administered intravenously on day 1 of each 21-day cycle.
- **In group B,** mosunetuzumab was administered intravenously as low and intermediate step-up doses on days 1 and 8 of cycle 1, with the target dose on day 15 and on day 1 of subsequent 21-day cycles.

# Response and survival

| | Mosunetuzumab NCT02500407 Ph 1/1b (dose escalation / expansion) | |
|---|---|---|
| Patients | 129 aNHL | 68 iNHL |
| Prior LoT, median<br>Refractory to last therapy<br>Prior CAR T-cell therapy | 3 (1-14)<br>106 (82%)<br>15 (12%) | 3 (1-11)<br>43 (63%)<br>4 (6%) |
| ORR / CR | 34.9% / 19.4% | 66.2% / 48.5% |
| Prior CART ORR / CR | 36.8% / 26.3% | |



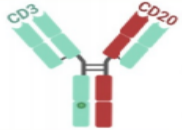



# Odronextamab, a human CD20×CD3 bispecific antibody in patients with CD20-positive B-cell malignancies (ELM-1): results from the relapsed or refractory non-Hodgkin lymphoma cohort in a single-arm, multicentre, phase 1 trial

*Rajat Bannerji, Jon E Arnason, Ranjana H Advani, Jennifer R Brown, John N Allan, Stephen M Ansell, Jeffrey A Barnes, Susan M O'Brien, Julio C Chávez, Johannes Duell, Andreas Rosenwald, Jennifer L Crombie, Melanie Ufkin, Jingjin Li, Min Zhu, Srikanth R Ambati, Aafia Chaudhry, Israel Lowy, Max S Topp*

**Lancet Haematol 2022; 9(5):e327-e339**

**odronextamab** **CD20 x CD3**




- fully human IgG4-based heterodimeric antibody
- monovalent CD20 and monovalent CD3ε binding
- Fc-dependent effector function-minimized antibody with Fc of the anti-CD3ε heavy chain modified to reduce Protein A binding
- common κ light chain from anti-CD3ε mAb

**Intravenous odronextamab every 2 weeks until disease progression or unacceptable toxicity**

- Step-up dosing schedule in cycle 1
- Once per week at target doses ranging from 0.1 mg to 320 mg during cycles 2–4 on days 1, 8, and 15 (each cycle was 21 days).
- After cycle 4, maintenance treatment every 2 weeks.

## Characteristics of the patients

| | Total (n=145) |
|---|---|
| Age | |
| Median | 67·0 (57·0–73·0) |
| ≥65 years | 86 (59%) |
| <65 years | 59 (41%) |
| Sex | |
| Male | 101 (70%) |
| Female | 44 (30%) |
| B-cell non-Hodgkin lymphoma diagnosis | |
| Diffuse large B-cell lymphoma | 85 (59%) |
| Follicular lymphoma grade 1–3a | 40 (28%) |
| Mantle cell lymphoma | 12 (8%) |
| Marginal zone lymphoma | 6 (4%) |
| Other* | 2 (1%) |
| Bulky disease according to investigator assessment | 49 (34%) |
| Median previous lines of therapy | 3 (2–5) |
| Previous autologous haematopoietic stem-cell transplantation | 12 (8%) |
| Previous CAR T-cell therapy | 42 (29%)† |
| Refractory to last line of therapy | 119 (82%) |
| Relapsed after last line of therapy | 15 (10%) |
| Refractory to anti-CD20 antibody in any line | 123 (85%) |
| Refractory to alkylator therapy in any line | 102 (70%) |

## Toxicity

| | Grade 1 or 2 | Grade 3 | Grade 4 | Grade 5 |
|---|---|---|---|---|
| Pyrexia | 105 (72%) | 2 (1%) | 0 | 0 |
| Cytokine release syndrome | 79 (54%) | 9 (6%) | 1 (1%) | 0 |
| Chills | 67 (46%) | 1 (1%) | 0 | 0 |
| Anaemia | 19 (13%) | 35 (24%) | 1 (1%) | 0 |
| Thrombocytopenia* | 20 (14%) | 11 (8%) | 9 (6%) | 0 |
| Headache | 36 (25%) | 0 | 0 | 0 |
| Nausea | 34 (23%) | 2 (1%) | 0 | 0 |
| Infusion-related reaction | 32 (22%) | 3 (2%) | 0 | 0 |
| Neutropenia* | 8 (6%) | 13 (9%) | 14 (10%) | 0 |
| Decreased appetite | 31 (21%) | 3 (2%) | 0 | 0 |

