Tarlatamab-dlle

An HCP Tool From AIM with Immunotherapy

Tarlatamab-dlle (Imdelltra) is a Bispecific T-cell Engager (BiTE®) immunotherapy targeting CD3 and a first-in-class, DLL3-targeting agent. It is indicated for the treatment of adult patients with extensive-stage small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.

The drug binds to both the SCLC cell (using DLL3) and the immune T cell (using CD3) to bring these cells together, so that the T cell recognizes and kills the cancer cell. DLL3 is the abbreviation for delta-like canonical Notch ligand 3, which is expressed in ~85-96% of SCLC cells and minimally expressed among normal tissues. Theories implicate a role for DLL3 in the promotion of growth, migration, and invasion of SCLC cells. Normally, this gene codes for a protein that regulates the Notch pathway in embryonic development. Sometimes cancer cells reactivate embryonic programs that were silenced as a part of normal human development after successful completion.

The indication for tarlatamab-dlle was approved under accelerated approval based on overall response rate and duration of response. The drug application was granted priority review, breakthrough designation, and orphan drug designation. The approval was based on results in the DeLLphi-301 clinical trial. Under accelerated approval, a drug's manufacturer must conduct additional trials to confirm that tarlatamab-dlle provides a clinical benefit.

In the clinical trial, the treated group was predicted to have a 15% response rate before the study began reflecting historical norms, but the group actually achieved 40% response rate after measuring tumor shrinkage. The major efficacy outcome measures from the DeLLphi-301 [NCT05060016] were overall response rate per RECIST 1.1 and duration of response, as assessed by blinded independent central review.

- Overall response rate was 40% and median duration of response was 9.7 months
- In patients with platinum-resistant SCLC, the overall response rate was 52%
- In patients with platinum-sensitive SCLC, the overall response rate was 31%
- Current treatments provided 6-12 months survival versus 14.3 months with 10 mg tarlatamab-dlle

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DRUG DOSAGE AND ADMINISTRATION

Tarlatamab-dlle should only be administered by a hospital or clinical facility with appropriate medical support to manage severe reactions such as cytokine release syndrome and neurologic toxicity, including immune effector cell–associated neurotoxicity syndrome.

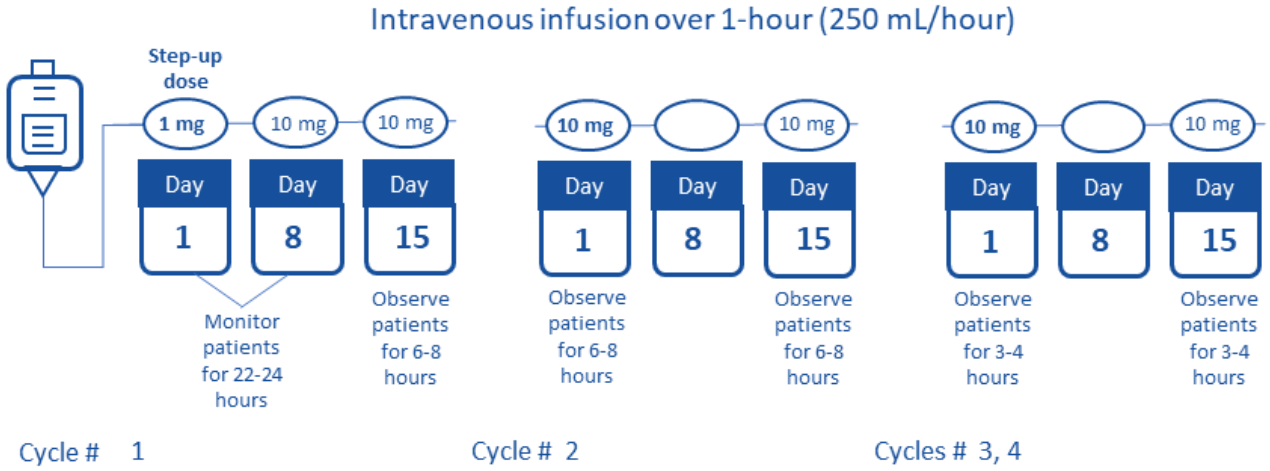
Tarlatamab-dlle is administered on days 1 and 8 in a hospital or inpatient setting. Patients should be monitored for 22-24 hours on the first cycle. The time is reduced with subsequent cycles (e.g. 6-8 hours, 3-4 hours, 2 hours, etc.), but patients are still monitored. Patients are also recommended to remain within 1-hour from their health care setting for 48 hours after the start of infusion, accompanied by a caregiver.

