Up Close with Glofitamab

This section provides an overview of glofitamab-gxbm (COLUMVI™).

- 🏷️ Indications
- 💊 Dosing and Administration
- ⚠️ CRS
- 🧠 Neurotoxicity (including ICANS)
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🏷️ Indications

FDA-Approved Indications

Glofitamab is **bispecific CD20-directed CD3 T-cell engager** indicated for the treatment of

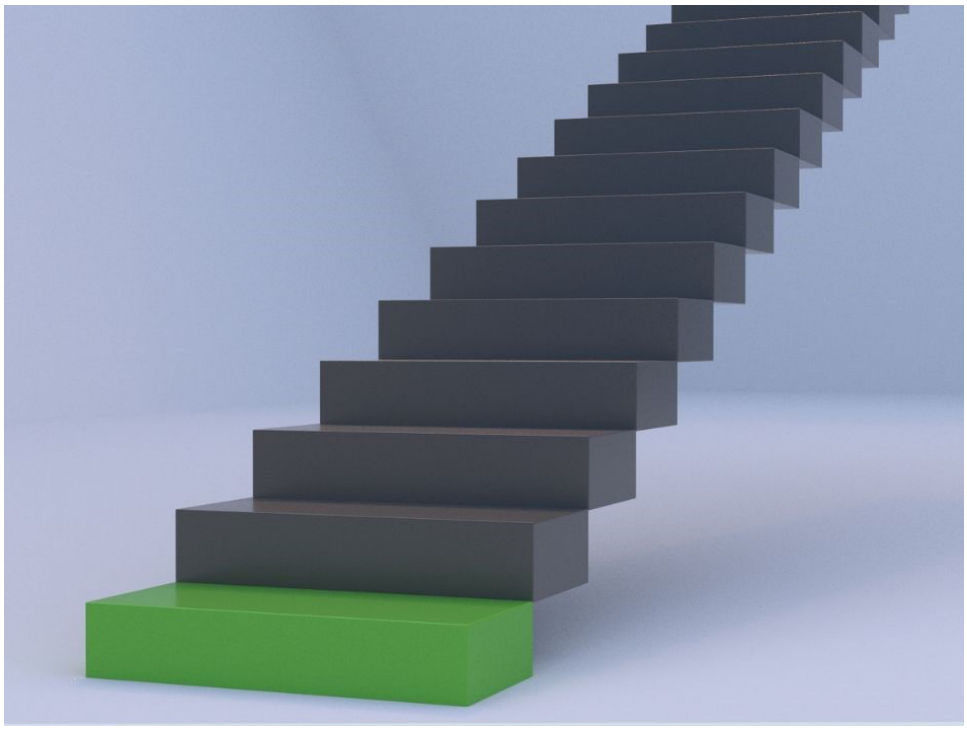
- Adult patients with **relapsed or refractory Diffuse Large B-Cell Lymphoma (DLBCL)**, not otherwise specified (NOS), or **Large B-Cell Lymphoma (LBCL)** arising from follicular lymphoma, **after 2 or more lines of systemic therapy**.

Note: These indications are approved under accelerated approval based on response rate and durability of response. Continued approval may be contingent upon verification of clinical benefit in confirmatory trials.

Guideline-Recommended Indications

- Glofitamab is recommended for **second line therapy for relapsed or refractory DLBCL when used in combination with gemcitabine and oxaliplatin.** This regimen may be used in ≤ 12 months or ≥ 12 months of relapsed disease.

💊 Dosing and Administration



Glofitamab is administered **intravenously (IV) as a 21-day cycle** for a maximum of 12 cycles, or until disease progression unacceptable toxicity. To reduce the risk of cytokine release syndrome, glofitamab as a **unique step-up dosing** schedule as shown below.

Prior to glofitamab administration, **all patients must receive obinutuzumab.** Obinutuzumab is used prior to glofitamab to deplete circulating and lymphoid tissue B-cells. The recommended dose of obinutuzumab is as followed:

- 1000 mg of obinutuzumab as a single intravenous dose (Cycle 1 Day 1)

Glofitamab 2 Step-Up Dosing Schedule			
Treatment Cycles		**Dose of Glofitamab / Route**	**Duration of Infusion**
Cycle 1	Day 1	Obinutuzumab[1] IV	4 hours[2]
	Day 8	2.5 mg[a] IV	
	Day 15	10 mg IV	
Cycle 2	Day 1	30 mg IV	4 hours[2]
Cycles 3 to 12	Day 1	30 mg IV	2 hours[3]

[1]Refer to obinuztumab dosing as described above
[2]Patients who experience CRS with their previous dose of glofitamab, may extend their infusion time up to 8 hours
[3]Patients who experience CRS with the previous dose of glofitamab, should have their infusion duration maintained at 4 hours
[a]All patients are required to be hospitalized during the first step-up dose (2.5 mg Cycle 1 Day 8) and for 24 hours following completion

