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Administration of GLOFITAMAB

Centers for Medicare & Medicaid Services
ICD-10 Coordination and Maintenance Committee Meeting
March 7-8, 2023

GLOFITAMAB is a T-cell-engaging bispecific antibody for the treatment of patients with relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL) who have received ≥2 prior systemic therapies

- **GLOFITAMAB** is the international, non-proprietary name* for the technology under consideration
- **Bispecific antibody** with a **novel 2:1 structure** designed to enable high-avidity, bivalent targeting of **CD20** on the surface of **B cells** and concomitant monovalent binding to **CD3** on **T cells**
- GLOFITAMAB induced **durable response rates** that were maintained after cessation of therapy with a **manageable safety** profile in an area of high unmet **medical need**
- **Off the shelf,** fixed-duration therapy administered as an **intravenous infusion (IV)**
- In the inpatient setting, GLOFITAMAB will be documented in the **"medication administration"** section of the medical record
- **Under consideration by CMS for an NTAP for FY2024**

* Subject to Food and Drug Administration (FDA) approval, the trade name for the product GLOFITAMAB will be finalized

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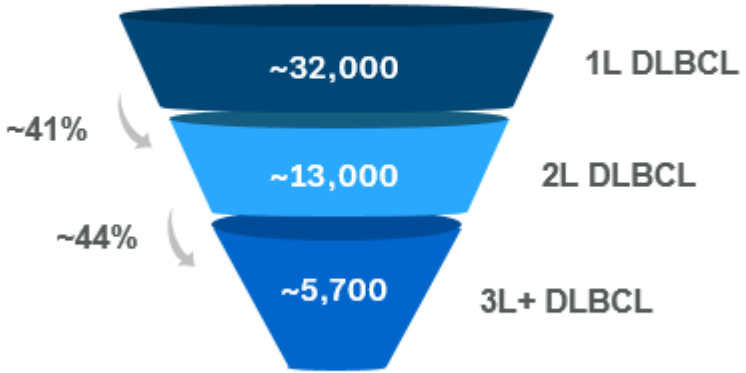
DLBCL IS THE MOST COMMON FORM OF NHL AND IS PRIMARILY A DISEASE OF OLDER PEOPLE

DLBCL is the most common form of NHL[1]

Estimated Treatment-Eligible DLBCL Cases in the US[2]



Patients with 3L+ DLBCL are heavily pretreated and highly refractory; many have exhausted all available treatment options. This is a patient cohort with substantial unmet clinical need

- DLBCL is an **aggressive** and **rapidly progressing** disease that involves the **malignant proliferation of B lymphocytes or B cells**[1,3]
- Median age of diagnosis is **66 years**[1,4]
- The rate of **new cases of DLBCL is 5.6 per 100,000** people per year; the death rate is **1.8 per 100,000** people per year[a,4]
- The **5-year relative survival is 64.6%** [4]
- The incidence of DLBCL cases in the US is approximately 30,000 new cases per year and is projected **to increase by 11% from 2020 to 2025** as a result of the aging population and the underlying higher incidence rate of DLBCL with older age[2]

[a]Rates are age-adjusted and based on 2015-2019 cases and deaths.

1L, first line; 2L, second line; 3L+, third line and greater; DLBCL, diffuse large B-cell lymphoma; NHL, non-Hodgkin lymphoma; US, United States.

1. American Cancer Society. Types of B-cell lymphoma. 2019:1-3. 2. Kanas G, et al. *Leuk Lymphoma*2022;63(1):54-63. 3. Liu Y, et al. *Am J Hematol*2019;94(5):604-16.
4. National Cancer Institute. NHL—diffuse large B-cell lymphoma. SEER 2022.

