

Administration of Tarlatamab-dlle

ICD-10 Coordination & Maintenance Committee Meeting

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Catherine Chan, U.S. Medical Lead, SCLC, Amgen, Inc.



IMDELLTRA™ - A Significant Clinical Advancement for Treatment of Extensive Stage Small Cell Lung Cancer (ES-SCLC)

- **IMDELLTRA™ – the first and only delta-like ligand 3 (DLL3) targeting Bispecific T-cell Engager (BiTE®) therapy** for ES-SCLC with disease progression on or after platinum-based chemotherapy
- **FDA approval** on May 16, 2024
- **Amgen, Inc. intends to submit a New Technology Add-on Payment (NTAP) application** for FY 2026

Unmet Medical need for ES-SCLC Patients With Limited Treatment Options and Poor Prognoses





- **Small Cell Lung Cancer (SCLC)** is one of the most aggressive and devastating solid tumors
- **Approximately 30-35,000 new SCLC cases** diagnosed in the U.S. each year¹
 - 2/3 of patients with SCLC are diagnosed with extensive-stage disease (ES-SCLC)²
- **Current prognosis is poor**
 - Median survival is approximately 12 months following initial therapy
 - Combining all stages, SCLC has a 7 percent estimated relative survival rate at 5 years³
- **≥ 75% of patients with SCLC experience disease progression**⁴
 - Despite initial high response rates to platinum-based first-line chemotherapy, SCLC patients quickly relapse and require subsequent treatment options

1. American Cancer Society, "Cancer Facts & Figures 2024," (January 14, 2024). Available at: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2024/2024-cancer-facts-and-figures-acs.pdf>. Accessed June 7, 2024. 2. Sabari JK, et al. Nat Rev Clin Oncol. 2017;14:549-561. 3. American Cancer Society. Lung Cancer Survival Rates. 2023. Available at: <https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/survival-rates.html>. Accessed June 7, 2024. 4. Rudin CM, et al. Nat Rev Dis Primers. 2021;7:3.

IMDELLTRA™ (tarlatamab-dlle) Product Overview

- IMDELLTRA™ is a bispecific delta-like ligand 3 (DLL3)-directed CD3 T-cell engager that binds to DLL3 expressed on the surface of cells, including tumor cells, and CD3 expressed on the surface of T cells. IMDELLTRA™ causes T-cell activation, release of inflammatory cytokines, and lysis of DLL3-expressing cells.
- IMDELLTRA™ is indicated for the treatment of adult patients with ES-SCLC with disease progression on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
 - In October 2023, IMDELLTRA™ was granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration (FDA)
 - On December 13, 2023, IMDELLTRA™ was granted Priority Review by the FDA.
 - On May 16, 2024, IMDELLTRA™ received FDA accelerated approval.

Administer IMDELLTRA™ in an Appropriate Healthcare Setting as a 1-Hour IV Infusion Every 2 Weeks (Q2W) After an Initial Step-Up Dosing Schedule to Reduce the Incidence and Severity of Cytokine Release Syndrome (CRS)

		 CONCOMITANT MEDICATION Pre-IMDELLTRA™ Dose	 IMDELLTRA™ ADMINISTRATION 1-hour IV infusion	 CONCOMITANT MEDICATION Post-IMDELLTRA™ Dose	 PATIENT MONITORING
STEP-UP DOSING SCHEDULE CYCLE 1	Day 1	8 mg IV dexamethasone (or equivalent) Within 1-hour prior to dose Flush IV line*	1 mg Step-up dose	1 L normal saline IV over 4–5 hours immediately following infusion	Monitor for 22–24 hours from the start of the IMDELLTRA™ infusion in an appropriate healthcare setting
	Day 8		10 mg		
	Day 15		10 mg		Observe for 6–8 hours post infusion
	On Day 1 and Day 8 of Cycle 1, recommend patients remain within 1 hour of an appropriate healthcare setting for a total of 48 hours from start of the IMDELLTRA™ infusion, accompanied by a caregiver.				
CYCLE 2	Day 1		10 mg		Observe for 6–8 hours post infusion
	Day 15				
CYCLE 3-4	Day 1		10 mg		Observe for 3–4 hours post infusion
	Day 15				
CYCLE 5+	Day 1		10 mg		Observe for 2 hours post infusion
	Day 15				

All IMDELLTRA™ infusions and monitoring should take place in an appropriate healthcare setting. Please see the full Prescribing Information for additional information on Dosing and Administration.