For Cycle 1, administer recommended concomitant medications before and after infusion to reduce the risk of cytokine release syndrome reactions. Additionally, tarlatamab-dlle is administered according to step-up dosing to reduce this risk.

The most common adverse reactions (≥20%) were cytokine release syndrome, fatigue, pyrexia, dysgeusia, decreased appetite, musculoskeletal pain, constipation, anemia and nausea. Grade 3 or 4 laboratory abnormalities (≥2%) include decreased lymphocytes, decreased sodium, increased uric acid, decreased total neutrophils, decreased hemoglobin, increased activated partial thromboplastin time, decreased potassium, increased aspartate aminotransferase, decreased white blood cells, decreased platelets, and increased alanine aminotransferase.

Tarlatamab-dlle for adult patients with extensive stage small cell lung cancer with disease progression on or after platinum-based chemotherapy:

Recommended dosing and administration



Note: For cycle 1, dexamethasone (8 mg) intravenously or an equivalent should be administered on treatment days 1 and 8 within 1-hour prior to administration with tarlatamab-dlle. On days 1, 8, and 15, 1 liter of normal saline should be administered intravenously over 4-5 hours immediately after completion of the drug infusion.

- Tarlatamab-dlle is given as a 1-hour IV infusion.
- Patients must be well hydrated before administration of tarlatamab-dlle.
- The intravenous catheter for concomitant medications can be used to administer the tarlatamab-dlle infusion
- For cycles 5 and subsequent infusions, patients should be observed for 2 hours post infusion.
- Prior to tarlatamab-dlle administration, evaluate complete blood count, liver enzymes and bilirubin before each dose.

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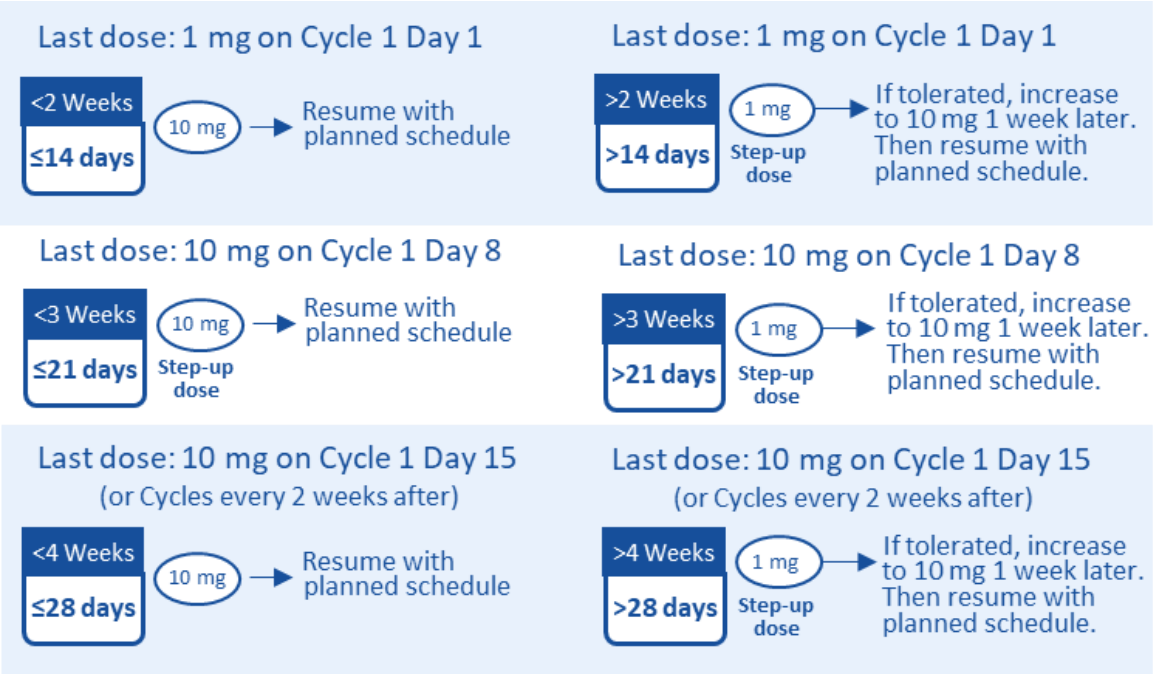
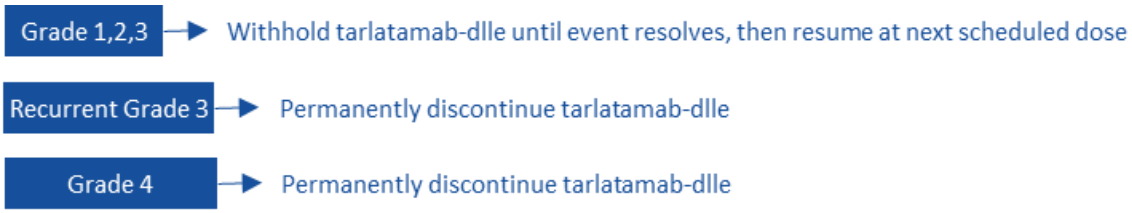
Restart dosing and administration



Note: If a dose of tarlatamab-dlle is delayed, restart the drug based on the dosing schedule below. Concomitant medication remains the same.