Recommendations for Restarting Therapy with Glofitamab after Dosage Delay				
Patient's Treatment History		**Last Dose Administered**	**Time Elapsed since Last Dose**	**Recommended Next Actions**
Medication	**Cycle 1**			
Obinutuzumab (pretreatment)	Day 1	1000 mg	≤ 2 weeks	Administer glofitamab 2.5 mg (Cycle 1 Day 8)[b], then resume with treatment plan as scheduled.
			> 2 weeks	Repeat obinutuzumab pretreatment. Then administer glofitamab 2.5 mg (Cycle 1 Day 8)[b], and resume treatment plan as scheduled.
Glofitamab	Day 8	2.5 mg	≤ 2 weeks	Administer glofitamab 10 mg (Cycle 1 Day 15)[c], then resume treatment plan as scheduled.
			> 2 to ≤ 4 weeks	Repeat glofitamab 2.5 mg (Cycle 1 Day 8)[b], then administer glofitamab 10 mg (Cycle 1 Day 15)[c]. Upon completion, resume treatment plan as scheduled.
			> 4 weeks	Repeat obinutuzumab pretreatment (Cycle 1 Day 1). Then administer glofitamab 2.5 mg (Cycle 1 Day 8)[b] and glofitamab 10 mg (Cycle 1 Day 15)[c]. Upon completion, resume treatment plan as scheduled.
	Day 15	10 mg	≤ 2 weeks	Administer glofitamab 30 mg (Cycle 2 Day 1) and resume treatment plan as scheduled.
			> 2 to ≤ 6 weeks	Readminister glofitamab 10 mg (Cycle 1 Day 15)[c]. Then administer glofitamab 30 mg (Cycle 2 Day 1) and resume treatment plan as scheduled.
			> 6 weeks	Repeat obinutuzumab pretreatment (Cycle 1 Day 1), glofitamab 2.5 mg (Cycle 1 Day 8)[b] and glofitamab 10 mg (Cycle 1 Day 15)[c]. Then administer glofitamab 30 mg (Cycle 2 Day 1) and resume treatment plan as scheduled.
Medication	**Cycle 2+**			
Glofitamab	Day 1	30 mg	≤ 6 weeks	Administer glofitamab 30 mg (Cycle 2 Day 1), then resume treatment plan as scheduled.
			> 6 weeks	Repeat Cycle 1 regimen as described above: obinutuzumab 1,000 mg pretreatment (Day 1), glofitamab 2.5 mg (Day 8)[b], and glofitamab 10 mg (Day 15)[c]. Then administer glofitamab 30 mg (Day 1 of next cycle) and resume treatment plan as scheduled.

[a]Refer to obinuztumab dosing as described above
[b]Patients who experience CRS with their previous dose of glofitamab, may extend their infusion time up to 8 hours
[c]Patients who experience CRS with the previous dose of glofitamab, should have their infusion duration maintained at 4 hours

Recommended Pre-Medications for Glofitamab Infusion			
Day of Treatment Cycle	**Patients Requiring Medications**	**Pre-Medication(s) / Route**	**Administration**
Cycle 1 (Day 8, 15) **Cycle 2 (Day 1)** **Cycle 3 (Day 1)**	All patients	Dexamethasone 20 mg* IV	Complete ≥1 hour prior to infusion.
		Diphenhydramine HCl 50 mg or equivalent antihistamine IV / PO	Complete ≥30 minutes prior to infusion
		Acetaminophen 500 mg to 1000 mg PO	Complete ≥30 minutes prior to infusion
Subsequent Cycles	All patients	Acetaminophen 500 mg to 1000 mg PO	Complete ≥30 minutes prior to infusion
		Diphenhydramine HCl 50 mg to 100 mg or equivalent antihistamine IV / PO	Administer orally or intravenously and complete at least 30 minutes prior to infusion.
	Patients who experienced any grade CRS with a previous dose	Dexamethasone 20 mg* IV	Complete ≥1 hour prior to infusion
PO, orally *If dexamethasone is unavailable, it is appropriate to administer prednisone 100 mg, prednisolone 100 mg, or methylprednisolone 80 mg intravenously			

Tumor Lysis Syndrome (TLS) Prophylaxis

- Before initiating glofitamab, **patients who are at risk for TLS** s**hould be administered anti-hyperuricemics**.
- Carefully monitor for adequate hydration status and appropriate care.

⚠️ CRS

What is it? Cytokine release syndrome (CRS) is a systemic inflammatory response that can occur when the immune system is activated and releases large amounts of cytokines—proteins that help regulate immune responses.

- **Signs and symptoms:** pyrexia, hypotension, hypoxia, dyspnea, chills, and tachycardia.
- CRS is frequently graded using the American Society for Transplantation and Cellular Therapy (ASTCT) consensus criteria.

Why it matters. CRS occurred in **70% of patients** in the clinical trial, NP30179.