- Prior to administration of IMDELLTRA™, evaluate complete blood count, liver enzymes, and bilirubin before each dose, and as clinically indicated
- After Days 1 and 8 of Cycle 1, extended monitoring in a healthcare setting is not required unless the patient experiences Grade ≥ 2 CRS, ICANS, or neurological toxicity during prior treatments.¹ See the IMDELLTRA™ full Prescribing Information for monitoring recommendations.

*The IV catheter for concomitant medications administration can be used to administer the IMDELLTRA™ infusion. To ensure patency, flush the IV catheter over 3–5 minutes using 0.9% Sodium Chloride for Injection.

CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; IV, intravenous.

IMDELLTRA™ (tarlatamab-dlle) prescribing information, Amgen.

IMDELLTRA™ Safety and Tolerability Profile from DeLLphi-300 and DeLLphi-301 Trials

Adverse reactions occurring in ≥ 15% of patients†

Adverse Reaction	IMDELLTRA™ (n=187)	
	Any Grade (%)	Grade 3 or 4 (%)
CRS‡	55.0	1.6
Fatigue§	51.0	10.0
Pyrexia	36.0	0.0
Dysgeusia	35.0	0.0
Decreased appetite	34.0	2.7
Musculoskeletal pain**	30.0	1.1
Constipation	30.0	0.5
Nausea	22.0	1.6
Dyspnea††	17.0	2.1
Cough	17.0	0.0

- IMDELLTRA™ has a BOXED WARNING in its product label regarding CRS and Neurological Toxicities, including Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS)
- The most common (> 20%) adverse reactions in patients were CRS, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, and constipation*
- Permanent discontinuation of IMDELLTRA™ due to adverse reactions occurred in 7% of patients*
- Dosage interruptions of IMDELLTRA™ due to adverse reactions occurred in 27% of patients. Adverse reactions that required dosage interruptions in ≥ 3% of patients included CRS (10%) and fatigue (3.2%)*

*Based on the pooled safety population of 187 patients enrolled in DeLLphi-300 and DeLLphi-301 who received IMDELLTRA™ 1 mg on Cycle 1 Day 1 followed by 10 mg on Days 8, 15, and then Q2W until disease progression or intolerable toxicity. †Graded using CTCAE Version 4.0 and Version 5.0. ‡Based on American Society for Transplantation and Cellular Therapy (ASTCT) 2019. §Includes fatigue and asthenia. **Includes myalgia, arthralgia, back pain, pain in extremity, neck pain, musculoskeletal chest pain, non-cardiac chest pain, and bone pain. ††Includes dyspnea and exertional dyspnea.

CRS, cytokine release syndrome; CTCAE, Common Terminology Criteria for Adverse Events; ES-SCLC, extensive-stage small cell lung cancer; Q2W, every 2 weeks.

IMDELLTRA™ (tarlatamab-dlle) prescribing information, Amgen.

Laboratory Abnormalities During Treatment With IMDELLTRA™ from DeLLphi-300 and DeLLphi-301 Trials

Laboratory abnormalities that worsened from baseline in ≥ 20% of patients†

Adverse Reaction	IMDELLTRA™ (n=187)	
	Any Grade (%)	Grade 3 or 4 (%)
Decreased lymphocytes	84.0	57.0
Decreased sodium	68.0	16.0
Decreased hemoglobin	58.0	5.0
Decreased potassium	50.0	5.0
Decreased white blood cells	44.0	3.8
Increased aspartate aminotransferase	44.0	3.2
Increased alanine aminotransferase	42.0	2.1
Decreased platelets	33.0	3.2
Decreased magnesium	33.0	1.6
Increased creatinine	29.0	0.5
Increased sodium	26.0	0.0
Increased alkaline phosphate	22.0	0.0
Decreased neutrophils‡	12.0	6.0

*Based on the pooled safety population of 187 patients enrolled in DeLLphi-300 and DeLLphi-301 who received IMDELLTRA™ 1 mg on Cycle 1 Day 1 followed by 10 mg on Days 8, 15, and then Q2W until disease progression or intolerable toxicity. †The denominator used to calculate the rate varied from 41 to 187 based on the number of patients with a baseline 534 value and at least 1 post-treatment value.

‡All Grade lab abnormalities occurring at a frequency of < 20% included decreased neutrophils.