- Dose reductions for tarlaramab-dlle are not recommended. The drug is either withheld until the event resolves or permanently discontinued.
- Suspected cytokine release syndrome requires monitoring patients who experience Grade 2 or higher with continuous cardiac telemetry and pulse oximetry.
- For severe or life-threatening cytokine release syndrome, administer tocilizumab or the equivalent, along with intensive monitoring in the ICU for supportive therapy. Lab testing and monitoring should occur for disseminated intravascular coagulation, hematology parameters, and function of the lungs, liver, heart and kidneys.

Dosage modification for cytokines release syndrome



- For Grade 2 and 3, when treatment resumes, patients should be monitored for 22-24 hours in a health care facility.
- ICU care is recommended for Grade 3 and 4, in addition to dexamethasone, vasopressor and oxygen support.

For ICANS (immune effector cell–associated neurotoxicity syndrome), at the first sign of neurologic toxicity (Grade 1), the drug is withheld until it resolves.

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SIDE EFFECTS AND MANAGEMENT

There are black boxed warnings for cytokine release syndrome and neurologic toxicity associated with tarlatamab-dlle. Both of these adverse effects are commonly seen with immunotherapies that activate T cells to kill cancer cells, including other BiTEs and CAR T-cell therapies.

A low percentage of patients (7%) permanently discontinued tarlatamab-dlle due to an adverse reaction. Approximately 13% of patients in the clinical trial on 10 mg of tarlatamab-dlle had to temporarily pause treatment or have their dose reduced, or both, due to adverse effects. Dosing interruptions due to an adverse reaction occurred in 27% of patients.

Serious adverse reactions

Serious adverse reactions occurred in 58% of patients receiving tarlatamab-dlle. The most common adverse reactions (≥20%) of tarlatamab-dlle were cytokine release syndrome (55%), fatigue (51%), pyrexia (36%), dysgeusia (36%), decreased appetite (34%), musculoskeletal pain (30%), constipation (30%), anemia (27%), and nausea (22%). The most common Grade 3 or 4 laboratory abnormalities (≥5%) were decreased lymphocytes, decreased sodium, increased uric acid, decreased total neutrophils, decreased hemoglobin, increased activated partial thromboplastin time, and decreased potassium.

Cytokine release syndrome

Cytokine-release syndrome primarily occurred during treatment cycle 1 or 2 in clinical trials. Most of the events in patients were grade 1 or 2 in severity. Grade 3 cytokine-release syndrome occurred in 1% of the patients in the 10-mg group. Withhold tarlatamab-dlle until cytokine-release syndrome resolves or permanently discontinue the drug based on severity.

ICANS (immune effector cell–associated neurotoxicity syndrome)

Another potentially serious side effect of tarlatamab-dlle is neurologic toxicity including ICANS (immune effector cell–associated neurotoxicity syndrome), which includes a host of neurological effects such as severe confusion, attention problems, tremor, and muscle weakness. For ICANS, at the first sign of neurologic toxicity (Grade 1), the drug is withheld until it resolves. One patient in the clinical trial on 10 mg of tarlatamab-dlle had to stop treatment because of ICANS. If the drug is withheld without resolution, permanently discontinue the drug based on severity.

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Recommended treatment interruptions and management

The table below shows management strategies for other side effects associated with tarlatamab-dlle.