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THE PROGNOSIS IS POOR FOR PATIENTS WHO DO NOT ACHIEVE SUSTAINED REMISSION WITH FIRST-LINE (1L) R-CHOP

Approximately 40% of Patients Will Require R/R Treatment

- Approximately 60% of patients will achieve long-term remission with R-CHOP[1-4]
- Of the remaining 40%, approximately 10% to 15% will have primary refractory disease and 20% to 25% will relapse, usually within the first 2 years of treatment[1-4]

Eligibility and Access to Curative Therapies Are Limited

- Approximately half of patients seeking 2L therapy are not eligible for ASCT or CAR T-cell therapy due to advanced age, comorbidities and/or the ability to tolerate treatment.[1]
- ASCT and CAR T-cell therapies are only available at a limited number of specialized/authorized centers that may require extensive patient travel and long wait times for CAR T-cell manufacturing slots[5-10]

Poor Duration of Response

- Median survival of patients who receive 2L treatments ranges from 10-12 months[2,11-13]
- Patients who initiate 3L treatment have a median overall survival of about 4-6 months[14]

1L, first line; 2L, second line; 3L, third line; CAR, chimeric antigen receptor; ASCT, autologous stem cell transplantation; DLBCL, diffuse large B-cell lymhoma; OS, overall survival; R-CHOP, rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; R/R, relapsed/refractory.

1. Sehn LH, et al. *N Engl J Med* 2021;384(9):842-58. 2. Crump M, et al. *Blood* 2017;130:1800-9. 3. Friedberg JW. *Hematology* 2011:498-505. 4. Kanas G, et al. *Leuk Lymphoma* 2022;63(1):54-63. 5. Delamater PL, et al. *Bone Marrow Transplant* 2016;51(2):241-8. 6. American Cancer Society. Treatment and survivorship fact page. Published March 2020. Accessed August 2022. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant/process.html. 7. Leukemia & Lymphoma Society. Facts about chimeric antigen receptor (CAR) T-cell therapy. www.LLSorg. 2020. 8. Avalere Health. Advancements in cell therapies require new patient support solutions. Published April 15, 2021. https://avalere.com/insights/advancements-in-cell-therapies-require-new-patient-support-solutions. 9. BMTInfonet. Medical centers that offer CAR T-cell therapy. Accessed October 13, 2022. www.bmtinfonet.org/transplant-article/medical-centers-offering-car-t-cell-therapy. 10. Caffrey M. Delays mean some miss window for CAR T-cell therapy, cardinal health data show. AJMC. Published January 25, 2021. https://www.ajmc.com/view/delays-mean-some-miss-window-for-car-t-cell-therapy-cardinal-health-data-show. 11. Liu Y, et al. *Am J Hematol* 2019;94(5):604-16. 12. Chien HC, et al. *Future Oncol* 2021;17:411-22. 13. Van Den Neste E, et al. *Bone Marrow Transplant* 2016;51(1):51-57. 14. Fox CP, et al. EHA 2021. Abstract EP539.

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ALTHOUGH THERE ARE TREATMENT OPTIONS FOR R/R DLBCL, THERE IS CURRENTLY NO STANDARD OF CARE (1/2)

Treatment landscape of FDA-approved non–CAR T-cell regimens in 2L+ DLBCL

Factor	Tafa-Len[1,2] L-MIND (n=80)	Pola-BR[3] GO29365 (n=40)	Selinexor[4] SADAL (n=127)	Lonca-T[5] LOTIS-2 (n=145)
ORR, % CR, %	57.5 40	62.5 50	28 12	48.3 24.1
Median DOR, months	43.9	12.6	9.3	10.3
Discontinuation due to AE, %	25[a,b]	33.3	17	23
Clinically significant adverse event, all grades (grade ≥3)	Infections[b] 73 (30)	Peripheral neuropathy 43.6 (0)	Nausea/vomiting 58 (6)/29 (2)	Edema or effusion 31 (5)
Limitations				
Low rate of CRs with poor durability			✓	✓
High toxicity/discontinuation rates, limiting use to certain situations or subgroups	✓	✓	✓	✓
Limited data on how to best sequence therapies that target CD19	✓			✓

Patient populations in these trials may be significantly different so this table is not intended to suggest cross-trial comparison

[a]Permanent discontinuation of tafasitamab or lenalidomide due to AE. Permanent discontinuation of tafasitamab due to AE occurred in 15%of patients. [b]From US Prescribing Information.
2L+, second line and greater; AE, adverse event; CAR, chimeric antigen receptor; CD19, cluster of differentiation 19; CR, complete response; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; FDA, Food and Drug Administration; Lonca-T, loncastuximab tesirine; ORR, overall response rate; Pola-BR, polatuzumab vedotin, bendamustine, and rituximab; R/R, relapsed/refractory; Tafa-Len, tafasitamab and lenalidomide; US, United States.

