Up Close with Mosunetuzumab

This section provides an overview of mosunetuzumab-axgb (LUNSUMIO™).

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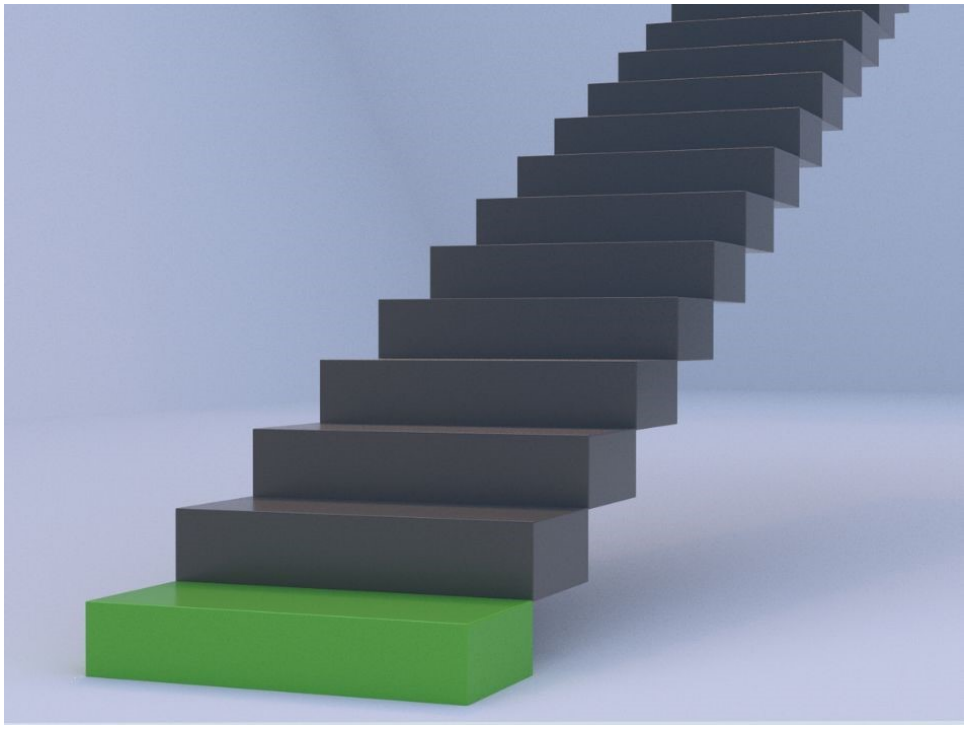
🏷️ Indications

Mosunetuzumab is **bispecific CD20-directed CD3 T-Cell engager** indicated for the treatment of:

- Adult patients with **relapsed or refractory follicular lymphoma**, who have previously received **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.

💊 Dosing and Administration



Mosunetuzumab is administered **intravenously (IV) in 21-day cycles** for **8 consecutive cycles**, or until disease progression and/or unacceptable toxicity. Mosunetuzumab has a **unique step-up dosing** schedule as shown below to reduce the risk of cytokine release syndrome (CRS).

Mosunetuzumab Step-Up Dosing Schedule			
Treatment Cycles		**Dose of Mosunetuzumab / Route**	**Duration of Infusion**
Cycle 1[a]	Day 1	1 mg IV	Administer over a minimum of 4 hours.
	Day 8	2 mg IV	
	Day 15	60 mg IV	
Cycle 2[a]	Day 1	60 mg IV	If infusions from Cycle 1 were well-tolerated, mosunetuzumab may be administered over 2 hours for subsequent cycles.
Cycle 3+[b]	Day 1	30 mg IV	

PO, orally

[a]Cycle 1 and 2 pre-medications (all patients)

- Premedicate with dexamethasone 20 mg IV or methylprednisolone 80 mg IV and complete at least 1 hour prior to infusion of mosunetuzumab.
- Premedicate with diphenhydramine 50 mg to 100 mg IV/PO or equivalent antihistamine and complete at least 30 minutes prior to infusion of mosunetuzumab.
- Premedicate with acetaminophen 500 mg to 1000 mg PO and complete at least 30 minutes prior to infusion of mosuntetuzumab.