Management of other notable side effects of tarlatamab-dlle

Adverse event	Common management guidance
Cytopenias	Grade 3 or 4 Neutropenia • Withhold tarlatamab-dlle until recovery to ≤Grade 2; consider G-CSF • Permanently discontinue if recovery to ≤Grade 2 does not occur within 3 weeks Febrile Neutropenia • Withhold tarlatamab-dlle until recovery to ≤Grade 2 and fever resolves Hemoglobin <8 g/dL • Withhold tarlatamab-dlle until hemoglobin is ≥8 g/dL Grade 3 or 4 Decreased Platelet Count • Withhold tarlatamab-dlle until count is ≤Grade 2 and no evidence of bleeding • Permanently discontinue if recovery to ≤Grade 2 does not occur within 3 weeks Recurrent Grade 4 Neutropenia or Recurrent Grade 4 Decreased Platelet Count • Permanently discontinue tarlatamab-dlle
Infections	All Grades • Withhold tarlatamab-dlle in the step-up phase until infection resolves Grade 3 (increased ALT or AST or bilirubin) • Withhold tarlatamab-dlle during the treatment phase until infection improves to ≤Grade 1 Grade 4 • Permanently discontinue tarlatamab-dlle
Hepatotoxicity	Grade 3 (increased ALT or AST or bilirubin) • Withhold tarlatamab-dlle until ≤Grade 1 Grade 4 • Permanently discontinue tarlatamab-dlle
Other adverse reactions	The general recommendation for remaining side effects: Grade 3 • Withhold tarlatamab-dlle until ≤Grade 1 or baseline • Consider discontinuation if the adverse reaction does not resolve within 28 days Grade 4 • Consider permanent discontinuation of tarlatamab-dlle

- Severity is based on National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE) Version 5.0.
- Educate patients and caregivers about side effects and the importance of reporting symptoms as soon as possible. Remind patients about the importance of staying on schedule.

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QUESTIONS & ANSWERS

Q. What is tarlatamab-dlle?

A. A prescription medicine used to treat adults with extensive stage small cell lung cancer, which has spread throughout the lung or to other parts of the body, and who have received treatment with chemotherapy that contains platinum, and it did not work or is no longer working. Its safety and efficacy is not known in children.

Q. What should I tell my clinician before receiving tarlatamab-dlle?

A. Tell them if you have an infection, are pregnant or plan to become pregnant, are breast feeding or plan to breastfeed. Tarlatamab-dlle may harm and unborn baby. Do not breastfeed while on tarlatamab-dlle and for 2 months after the last dose of the drug.

Q. What should be avoided while receiving tarlatamab-dlle?

A. Patients should not drive, operate heavy or potentially dangerous machinery or do other dangerous activities, including work-related activities, during treatment. Dizziness and other signs like confusion could be symptoms of neurological problems.

Q. How is tarlatamab-dlle received?

A. Tarlatamab-dlle is an intravenous infusion administered through a needle place in a vein that is given over a 1-hour period. The treatment schedule is divided into cycles that are 28 days in length, with the treatment given on days 1, 8, or 15, depending on the cycle. The total number of cycles received by each patient will be determined by their health care provider.

Q. What are possible side effects of tarlatamab-dlle?

A. Decreased blood cell counts are common with treatment. Tarlatamab-dlle may cause serious infections that can lead to death. Tarlatamab-dlle may case increased liver enzymes and bilirubin in the blood. Allergic reactions may be severe. The most common side effects are muscle or bone pain, a bad or metallic taste in the mouth, constipation, decreased appetite, fever, nausea, and tiredness.

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PATIENT RESOURCES

ADDITIONAL INFORMATION RESOURCES

American Cancer Society
Patient programs, services, 24/7 hotline, etc
https://www.cancer.org/

National Cancer Institute
Information about cancer types, treatment, side effects, find a clinical trial, etc
https://www.cancer.gov/

FINANCIAL ASSISTANCE

Cancer Financial Aid Coalition
Facilitates communication, educates and advocates for patients.
www.cancerfac.org

Centers for Medicare and Medicaid Services (CMS)
Apply to determine if you are eligible for government assistance.
www.cms.gov or www.medicare.gov
800-633-4227

Lazarex Foundation
Provides assistance with travel costs for clinical trial participation. Ask your social work counselor for a referral if you have been consented to a clinical trial for melanoma.
www.lazarex.org

Needymeds
Database to search for free or low-cost medications, help with medical transportation and other resources.
www.needymeds.org

Patient Advocate Foundation
Provides assistance with mediation, financial stability, and other assistance. Funds subject to availability. Patient must meet their eligibility for financial assistance.
www.patientadvocate.org
800-532-5274

The Sam Fund for Young Adult Survivors of Cancer
The Sam Fund for Young Adult Survivors of Cancer assists ages 21-39 with their transition into post-treatment life. This program distributes grants and scholarships in an effort to enable survivors to pursue goals.
www.thesamfund.org
info@thesamfund.org

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PRESCRIPTION ASSISTANCE

CancerCare Co-Payment Assistance Foundation
Helps with the cost of medication. Availability of funds for patients with specific cancers is subject to availability.
www.cancercarecopay.org
1-866-552-6729