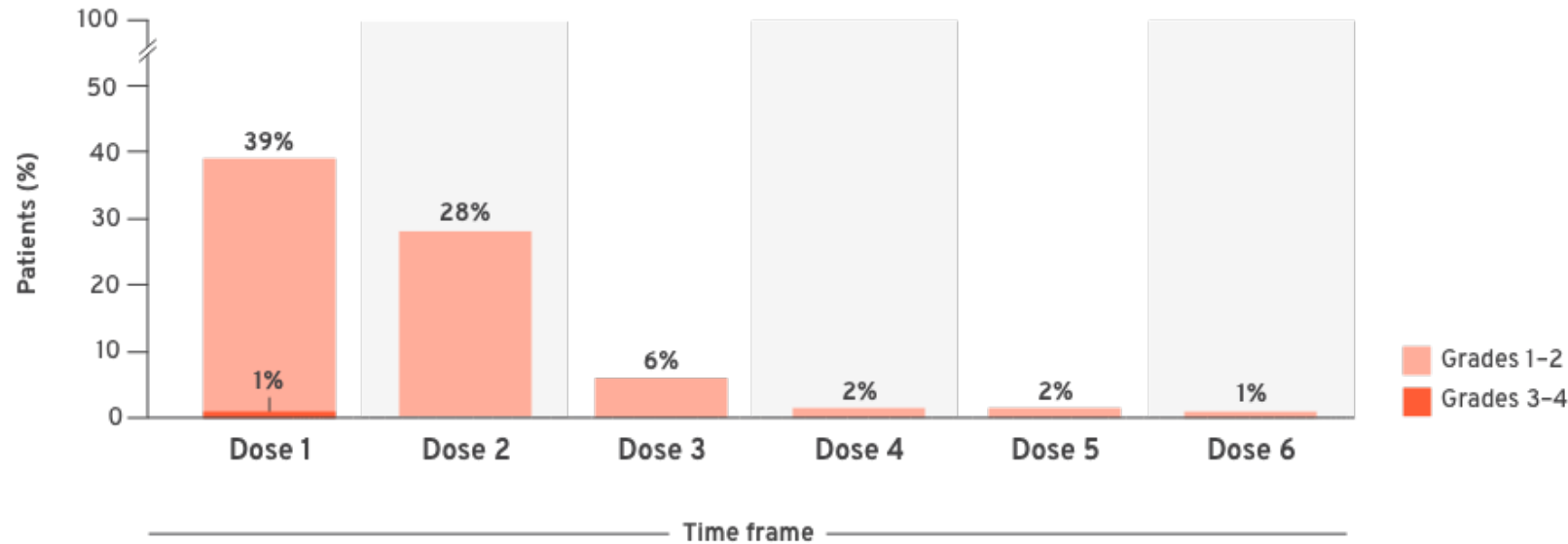
ES-SCLC, extensive-stage small cell lung cancer; Q2W, every 2 weeks.

IMDELLTRA™ (tarlatamab-dlle) prescribing information, Amgen.



Most CRS Events Were Grade 1 and Occurred Following the First Two Doses of IMDELLTRA™ 1,*

CRS events across treatment doses in the DeLLphi-301 study^{2,†}



- 34% (n=64/187), 19% (n=36/187), 1.1% (n=2/187), and 0.5% (n=1/187) of patients experienced Grade 1, 2, 3, and 4 CRS, respectively^{1,*}
- Recurrent CRS occurred in 24% of patients treated with IMDELLTRA™, including 18% Grade 1 and 6% Grade 2^{1,*}

In the DeLLphi-300 and DeLLphi-301 pooled safety population, most events (43%) of CRS occurred after the first dose, with 29% of patients experiencing any Grade CRS after the second dose and 9% following the third dose or later. Following the Day 1, Day 8, and Day 15 infusions, 16%, 4.3%, and 2.1% of patients experienced \geq Grade 2 CRS, respectively.^{1,*}

*Based on the pooled safety population of 187 patients enrolled in DeLLphi-300 and DeLLphi-301 who received IMDELLTRA™ 1 mg on Cycle 1 Day 1 followed by 10 mg on Days 8, 15, and then Q2W until disease progression or intolerable toxicity.¹ †Based on 133 patients who received IMDELLTRA™ 10 mg in the DeLLphi-301 study.²

CRS, cytokine release syndrome; Q2W, every 2 weeks.