1. Duell J, et al. *Haematologica* 2021;106(9):2417-26. 2. MONJUVI (tafasitamab-cxix) [prescribing information]. Boston, MA: Morphosys; July 2020. 3. Sehn LH, et al. *J Clin Oncol* 2020;155-65.
4. Kalakonda N, et al. *Lancet* 2020; 7(7):e511-22. 5. Caimi PF, et al. *Lancet Oncol* 2021;22(6):790-800.

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Treatment landscape of FDA-approved CAR T-cell regimens in 2L+ DLBCL

Factor	Axi-Cel[1,2] 3L+: ZUMA-1[a] (n=101)	Axi-Cel[1,2] 2L: ZUMA-7 (n=180)	Liso-Cel[1,3] 3L+: TRANSCEND[a] (n=256)	Liso-Cel[1,3] 2L: TRANSFORM (n=92)	Tisa-Cel[1] 3L+: JULIET[a] (n=115)
ORR, %	74	83	73	86	52
CR, %	54	65	53	66	40
Median DOR, months	11.1	26.9	NR	NR	NR
All-grade CRS, %	92	92	42	45	58
Grade ≥3 CRS, %	10	6	2	1	22
All-grade NEs, %	67	60	30	12	21
Grade ≥3 NEs, %	32	21	10	4	11

Patient populations in these trials may be significantly different so this table is not intended to suggest cross-trial comparison

Limitations of CAR T-cell therapy

- Long waiting periods to access manufacturing slots
- 12 states have no available CAR T-cell sites
- Relocation near treatment site for 4 weeks after infusion
- Advised driving restriction for at least 8 weeks
- Poor tolerability, especially in older patients and patients with comorbidities
- High rates of CRS
- Potential for severe neurotoxicity
- Requires chemotherapy lymphodepletion

There is an unmet need for more options that offer durable efficacy with a manageable safety in R/R DLBCL

[a]Understanding of data from CAR T-cell studies evolved over time. Data are based on recent review authored by the lead investigators from ZUMA-1, TRANSCEND, and JULIET.[1]
2L, second line; Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DLBCL, diffuse large B-cell lymphoma; DOR, duration of response; Liso-cel, lisocabtagene maraleucel;NE, not evaluable; NE, neurological event; NR, not reached; ORR, overall response rate; R/R, relapsed/refractory; Tisa-cel, tisagenlecleucel.
1. Westin JR, et al. *Am J Hematol*2021;96(10):1295-1312. 2. Locke FL, et al. *N Engl J Med*2021;386:640-54. 3. Kamdar M, et al. *Lancet*2022;399:2294-308.

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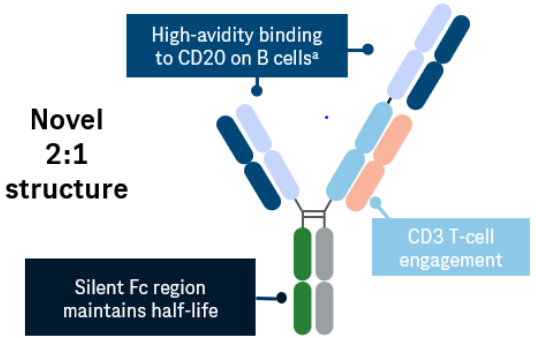
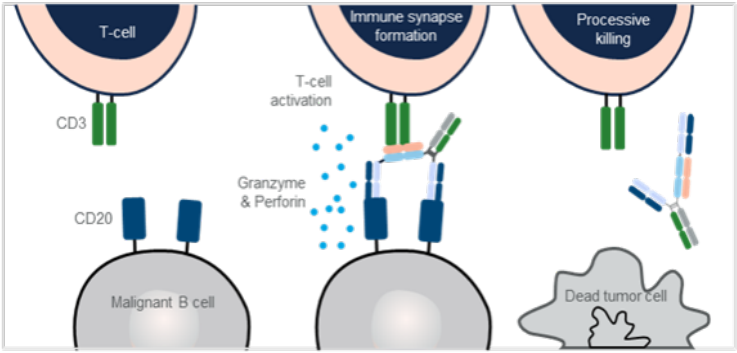
GLOFITAMAB IS A T-CELL-ENGAGING BISPECIFIC ANTIBODY WITH A NOVEL 2:1 STRUCTURE