- **Most CRS events** occurred during **Cycle 1**, with the **highest events** occurring on the initiation of glofitamab **(Cycle 1 Day 8)**.
    - All events were **primarily Grade 1 or 2**, however due to the significantly increased risk of CRS, **all patients are required to be hospitalized during the first step-up dose** (2.5 mg Cycle 1 Day 8) and **for 24 hours following completio**n.
- The **median time to onset of CRS** across all doses was **14 hours** following the initial step-up dose of glofitamab (range: 5 to 74 hours) post-administration.
- The **median duration** of CRS was **2 days** (range: 1 to 14 days) and resolved in 98% of cases.
- Additionally, any patient that experiences

- **CRS during Cycle 1**, regardless of the grade, **should be hospitalized during and for 24 hours** following **completion of the second step-up dose** of glofitamab (10 mg on Cycle 1 Day 15).
- **Grade ≥ 2 CRS during or following subsequent doses** of glofitamab (Day 1 of Cycle 2+) **should be hospitalized during and for 24 hours following completion** of infusion.

The bottom line. CRS was primarily low-grade, predictable, and manageable.

🧠 Neurotoxicity (including ICANS)

What is it? Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) is characterized by various neurological symptoms resulting from the activation of the immune system and the resultant inflammatory processes.

- **Signs and symptoms:** encephalopathy, headaches, seizures, aphasia, motor deficits, ataxia, and tremor.
- ICANS is frequently graded using the ASTCT consensus criteria.

Why it matters. ICANS of any grade occurred in **4.8%** of patients in the clinical trial. However, the more common neurological toxicities associated with glofitamab were dizziness/vertigo, confusion, peripheral neuropathy, and headache.

- ICANS resolved in most cases and lasted a few days.

- Care teams should **monitor patients for any signs and symptoms of neurological toxicity**, including headache, peripheral neuropathy, vertigo/dizziness and confusional state.
    - Coadministration of any other neurologically acting agents may increase the risk of neurotoxicity.
    - Consider **withholding or permanently discontinuing** glofitamab **based on severity** of ICANS.

The bottom line. ICANS was uncommon and primarily low-grade.

🚨 Other Toxicities

Glofitamab may cause other adverse reactions such as **infections, tumor flares, or embryo-fetal toxicity**.

Why it matters. In addition to the risks of CRS and neurotoxicity (including ICANS), care teams need to be on the lookout for other **glofitamab**-associated toxicities.

Infections. Glofitamab can cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **16% of patients**, with **Grade 3 or 4 infections in 10%**, and **fatal infections in 4.8%**.
    - The most common serious infections reported were pneumonia, sepsis, and increased risk of COVID-19 acquired infections.

The bottom line. Care teams should **monitor patients for signs of infection before and during treatment**; treat appropriately.

- Avoid administration in patients with active infections; withhold or discontinue glofitamab based on severity.
- Consider providing *Pneumocystis jirovecii pneumonia* (PJP), herpes virus, and cytomegalovirus prophylaxis before starting glofitamab for those who may be at increased risk.

Cytopenias. Glofitamab may cause cytopenias, including thrombocytopenia and neutropenia.

- In the clinical trial, **neutropenia and thrombocytopenia** occurred in **56% of patients** whereas f**ebrile neutropenia** occurred in **3.4% of patients**.

The bottom line. Care teams should **monitor complete blood counts throughout treatment**.

- **Withhold or discontinue** glofitamab **based on severity of the cytopenia**.
  - Neutropenia (ANC < 0.5 x 10^9/L) and/or
  - Thrombocytopenia (platelets < 50 x 10^9/L)

Embryo-Fetal Toxicity. Glofitamab may cause fetal harm when administered to a pregnant woman.

- Advise **females of reproductive potential** to use effective contraception **during treatment and for 1 month after the last dose**.
- Verify pregnancy status before initiating glofitamab.

Use in Specific Populations.

- **Lactation:** Human immunoglobulin-G (IgG) is present in human milk, and therefore there is a potential for glofitamab absorption leading to B-cell depletion. Advise women not to breastfeed during treatment and for 1 month after the last dose.
- **Geriatric Use** (in NP3071):
  - No overall difference identified in efficacy of glofitamab use in patients 65 years of age or older when compared to younger patients.
  - Higher rate of fatal adverse reactions, mainly infections, including COVID-19, in patients ≥ 65 years old compared to younger adults.
- **Pediatric Use:** At this time, no safety and effectiveness data has been established in pediatric patients.

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References

1. Glofitamab (COLUMVI™) [package insert]. Genentech, Inc. San Francisco, CA. 2023.
2. Lee DW, Santomasso BD, Locke FL, et al. ASTCT Consensus Grading for Cytokine Release Syndrome and Neurologic Toxicity Associated with Immune Effector Cells. *Biol Blood Marrow Transplant*. 2019;25(4):625-638. doi:10.1016/j.bbmt.2018.12.758.
3. Dickinson MJ, Carlo-Stella C, Morschhauser F, et al. Glofitamab for relapsed or refractory diffuse large B-cell lymphoma. *N Engl J Med.* 2022;387(24):2220-2231. doi:10.1056/NEJMoa2205183.
4. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas V2.2025. National Comprehensive Cancer Network, Inc. 2025. Accessed March 4, 2025.