1. IMDELLTRA™ (tarlatamab-dlle) prescribing information, Amgen. 2. Ahn M-J, et al. *N Engl J Med*. 2023. doi:10.1056/NEJMoa2307980.

Onset, Duration, and Management of CRS With IMDELLTRA™

13.5
hours

Median onset of all Grade CRS from most recent dose of IMDELLTRA™^{1,*}
(1–268 hours)

4
days

Median duration^{2,†}
(IQR: 2–6 days)

The median time to onset of Grade ≥ 2 CRS from the most recent dose was 14.6 hours (2–566 hours)^{1,*}

If CRS symptoms arise, manage according to the recommended dosage modifications and management strategies. Hospitalization is recommended for patients who experience Grade 2 or higher CRS.

^{*}Based on the pooled safety population of 187 patients enrolled in DeLLphi-300 and DeLLphi-301 who received IMDELLTRA™ 1 mg on Cycle 1 Day 1 followed by 10 mg on Days 8, 15, and then Q2W until disease progression or intolerable toxicity.¹

[†]Based on DeLLphi-301 safety data in patients who received IMDELLTRA™ 10 mg (n=133) and those who received IMDELLTRA™ 100 mg (n=87).²

CRS, cytokine release syndrome; IQR, interquartile range; Q2W, every 2 weeks.

1. IMDELLTRA™ (tarlatamab-dlle) prescribing information, Amgen. 2. Ahn M-J, et al. *N Engl J Med*. 2023;389:2063-2075.

Management of CRS for IMDELLTRA™ is Based on Severity

Dosage modifications and management strategies*

Grade	Dosage Modifications	Management Strategies
Grade 1	Withhold IMDELLTRA™ until event resolves, then resume IMDELLTRA™ at the next scheduled dose	Administer symptomatic treatment (e.g., acetaminophen) for fever
Grade 2	Withhold IMDELLTRA™ until event resolves, then resume IMDELLTRA™ at the next scheduled dose	<ul style="list-style-type: none"> • Recommend hospitalization for a minimum of 24 hours with cardiac telemetry and pulse oximetry • Administer symptomatic treatment (eg, acetaminophen) for fever • Administer supplemental oxygen and IV fluids when indicated • Consider dexamethasone[†] (or equivalent) 8 mg IV • Consider tocilizumab (or equivalent) <p>When resuming treatment at the next planned dose, monitor patients from the start of the IMDELLTRA™ infusion for 22 to 24 hours in an appropriate healthcare setting.</p>
Grade 3	<ul style="list-style-type: none"> • Withhold IMDELLTRA™ until the event resolves, then resume IMDELLTRA™ at the next scheduled dose • For recurrent Grade 3 events, permanently discontinue IMDELLTRA™ 	<p>In addition to Grade 2 treatment:</p> <ul style="list-style-type: none"> • Recommend intensive monitoring (e.g., ICU care) • Administer dexamethasone[†] (or equivalent) 8 mg IV every 8 hours up to 3 doses • Vasopressor support as needed • High-flow oxygen support as needed • Recommend tocilizumab (or equivalent) • Prior to the next dose, administer concomitant medications as recommended for Cycle 1 <p>When resuming treatment at the next planned dose, monitor patients from the start of the IMDELLTRA™ infusion for 22 to 24 hours in an appropriate healthcare setting.</p>
Grade 4	Permanently discontinue IMDELLTRA™	<ul style="list-style-type: none"> • ICU care • Per Grade 3 treatment • Recommend tocilizumab (or equivalent)

*Based on ASTCT Consensus Grading (2019). [†]Taper steroids per standard-of-care guidelines.

ASTCT, American Society for Transplantation and Cellular Therapy; CRS, cytokine release syndrome; ICU, intensive care unit; IV, intravenous.

IMDELLTRA™ (tarlatamab-dlle) prescribing information, Amgen.

Documentation of Administration

- IMDELLTRA™ administration should be documented consistent with the documentation associated with other intravenous injections.
- Documentation of administration within the medical record would most commonly be found in the Medication Administration Record (MAR), physician orders, and progress notes.

Summary

- Outcomes are poor for SCLC patients with disease progression after initial platinum-based chemotherapy
- Existing therapies have limitations including efficacy and safety
- Tarlatamab-dlle has a unique mechanism of action and is the first FDA-approved bispecific antibody therapy for SCLC