GLOFITAMAB is a bispecific antibody with a novel 2:1 structure designed to enable high-avidity, bivalent targeting of CD20 on the surface of B cells and concomitant monovalent binding to CD3 on T cells



- Binding to CD3 activates the T cell, which induces T-cell proliferation and targeted killing of B cells [1]
- The novel 2:1 structure enables high-avidity, bivalent binding to CD20 that can result in activity against malignant B cells even under low effector-to-target cell ratios[2,3]
- The half-life is maintained due to the intact Fc region, allowing for a relatively simple dose schedule



GLOFITAMAB will be used to treat patients with R/R DLBCL who have progressed after ≥2 prior lines of therapy

[a]Obinutuzumab binds to the same CD20 epitope as GLOFITAMAB.
CD3, cluster of differentiation 3; CD20, cluster of differentiation 20; DLBCL, diffuse large B-cell lymphoma; Fc, fragment crystallizable; R/R, relapsed/refractory.
1. Broske AE, et al. *Blood Adv* 2022;6(3):1025-37. 2. Bacac M, et al. *Clin Cancer Res* 2018;24(19):4785-97. 3. Bacac M, et al. *Blood* 2016;128(22):1836. 4. Wang X, et al. *Protein Cell* 2018;9(1):63-73.

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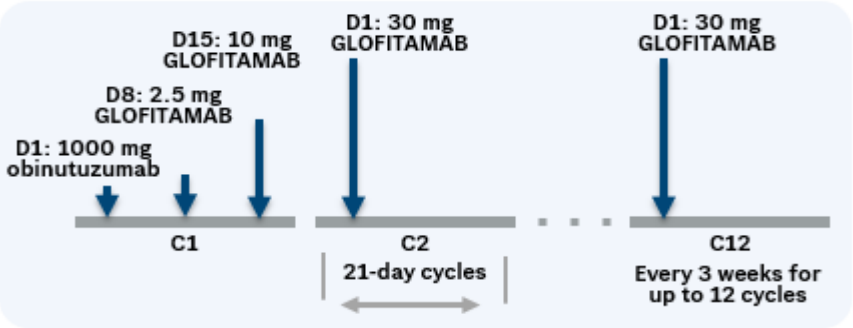
NCT03075696: A DOSE EXPANSION STUDY OF GLOFITAMAB AS A SINGLE AGENT AND IN COMBINATION WITH OBINUTUZUMAB IN R/R DLBCL[1]

GLOFITAMAB administration

- Simple dose schedule and fixed-duration therapy
- Obinutuzumab is administered on the first day of cycle 1, followed by 2.5 mg of glofitamab on Day 8 and 10 mg of glofitamab on day 15 of cycle 1. These measures are to reduce the risk of CRS
- Following cycle 2, glofitamab is given on day 1 of every subsequent cycle. Each cycle is 21 days
- The maximum number of cycles is 12. Treatment can be completed to 8.5 months



Key inclusion criteria

- DLBCL (DLBCL NOS, HGBCL, transformed FL or PMBCL)
- ECOG PS 0-1
- ≥2 prior regiments, including at least 1 anti-CD20 Ab and 1 anthracycline

Primary objective

- CR (best response) rate by PET/CT assessed by an independent review committee[2]

Baseline characteristics (N=155)

- Median age: 66 years (range, 21-90)
- Stage III–IV disease: 75.3%
- Median number of prior lines: 3 (range, 2–7)
  - 2 prior lines: 40.3%
  - ≥3 prior lines: 59.7%
- Prior CAR T-cell therapy: 33.1%
  - Refractory to CAR T-cell therapy: 90.2%
- Refractory to any prior therapy: 90.3%
- Refractory to last therapy: 85.7%