Medicine Assistance Tool
Database to search for patient assistance resources offered by pharmaceutical companies.
www.medicineassistancetool.org/

Patient Advocate Foundation Co-Pay Relief
Provides direct financial support to patients who medically qualify. Funds subject to availability.
https://copays.org
1-866-512-3861

Good Days
Provides assistance with insurance co-pays, and prescription medications. Funds subject to availability.
www.mygooddays.org

Health Well Foundation
For patients who cannot afford insurance premiums, co-payments, co-insurance, or other out-of-pocket health care costs. Funds for patients subject to availability. Patient must also meet eligibility for financial assistance.
www.healthwellfoundation.org or grants@healthwellfoundation.org
1-800-675-8416

The Assistance Fund, Inc
Provides prescription copay and financial assistance, including health insurance premiums. Funds subject to availability.
www.theassistancefund.org
https://tafcares.org
1-855-845-3663

PAN Foundation
Provides financial assistance to cover out-of-pocket treatment costs. Funds subject to availability.
www.panfoundation.org
1-866-316-PANF (7263)

Patient Assistance Program
Comprehensive database of patient assistance programs offering free medications.
www.rxassist.org
info@rxassist.org

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HOUSING

American Cancer Society – Hope Lodge
Provides free housing during treatment appointments. Requires a referral from your social worker.
www.cancer.org/
1-800-227-6333

American Cancer Society – Extended Stay America
Partnership to offer discounted rooms for patients who have to be away from home for cancer treatment.
https://www.cancer.org/about-us/our-partners/extended-stay-america.html
1-800-227-2345

Healthcare Hospitality Network
Connects patients and their caregivers looking for lodging near their healthcare provider
https://members.hhnetwork.org/locate-a-house
1-800-318-8861

Joe's House
Helping patients with cancer find lodging throughout the U.S.
https://www.joeshouse.org/lodging?state=0
1-877-563-7468

National Council of State Housing Agencies
Emergency rental assistance programs available by state. Federal grants still available in some areas.
https://www.ncsha.org/emergency-housing-assistance/

TRANSPORTATION (AIR AND GROUND)

Air Charity Network
Provides access for people in need who are seeking free air transportation to specialized health care facilities
http://aircharitynetwork.org/
1-877-621-7177

Corporate Angel Network
Nonprofit organization that helps cancer patients by arranging free travel on corporate aircraft
https://www.corpangelnetwork.org/
info@corpangelnetwork.org
1-914-328-1313

Medicaid
Ground transportation only. Sets up rides and provides mileage reimbursement for Medicaid patients only.
1-877-633-8747

Mercy Medical Angels
Provides free medical transportation (flights, gas cards, bus and train tickets) for patients with financial needs who need to travel more than 50 miles. Patients must meet their eligibility for financial assistance.
www.mercymedical.org/

Pilots for Patients
Provides free flights to people in need of medical treatment. Patient must be medically stable to fly and be ambulatory. Ask your social worker about a referral.
www.pilotsforpatients.org
318-322-5112

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ADDITIONAL RESOURCES

Ahn M, Cho BC, Felip E et al. Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. *N Engl J Med*. 2023;389(22):2063-2075. doi: 10.1056/NEJMoa2307980.

Paz-Ares L, Champiat S, Lai WV 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 Clinic Oncol*. 2023;41(16). doi.org/10.1200/JCO.22.0282.

NCBI Gene Entry for DLL3 - DLL3 delta like canonical Notch ligand 3 [Homo sapiens (human)]. https://www.ncbi.nlm.nih.gov/gene/10683. Accessed June 14, 2024. Updated March 5, 2024.

IMDELLTRA (tarlatamab-dlle) [prescribing information]. Thousand Oaks, CA 91320-1799, USA: Amgen Inc.; 2024. Available at: https://www.pi.amgen.com/-/media/Project/Amgen/Repository/pi-amgen-com/Imdelltra/imdelltra_fpi.pdf . Revised May 2024. Accessed June 24, 2024.

National Cancer Institute of the National Institutes of Health. Tarlatamab Shows Promise for Some People with Small Cell Lung Cancer. https://www.cancer.gov/news-events/cancer-currents-blog/2023/tarlatamab-previously-treated-sclc. Accessed June 17, 2024. Updated May 16, 2024.

U.S. FDA release. FDA grants accelerated approval to tarlatamab-dlle for extensive stage small cell lung cancer. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-tarlatamab-dlle-extensive-stage-small-cell-lung-cancer. Accessed June 14, 2024. Updated May 16, 2024.

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