**ICAN**

- 18 (12%): grade 3: 4 (3%); no grade 4-5
- All reversible, median 3 days

# Response

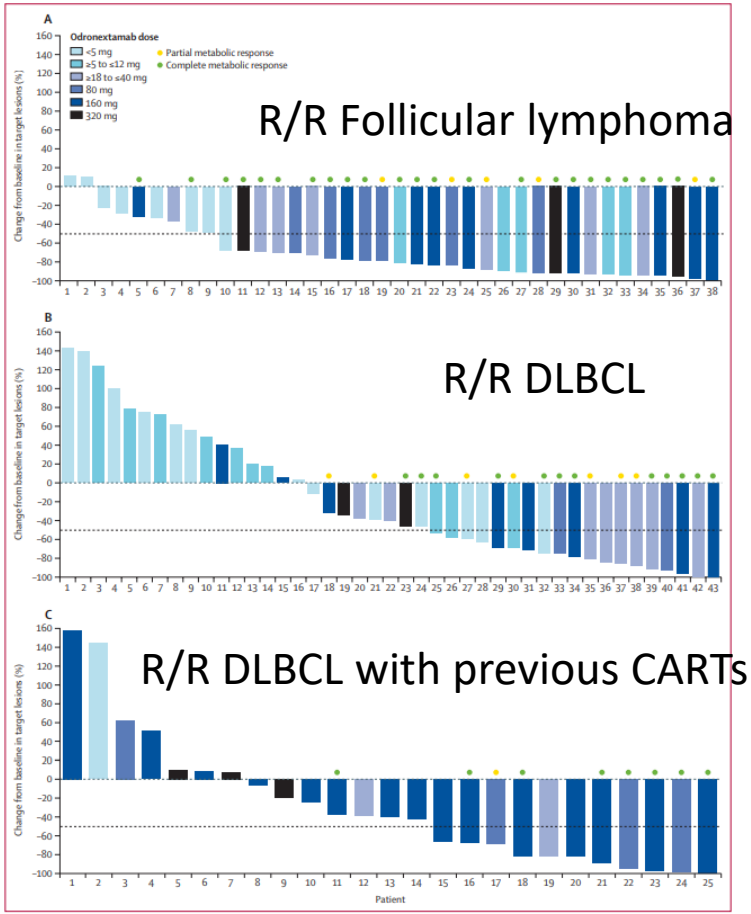
| | Relapsed or refractory follicular lymphoma grade 1–3a (n=40) | Relapsed or refractory diffuse large B-cell lymphoma without previous CAR T-cell therapy (n=49) | Relapsed or refractory diffuse large B-cell lymphoma with previous CAR T-cell therapy (n=33) |
|---|---|---|---|
| Objective response (complete or partial) | 31 (78%; 61·5–89·2) | 19 (39%; 25·2–53·8) | 11 (33%; 18·0–51·8) |
| Best overall complete tumour response | 25 (63%; 45·8–77·3) | 12 (24%; 13·3–38·9) | 8 (24%; 11·1–42·3) |
| Time to first response, months | 1·2 (1·0–2·5) | 1·4 (1·0–2·6) | 1·1 (0·8–2·5) |
| Estimated duration of response, months | 12·7 (95% CI 6·1–NE) | 4·4 (95% CI 2·9–NE) | NR (95% CI 1·6–NE) |
| Estimated duration of complete response, months | 14·5 (95% CI 8·8–NE) | NR (95% CI 4·0–NE) | NR (95% CI NE–NE) |
| Observed duration of complete response, months | 9·9 (3·9–19·9) | 10·3 (4·2–21·4) | 7·4 (2·6–15·8) |

**DLBCL > 80 mg ORR 53% / CR 53%**

**DLBCL post CART > 80 mg ORR 33% / CR 27%**

Recommended dose for expansion

- 80 mg in FL
- 160 mg in DLBCL



# Open questions

| | Bispecific antibodies | CARTs |
|---|---|---|
| Readily avaliable | 👍 | |
| Fixed treatment | | 👍 |
| Outpatient Tx | 👍 | |
| Less CRS / ICAN<br>- Step-up dosing<br>- Pre tx anti CD20<br>- SC formulation | 👍 | |
| Less Infections | 👍? | |
| Long-term efficacy | | 👍 |
| Higher probability of combinations | 👍? | |
| Sequencing | | 👍 |
| Less costs | 👍? | |

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| Less costs | 👍? | |

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