Ab, antibody; C, cycle; CAR, chimeric antigen receptor; CD20, cluster of differentiation 20; CR, complete response; CRS, cytokine release syndrome; D, day; DLBCL, diffuse large B-cell lymphoma; ECOG PS, Eastern Clinical Oncology Group performance status; FL, follicular lymphoma; HGBCL, high-grade B-cell lymphoma; N, number; NOS, not otherwise specified; PET/CT, positron emission tomography/computed tomography; PMLBCL, primary mediastinal large B-cell lymphoma; Q3W, every 3 weeks; R/R, relapsed/refractory.

1. Dickinson M, et al. ASCO 2022. Oral 7500. 2. Cheson BD, et al. *J Clin Oncol* 2007;25:579–8.

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GLOFITAMAB MET ITS PRIMARY ENDPOINT IN HEAVILY PRETREATED PATIENTS WITH DLBCL, WHERE THE MAJORITY ARE HIGHLY REFRACTORY

Efficacy endpoint	GLOFITAMAB 2.5/10/30 mg (N=155)
CR rate,[a] n (%)	**61 (39.4%)** [95% CI, 31.6-47.5]
ORR,[a] n (%)	**80 (51.6%)** [95% CI, 43.5-59.7]

- Median duration of follow-up: 12.6 months (range, 0-22)
- Responses were achieved early: median time to first CR was 42 days (95% CI, 42-44)

Patients achieved a similar CR rate regardless of having 2 or ≥3 prior lines of therapy, being younger or older than 65 years, or having prior CAR T-cell therapy

[a]Best response by intent-to-treat population.
CAR, chimeric antigen receptor; CI, confidence interval; CR, complete response; DLBCL, diffuse large B-cell lymphoma; IRC, independent review committee; ORR, overall response rate; R/R, relapsed/refractory.
Dickinson M, et al. ASCO 2022. Oral 7500.

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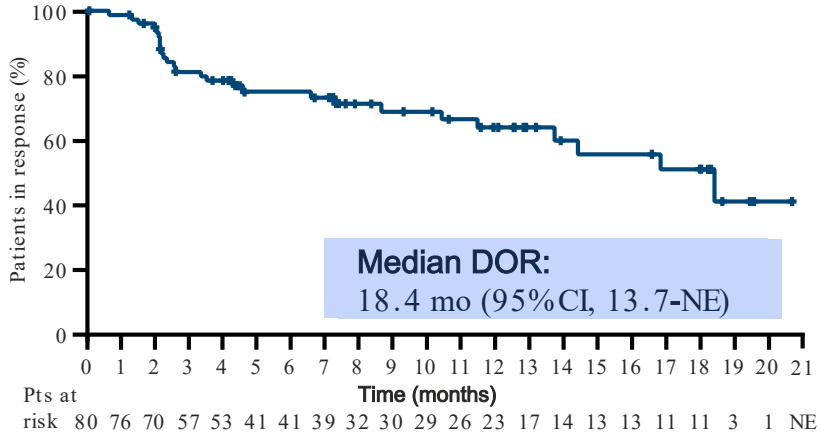
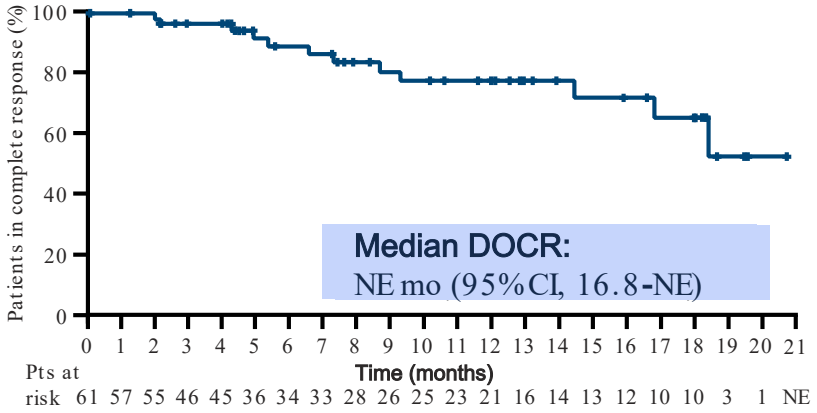
GLOFITAMAB INDUCED DURABLE RESPONSES THAT WERE MAINTAINED AFTER CESSATION OF THERAPY

