Up Close with Tarlatamab

This resource provides an overview of tarlatamab-dlle (IMDELLTRA®).

Indications

Dosing & Administration

Cytokine Release Syndrome (CRS)

Neurotoxicity (including ICANS)

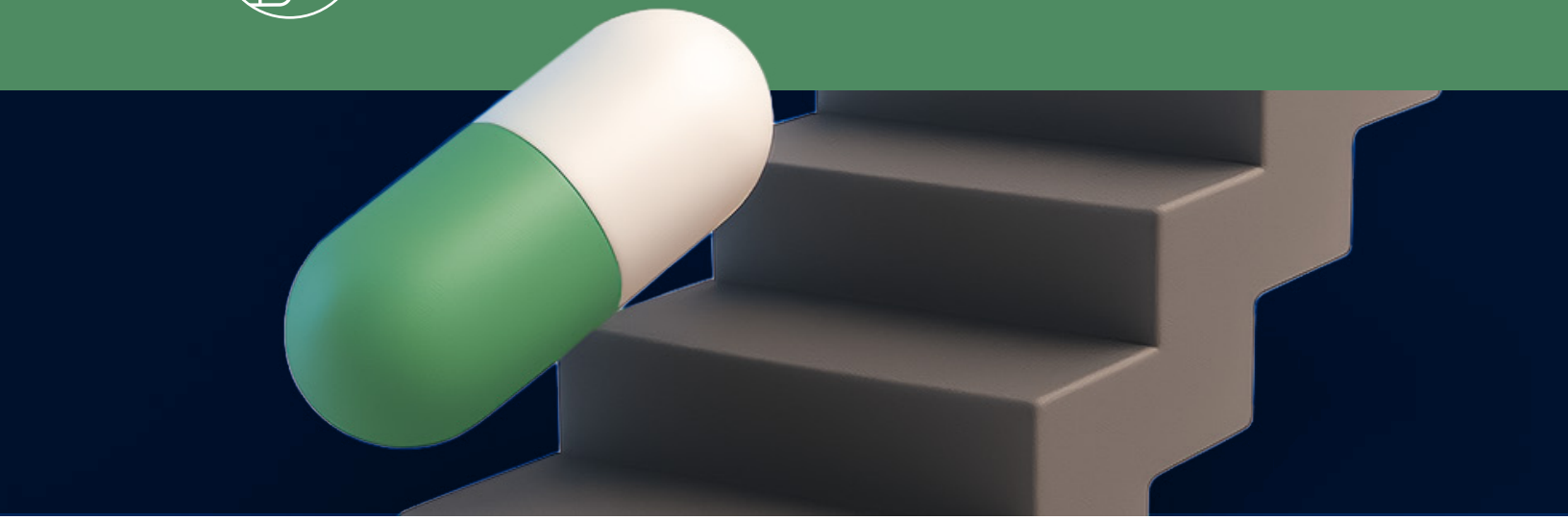
Other Toxicities

Indications

Tarlatamab is a **bispecific delta-like ligand 3 (DLL3)-directed CD3 T-cell engager** indicated for the treatment of adult patients with:

- **Extensive stage small cell lung cancer (ES-SCLC)** with **disease progression on or after platinum-based chemotherapy**

Dosing & Administration



Tarlatamab is administered via an **intravenous (IV) infusion over 1 hour** (rate of 250 mL/hour) with unique **step-up dosing** only during Cycle 1 (Days 1, 8, and 15) to reduce the risk and severity of cytokine release syndrome (CRS) as shown below.