[b]Cycle 3+ premedications (any patient that experienced CRS of any grade with a previous dose)

- Premedicate with dexamethasone 20 mg IV or methylprednisolone 80 mg IV and complete at least 1 hour prior to infusion of mosunetuzumab.
- Premedicate with diphenhydramine HCl 50 mg to 100 mg IV/PO or equivalent antihistamine and complete at least 30 minutes prior to infusion of mosunetuzumab.

- Premedicate with acetaminophen 500 mg to 1000 mg PO and complete at least 30 minutes prior to infusion of mosunetuzumab.

There are **specific recommendations** for the number of cycles recommended, pending response to mosunetuzumab.

- For patients **who achieve a <u>complete</u> response upon completion of cycle 8:**
  - No further subsequent treatment is required.
- For patients **who receive a <u>partial response or have stable disease</u> in response to mosunetuzumab after 8 cycles:**
  - Patients should receive an additional 9 cycles of mosunetuzumab (17 total).

Recommendations for Restarting Therapy with Mosunetuzumab After Dosage Delay			
Patient's Treatment History		**Time Elapsed Since Last Dose**	**Recommended Next Actions**
Cycle 1			
Day 1	1 mg	1 to 2 weeks	Administer 2 mg (Cycle 1 Day 8), then continue treatment plan as scheduled.
		> 2 weeks	Repeat 1 mg (Cycle 1 Day 1), then administer 2 mg (Cycle 1 Day 8) and resume treatment plan as scheduled.
Day 8	2 mg	1 to 2 weeks	Administer 60 mg (Cycle 1 Day 15), then resume treatment plan as scheduled.
		> 2 to < 6 weeks	Repeat 2 mg (Cycle 1 Day 8), then administer 60 mg (Cycle 1 Day 15), then resume treatment plan as scheduled.
		≥6 weeks	Repeat 1 mg (Cycle 1 Day 1), 2 mg (Cycle 1 Day 8), and then administer 60 mg (Cycle 1 Day 15) and resume treatment plan as scheduled.
Day 15	60 mg	1 to < 6 weeks	Administer 60 mg (Cycle 2 Day 1), then resume treatment plan as scheduled.
		≥6 weeks	Repeat 1 mg (Cycle 2 Day 1), 2 mg (Cycle 2 Day 8), then administer 60 mg (Cycle 2 Day 15). Upon completion, administer 40 mg (Cycle 3 Day 1) and resume treatment plan as scheduled.
Cycle 2			
Day 1	60 mg	3 to < 6 weeks	Administer 30 mg (Cycle 3 Day 1) and continue treatment plan as scheduled.
		≥ 6 weeks	Repeat 1 mg (Cycle 3 Day 1), 2 mg (Cycle 3 Day 8), and then administer 30 mg (Cycle 3 Day 15). Upon completion, administer 30 mg (Cycle 4 Day 1), and resume treatment plan as scheduled.
Cycle 3+			
Day 1	30 mg	3 to < 6 weeks	Administer 30 mg and continue treatment plan as scheduled.
		≥ 6 weeks	Repeat 1 mg on Day 1 and 2 mg on Day 8 of the next cycle. Upon completion, administer 30 mg on Day 15.[a] Moving forward, administer 30 mg on Day 1 of each subsequent cycle.
[a]Administer pre-medications as described below for Days 1, 8, and 15 of doses in the next cycle			

⚠️ 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 **44%** of patients in the study GO29781.

- **Most CRS events** occurred **during Cycle 1**, with the **highest events occurring** on **Day 15 of Cycle 1**, which coincides with the **highest administered** dose of mosunetuzumab (**60 mg**).
    - The **median time to onset** of CRS across all doses was **27 hours** (range: 1 to 72 hours) post-administration.
        - Cycle 1 Day 1: ~5 hours
        - Cycle 1 Day 8: ~28 hours
        - Cycle 1 Day 15: ~25 hours
        - Cycle 2 Day 1: ~46 hours
    - The **median duration** of CRS was **3 days** (range: 1 to 29 days).
- **Concurrent neurological adverse reactions** associated with CRS **occurred in 6% of patients**, including, but not limited to anxiety, confusion, and headache.