Duration of overall response by IRC



	n=80
Median DOR follow-up, months (range)	10.6 (0-21)
12-month DOR, % (95% CI)	**63.6 (51.1 -76.2)**
ORs ongoing at CCOD, n (%)	53 (66.3)

Duration of complete response by IRC



	n=61
Median DOCR follow-up, months (range)	10.6 (0-21)
12-month DOCR, % (95% CI)	**77.6 (64.3 -90.8)**
CRs ongoing at CCOD, n (%)	49 (80.3)

CCOD, clinical cutoff date; CI, confidence interval; CR, complete response; DOCR, duration of complete response; DOR, duration of response; IRC, independent review committee; NE, not estimable; OR, overall response; PFS, progression-free survival; pts, patients; SPD, sum of the products of diameters.
Dickinson M, et al. ASCO 2022. Oral 7500.

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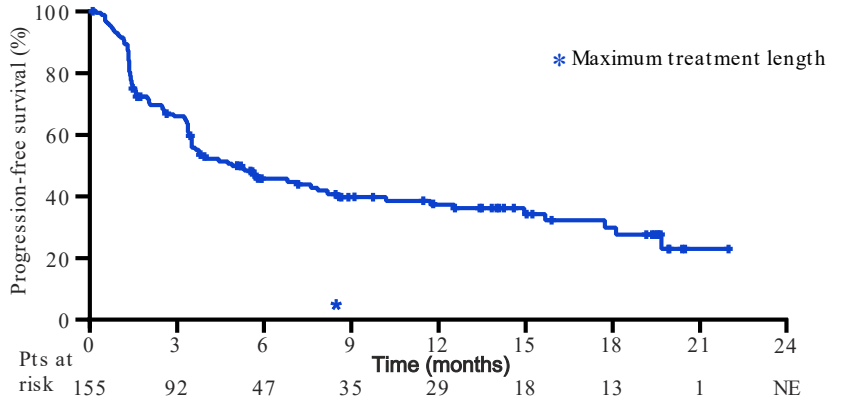
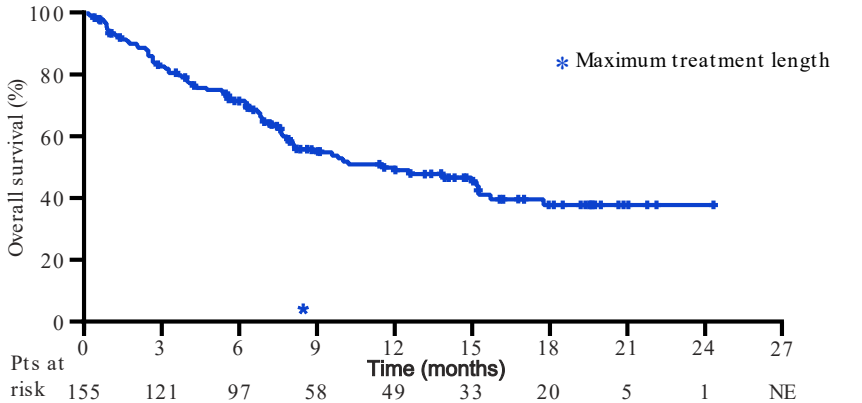
FOR PATIENTS TREATED WITH GLOFITAMAB, MEDIAN PFS WAS 4.9 MONTHS AND MEDIAN OS WAS 11.5 MONTHS

Progression-free survival by IRC



	N=155
Median PFS follow-up, months (range)	12.6 (0-22)
Median PFS, months (95%CI)[b]	4.9 (3.4-8.1)
6-month event-free rate, %(95%CI)	45.5 (37.2-53.8)
12-month event-free rate, %(95%CI)	37.1 (28.5-45.8)

Overall survival [a]



	N=155
Median OS, months (95%CI)[b]	11.5 (7.9-15.7)
12-month OS rate, %(95%CI)	49.8 (41.1-58.5)

[a]Including 5 deaths due to COVID-19. [b]Kaplan-Meier estimates.
CI, confidence interval; IRC, independent review committee; OS, overall survival; PFS, progression-free survival.
Dickinson M, et al. ASCO. 2022. Oral 7500.