Tarlatamab Dosing Schedule

Dosing Schedule	Day of Treatment	Tarlatamab Dose / Route		Administration Instructions	Tarlatamab Monitoring Recommendations
Cycle 1 (Step-Up)[a]	Day 1	Step-up dose 1	1 mg IV	Administer over a 1-hour infusion at an appropriate healthcare setting.	Monitor patients from the start of infusion for 22 to 24 hours in an appropriate healthcare setting. Recommend that patients remain within 1 hour of an appropriate healthcare setting for a total of 48 hours from start of the infusion accompanied by a caregiver.
	Day 8	10 mg IV			
	Day 15	10 mg IV			Observe patients for 6-8 hours post infusion.[b]
Cycle 2	Day 1	10 mg IV		Administer over a 1-hour infusion at an appropriate healthcare setting.	Observe patients for 6-8 hours post infusion.[b]
	Day 15	10 mg IV			
Cycles 3-4	Day 1	10 mg IV		Administer over a 1-hour infusion at an appropriate healthcare setting.	Observe patients for 3-4 hours post infusion.[b]
	Day 15	10 mg IV			

Tarlatamab Dosing Schedule - continued

Dosing Schedule	Day of Treatment	Tarlatamab Dose / Route	Administration Instructions	Tarlatamab Monitoring Recommendations
Cycles 5+	Day 1	10 mg IV	Administer over a 1-hour infusion at an appropriate healthcare setting.	Observe patients for 2 hours post infusion.[b]
	Day 15	10 mg IV		

[a]Administer concomitant medication before and after tarlatamab infusion **(Cycle 1 only)**

- Prior to tarlatamab infusion (Cycle 1 Days 1 and 8):
  - Administer 8 mg of dexamethasone intravenously (or equivalent) within 1 hour of tarlatamab infusion
- Post-tarlatamab infusion (Cycle 1 Days 1 and 8):
  - Administer 1 liter of normal saline intravenously over 2-4 hours immediately following completion of tarlatamab infusion

[b]Extended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥ 2 CRS, ICANS or neurologic toxicity during prior treatments

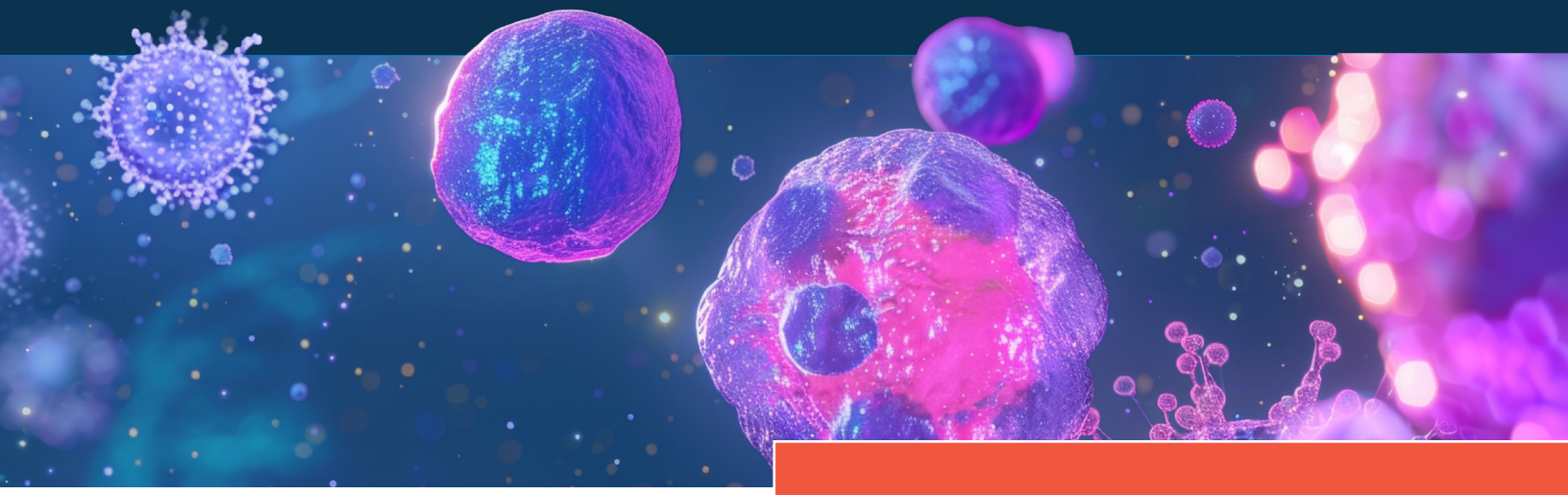
Recommendations for Restarting Tarlatamab Following Dose Delay