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 was reported in **1% of patients** in the clinical trial, however across a broader clinical trial population, ICANS **occurred or was suspected in 2.1%** of trial participants.

- The **time to onset** of ICANS or suspected ICANS was **17 days** (range: 1 to 48 days).
- ICANS resolved in most cases and lasted a few days.

The bottom line. ICANS was uncommon, primarily low-grade, and resolved in the majority of cases over a few days.

🚨 Other Toxicities

Mosunetuzumab can cause other adverse reactions such as **opportunistic infections, cytopenia, tumor flares, hemophagocytic lymphohistiocytosis, and 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 **mosunetuzumab-**associated toxicities.

Infections. Mosunetuzumab may cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **17% of patients,** with **Grade 3 or 4 infections in 14%**, and **fatal infections in 0.9%**.
    - The most common serious infections reported were pneumonia, sepsis, and upper respiratory tract 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 mosunetuzumab based on severity.

Cytopenias. Mosunetuzumab may cause serious or severe cytopenias, including anemia, neutropenia, and thrombocytopenia.

- In GO29781, **Grade 3 or 4 cytopenias** occurred in **up to 38% of patients** enrolled in the trial.
    - **Neutropenia, thrombocytopenia, and anemia** were reported in **38%, 12%, and 19%**, respectively.

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

- **Withhold or discontinue mosunetuzumab based on neutropenia severity**; consider prophylactic granulocyte colony-stimulating factor.

Tumor Flare. Mosunetuzumab may cause serious or severe tumor flare.

- Among the patients enrolled in GO29781, **4% of patients experienced tumor flare**.
    - Manifestations included, but were not limited to localized pain, swelling and pain at lymphoma lesions, tumor inflammation, and new or worsening pleural effusions.

The bottom line. Care teams should **monitor patients with bulky tumors or tumors in proximity to chest and airways**.

- Additionally, care teams should carefully **monitor patients for signs and symptoms of compression or obstruction due to a mass**, secondary to tumor flare.
- If these clinical manifestations are present, patients should be treated according to their institution's standard treatment.

Hemophagocytic Lymphohistiocytosis. Mosunetuzumab may cause a serious or fatal condition of hemophagocytic lymphohistiocytosis (HLH). HLH is a potentially life-threatening, hyperinflammatory syndrome that is not associated with CRS.

- Reports of HLH occurred in 0.5% (7/1536) of patients enrolled in a broader population of clinical trial. Of those 7 cases, 6 patients had fatal outcomes.
    - Manifestations of HLH include fever, hemophagocytosis, coagulopathy, splenomegaly, hepatitis, elevated ferritin, and cytopenias.

The bottom line. Care teams should **monitor for signs and symptoms of HLH**, and when the clinical presentation of CRS seems atypical and/or prolonged, patients should be considered for HLH.

- **Patients who are suspected to have HLH** should **withhold mosunetuzumab treatment** and should be treated for HLH per recommendations of practice guidelines.

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

- Advise **females of reproductive potential** to use effective contraception d**uring treatment and for 3 months after the last dose**.
- Verify pregnancy status before initiating mosunetuzumab.

Use in Specific Populations

- **Lactation Use:** Advise women not to breastfeed during treatment and for 3 months after the last dose.
- **Geriatric Use:** At this time, there are no differences in safety or effectiveness of mosunetuzumab use in in patients ≥ 65 years old compared to younger adults.
- **Pediatric Use:** The safety and efficacy of mosunetuzumab has not been established in pediatric patients.

Updated: 03/21/2025

References:

1. Mosunetuzumab (LUNSUMIO™) [package insert]. Genentech, Inc. San Francisco, CA. 2024.
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. Budde LE, Sehn LH, Matasar M, et al. Safety and efficacy of mosunetuzumab, a bispecific antibody, in patients with relapsed or refractory follicular lymphoma: a single-arm, multicentre, phase 2 study. *Lancet Oncol.* Published online July 5, 2022. doi:10.1016/S1470-2045(22)00335-7.