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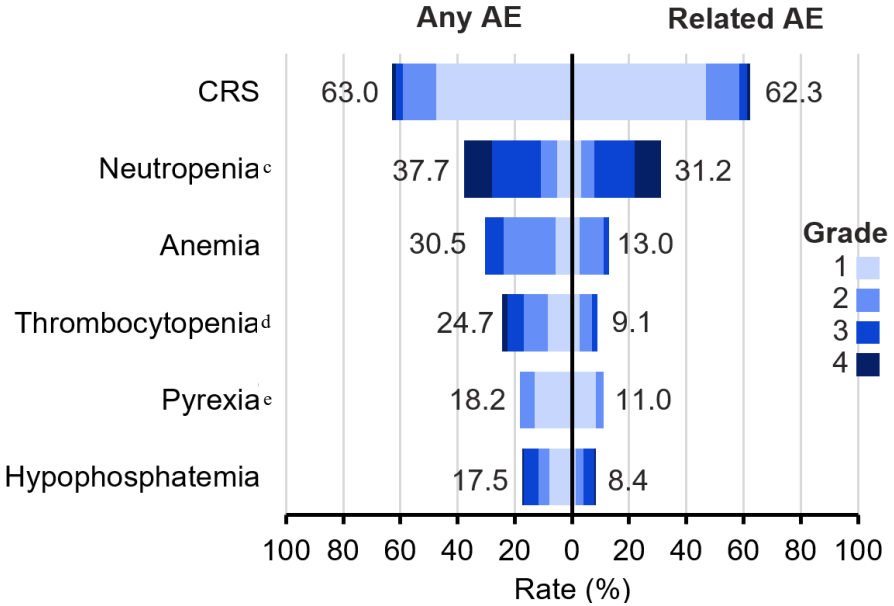
GLOFITAMAB DEMONSTRATED A MANAGEABLE SAFETY PROFILE WITH LOW RATE OF TREATMENT DISCONTINUATIONS

n (%)[a]	N=154
Median no. of cycles received (range)	5 (1-13)
Median relative dose intensity, %(range)	100 (94-100)
AEs	152 (98.7)
Related AEs	140 (90.9)
Grade 3 or 4 AEs	87 (56.5)
Related AEs	64 (41.6)
Serious AEs	73 (47.4)
Related AEs	46 (29.9)
Grade 5 (fatal AEs)	8 (5.2)[b]
Related AEs	0
AEs leading to treatment discontinuation	14 (9.1)
Related AEs	5 (3.2)

AEs (≥15%) by grade and relationship with GLOFITAMAB



[a]Unless otherwise specified. [b]COVID-19/COVID-19 pneumonia (n=5); sepsis (n=2); delirium (n=1). [c]Includes neutrophil count decreased. [d]Includes platelet count decreased. [e]Pyrexia events separate from CRS.
AE, adverse event; CRS, cytokine release syndrome..
Dickinson M, et al. ASCO. 2022. Oral 7500.