Last Administered Cycle/Day of Tarlatamab	Last Dose of Tarlatamab Administered	Time Since Last Administered Dose of Tarlatamab	Recommended Action[a]
Cycle 1 Day 1	1 mg	≤ 14 days	Administer tarlatamab 10 mg, then resume the treatment plan as scheduled.
		> 14 days	Administer tarlatamab step-up dose 1 mg. If dose is tolerated, increase to 10 mg (one week later) and resume treatment plan as scheduled.
Cycle 1 Day 8	10 mg	≤ 21 days	Administer tarlatamab 10 mg, then resume the treatment plan as scheduled.
		> 21 days	Administer tarlatamab step-up dose 1 mg. If dose is tolerated, increase to 10 mg (one week later) and resume treatment plan as scheduled.
Cycle 1 Day 15 and Subsequent cycles every 2 weeks thereafter	10 mg	≤ 28 days	Administer tarlatamab 10 mg, then resume the treatment plan as scheduled.
		> 28 days	Administer tarlatamab step-up dose 1 mg. If dose is tolerated, increase to 10 mg (one week later) and resume treatment plan as scheduled.

[a]Administer concomitant medication before and after tarlatamab infusion **(Cycle 1 only)**

- Prior to tarlatamab infusion (Cycle 1 Days 1 and 8):
  - Administer 8 mg of dexamethasone intravenously (or equivalent) within 1 hour of tarlatamab infusion
- Post-tarlatamab infusion (Cycle 1 Days 1 & 8):
  - Administer 1 liter of normal saline intravenously over 2-4 hours immediately following completion of tarlatamab infusion

Cytokine Release Syndrome



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:

- Chills
- Low tissue oxygen level
- Fever
- Rapid heartbeat
- Low blood pressure
- Trouble breathing

CRS is frequently graded using the American Society for Transplantation and Cellular Therapy (ASTCT) consensus criteria.

THE BOTTOM LINE:

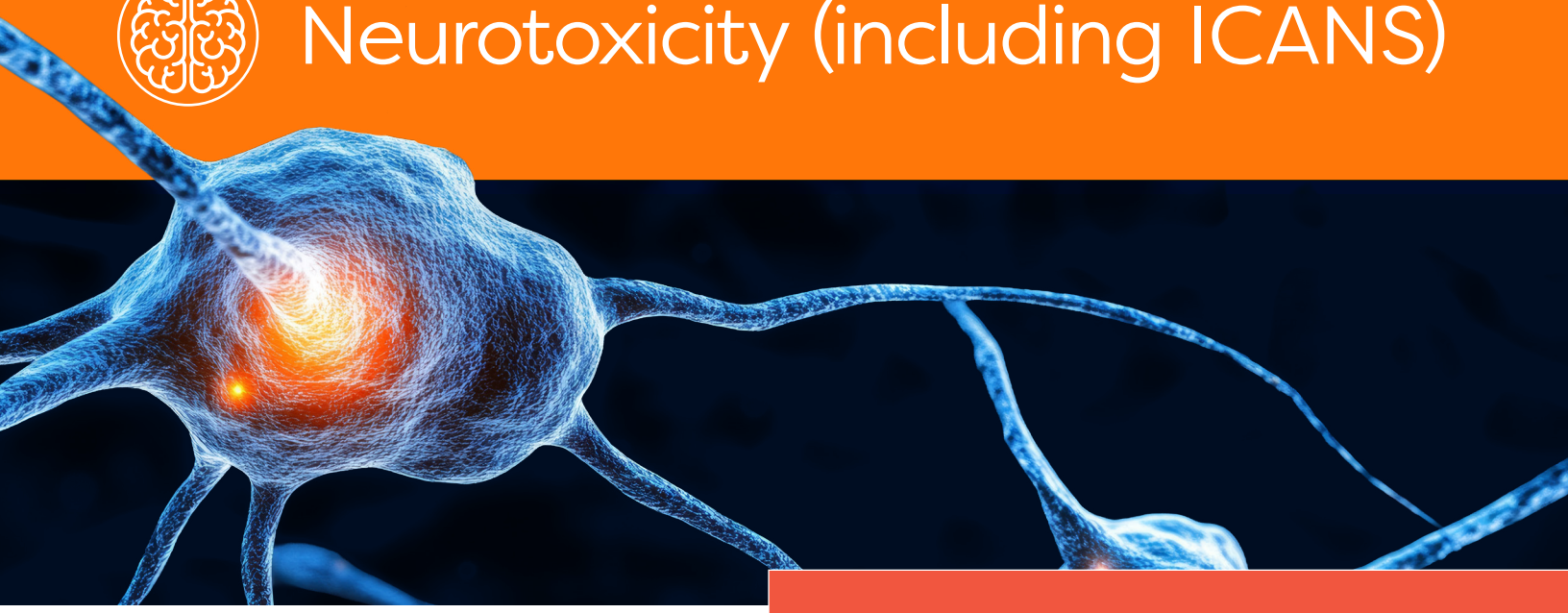
CRS is common, occurs primarily during Cycle 1, and is usually Grade 1 or 2; severe and life-threatening events can occur.