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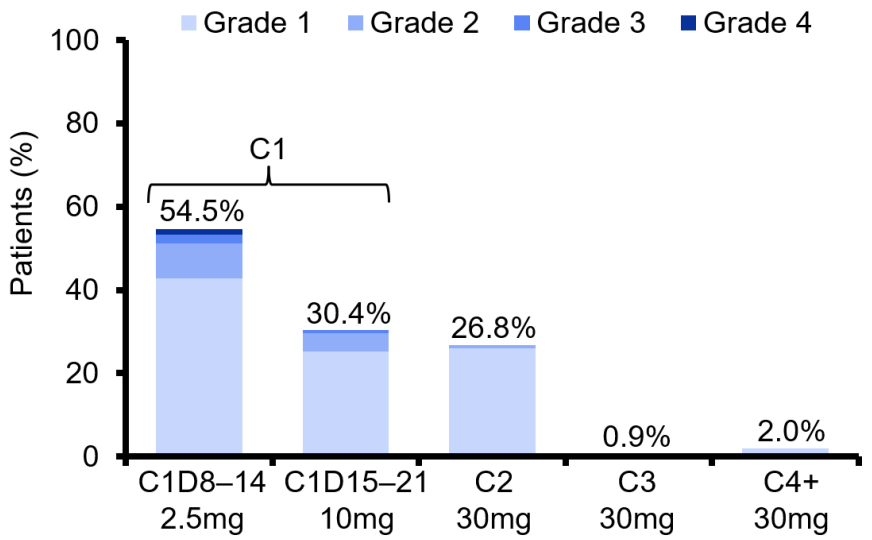
CRS WAS MOSTLY LOW GRADE AND OCCURRED PRIMARILY AFTER THE INITIAL DOSES OF GLOFITAMAB TREATMENT

n (%)	N=154
CRS (any grade)[a]	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)
Median CRS duration, hours (range)	30.63 (0.5-316.7)
Corticosteroids for CRS management	27/97 (27.8)
Tocilizumab for CRS management	31/97 (32.0)
Neurologic AEs (all grades)[b]	59 (38.3)
Grade ≥3	5 (3.2)
ICANS (all grades)[c]	12 (7.8)
Grade ≥3	4 (2.6)

CRS by cycle and grade[d]



[a]CRS was graded by investigator according to Lee 2014 criteria (and grade by the ASTCT criteria was derived based on reported data). [b]Neurologic AEs include AEs reported in Nervous System Disorders and Psychiatric Disorders System Organ Class. [c]Neurologic AEs potentially consistent with ICANS. [d]One patient had grade 1 CRS following obinutuzumab pretreatment due to CAR T-cell re-expansion.
AE, adverse event; ASTCT, American Society for Transplantation and Cellular Therapy; C, cycle; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; D, day; ICANS, immune effector cell-associated neurotoxicity syndrome.
Dickinson M, et al. ASCO 2022. Oral 7500.

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GLOFITAMAB DEMONSTRATED CLINICALLY MEANINGFUL OUTCOMES WITH A MANAGEABLE SAFETY PROFILE IN R/R DLBCL

T-Cell–Engaging Bispecific Antibody

- GLOFITAMAB is a T-cell–engaging bispecific monoclonal antibody that demonstrated clinically meaningful outcomes for patients with 3L+ DLBCL in a pivotal phase II setting
  - Patients in the pivotal cohort were heavily pretreated (40.3% with 2 prior lines and 59.7% with ≥3 prior lines) and highly refractory (90.3% refractory to any prior therapy)
  - Approximately one-third of the patients had prior CAR T-cell therapy, and 90.2% of those patients were refractory to CAR T-cell therapy

Clinically Meaningful Responses

- The CR rate was 39.4% in this difficult-to-treat patient population
  - CRs were achieved early (median time to response: 42 days) and were durable (mDOR: not estimable; 12-month DOCR: 77.6%)

Manageable Safety Profile

- GLOFITAMAB was well tolerated with a low rate of treatment discontinuations (9.1%)
  - The most frequent AE was CRS, with the majority being grade 1 (fever) and occurring on the initial dose

Fixed-Duration Therapy

- GLOFITAMAB is a promising off-the-shelf therapy, with a simple and fixed-duration dosing schedule (every 3 weeks for a maximum of 12 cycles). Treatment can be completed in up to 8.3 months

3L+, third line and greater; AE, adverse event; CAR, chimeric antigen receptor; CR, complete response; CRS, cytokine release syndrome; DOCR: duration of complete response; DLBCL, diffuse large B-cell lymphoma; mDOR, median duration of response; R/R, relapsed/refractory.
Dickinson M, et al. ASCO 2022. Oral 7500.

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Thank you