Why it matters:

CRS occurred in 57% of patients who received tarlatamab in the studies DeLLphi-300 and DeLLphi-301.

- Most CRS events occurred during **Cycle 1**, with the highest events occurring with the first dose of tarlatamab (73%), followed by the second dose (60%) and third or subsequent doses (15%).
  - **Grade ≥ 2 CRS events** occurred on the following days of Cycle 1
    - Day 1 (24%)
    - Day 8 (8%)
    - Day 15 (1%)
  - CRS events were primarily Grade 1 (39%) with Grade 3 and 4 events occurring in 1.7% and 0.2% of patients, respectively.
- The **median time to onset** of CRS following administration of the most recent dose of tarlatamab was 16 hours.
  - The median time to onset of Grade ≥ 2 CRS events following administration of the most recent dose of tarlatamab was 15 hours (range: 1 to 15).
- Care teams should monitor patients for signs/symptoms of CRS during treatment with tarlatamab.
  - **At first sign of CRS**, care teams should **immediately stop the tarlatamab infusion** and evaluate the patient for the need for hospitalization and supportive care measures.

Neurotoxicity (including ICANS)



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

Signs and symptoms:

- Confusion
- Dizziness
- Headache
- Memory issues
- Motor Deficits
- Shaking
- Trouble finding or words speaking

ICANS is frequently graded using the ASTCT consensus criteria.

Why it matters:

Neurologic toxicity, including ICANS, occurred in **65%** of patients in a pooled analysis of the two clinical trials, **7%** of which were reported as **Grade ≥ 3**.

- **Neurologic toxicity consistent with ICANS** was reported in **10%** of patients treated with tarlatamab, including **recurrent** events in **1.5%** of patients.
  - Grade ≥ 2 ICANS events occurred on the following days of Cycle 1: Day 1 (1.3%), Day 8 (1.3%), and Day 15 (0.4%); however, most patients experienced ICANS after receiving tarlatamab on Cycle 1 Day 8 (3.6%).
- The **median time to onset** of ICANS following administration of the **first** dose of tarlatamab was **16 days** (range: 1 to 862), though it can occur at any point several weeks following its administration.
- The **median time to resolution** of ICANS was **4 days.**
- Care teams should advise their patients to avoid driving or operating heavy machinery in the event of any neurologic symptoms, until these events resolve.
  - Tarlatamab **may need to be withheld or permanently discontinued based on the severity.**

THE BOTTOM LINE:

ICANS is less common than other neurologic toxicities but may be life-threatening or fatal. Onset may be delayed, and ICANS can occur concurrently with CRS, after CRS resolves, or in the absence of CRS.

Other Toxicities

Tarlatamab may cause other adverse reactions, such as **cytopenias, infections, hypersensitivity, hepatotoxicity, 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 tarlatamab-associated toxicities.

Infections. Tarlatamab may cause serious and fatal infections.

- **Serious infections**, including opportunistic infections, occurred in **43%** of patients with **Grade 3 or 4** infections reported in **14%** of patients.
  - The most frequently reported infections included were COVID-19, pneumonia, urinary tract infections, and upper respiratory tract infections.

THE BOTTOM LINE:

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

- **Based on severity**, tarlatamab **may need to be withheld or permanently discontinued**.

Cytopenias. Tarlatamab may cause cytopenias which include: thrombocytopenia, anemia, and neutropenia.

- Laboratory abnormalities included decreased hemoglobin in 56%, decreased platelets in 30%, and decreased neutrophils in 16% of patients.
  - These events included **Grade 3 or 4** neutropenia, anemia, and thrombocytopenia in **9%**, **4.7%**, and **2.2%**, respectively.
- **Febrile neutropenia** occurred in **1.5%**.

THE BOTTOM LINE:

Perform a **complete blood count** before every tarlatamab dose through Cycle 5 Day 15 and before the Day 1 dose of each cycle beginning with Cycle 6. Monitor more frequently as clinically indicated.

- Temporarily **withhold or permanently discontinue** tarlatamab based on the **severity of the cytopenia.**

Hepatotoxicity. Tarlatamab may cause hepatotoxicity, which can include elevated liver enzymes (alanine aminotransferase [ALT], aspartate aminotransferase [AST]) and total bilirubin.

- Elevated **AST and ALT** occurred in **43% and 39%** of patients, respectively; elevated **total bilirubin** occurred in **16%**.
  - **Grade 3 or 4 elevations in AST** occurred in **3.2%** of patients, and in ALT in **2.5%**.
  - **Grade 3 or 4 elevations in total bilirubin** occurred in **1.3%** of patients.

THE BOTTOM LINE:

Monitor **AST, ALT, and total bilirubin** before starting tarlatamab and as clinically indicated during treatment.

- **Treatment with tarlatamab** may need to be **temporarily held or permanently discontinued based on severity**.

Hypersensitivity. Tarlatamab may cause severe hypersensitivity reactions, including but not limited to rash or bronchospasm.

THE BOTTOM LINE:

Care teams should **monitor their patients for any signs or symptoms of hypersensitivity** during treatment with tarlatamab.

- Care teams may need to **consider a temporary hold or permanent discontinuation based on severity**.

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

- Advise **females of reproductive potential** to use effective contraception **during treatment** and **for 2 months** after the last dose.
- Verify pregnancy status before initiating tarlatamab.

Use in Specific Populations

- **Lactation:** Advise women not to breastfeed during treatment and for **2 months** after the last dose.
- **Pediatric Use:** The safety and efficacy of tarlatamab have not been established in the pediatric population.
- **Geriatric Use:** Of the total number of tarlatamab-treated patients in these studies, 51% were 65 years of age and older and 11% were 75 years of age or older. No overall differences in safety or effectiveness were observed between these patients and younger patients.

References:

1. Imdelltra. Prescribing information. Amgen Inc.; 2025. Accessed July 16, 2026. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761344s001lbl.pdf

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. Paz-Ares L, Goldman JW, Goto K, et al. Tarlatamab, a first-in-class DLL3-targeted bispecific T-cell engager, in recurrent small-cell lung cancer: an open-label, phase I study. *J Clin Oncol.* 2023;41(16):2893-2903. doi:10.1200/JCO.22.02823

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5. Mountzios G, Sun L, Cho BC, et al. Tarlatamab in Small-Cell Lung Cancer after Platinum-Based Chemotherapy. *N Engl J Med.* 2025;393(4):349-361. doi:10.1056/NEJMoa2502099