Health Technology Briefing
May 2025

Tarlatamab for treating relapsed small cell lung cancer after platinum-based chemotherapy

Company/Developer	Amgen Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 37106	NICE ID: Not Available	UKPS ID: 675113

Licensing and Market Availability Plans

Currently in phase III/II clinical trials.

Summary

Tarlatamab is in clinical development for the treatment of relapsed small cell lung cancer (SCLC) after platinum-based first-line chemotherapy. SCLC is a disease in which malignant (cancer) cells form in the tissues of the lung. SCLC is a particularly aggressive form of the disease and tends to spread faster than non-SCLC, with more than two third of people with SCLC having metastatic disease at the time of diagnosis. Metastasis is when cancer spreads from its original location to other areas of the body. Despite being both a chemo- and radiation-sensitive malignancy, SCLC recurrence occurs in most cases and negatively impacts patients' prognosis. There is an unmet need for second line treatment options for relapsed SCLC.

Tarlatamab is a type of protein that binds both to a specific target on SCLC cancer cells called delta-like ligand 3 (DLL3) and to a type of immune cell called T-cells. By binding to both the cancer cells and the T-cells, the T-cells become activated and therefore able to kill cancer cells. It is administered as an intravenous infusion into the blood stream. If licensed for second-line treatment, tarlatamab will offer an additional treatment option for relapsed SCLC.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Proposed Indication

Treatment of relapsed small cell lung cancer (SCLC) with after platinum-based first-line chemotherapy.[1]

Technology

Description

Tarlatamab (AMG-757) is a bispecific delta-like ligand 3 (DLL3)-directed CD3 T-cell engager that binds to DLL3 expressed on the surface of tumour cells and CD3 expressed on the surface of T cells. The bispecific binding of tarlatamab to T cells and DLL3-positive tumour cells triggers T-cell activation, production of inflammatory cytokines, release of cytotoxic proteins, which results in redirected lysis of tumour cells.[2]

Tarlatamab is in development for relapsed SCLC after platinum-based first-line chemotherapy. In the ongoing phase III and II trials (NCT05740566, NCT06745323), tarlatamab is administered as an intravenous (IV) infusion during the treatment period.[1,3]

Key Innovation

SCLC is an aggressive malignancy for which very few patients achieve long term disease control; response to most treatments is transient and second line treatment options are limited.[4] Relapsed SCLC is said to be incurable and available treatments are provided with palliative intent.[5] DLL3 is a notch ligand aberrantly expressed on the surface of up to 85% of SCLC cells and minimally expressed in normal tissues, making it an attractive therapeutic target. Tarlatamab is a bispecific T cell engager (BiTE) molecule designed to bind DLL3 on target cancer cells and CD3 on T cells, thereby driving T cell-dependent killing of tumour cells.[4] This addresses a key driver of disease in relapsed SCLC.

If licensed, tarlatamab will offer an additional treatment option for relapsed SCLC.

Regulatory & Development Status

Tarlatamab currently has Marketing Authorisation in the UK for the treatment of adult patients with extensive-stage SCLC with disease progression on or after at least two prior lines of therapy including platinum-based chemotherapy.[2]

Tarlatamab is in phase III/II clinical development for:[6]

- extrapulmonary small cell carcinoma
- neuroendocrine carcinoma
- DLL3 expressing tumours
- gliomas

Tarlatamab has an orphan drug designation in the UK and EU in 2024 for SCLC.[7,8]

Patient Group

Disease Area and Clinical Need

There are two main types of primary lung cancer: non-SCLC and SCLC. SCLC gets its name from how the cancer looks under the microscope.[9] SCLCs are also classed as neuroendocrine tumours. Neuroendocrine tumours are rare tumours that develop in cells of the neuroendocrine system. In SCLC, the tumour starts in the neuroendocrine cells of the lung.[10] SCLC is a particularly aggressive form of lung cancer and tends

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

to spread faster than non-SCLC, with most people with SCLC having metastatic disease at the time of diagnosis.[11] Symptoms of SCLC include chest pain, lingering cough, trouble breathing, face and neck swelling, severe tiredness, loss of appetite, weight loss, etc.[12] Factors that increase the risk of getting lung cancer include smoking, older age, exposure to second-hand smoke, air pollution, radiation, a family history of lung cancer, testing positive for human immune-deficiency virus (HIV), etc.[12]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2017-2019). In females in the UK, lung cancer is the 2nd most common cancer, with around 23,800 new cases every year (2017-2019). In males in the UK, lung cancer is the 2nd most common cancer, with around 25,400 new cases every year (2017-2019). Incidence rates for lung cancer in the UK are highest in people aged 80 to 84 (2017-2019).[13] SCLC makes up about 1 in 7 lung cancers (about 15%).[9] In England, 2023-24, there were 125,652 finished consultant episodes (FCE) and 106,130 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34) which resulted in 220,815 FCE bed days and 81,951 day cases.[14] There are around 34,800 lung cancer deaths in the UK every year, averaging at 95 every day (2017-2019). Lung cancer is the most common cause of cancer death in the UK, accounting for 21% of all cancer deaths (2017-2019).[13] For patients in England diagnosed with lung cancer between 2016 and 2020, the 1-year and 5-year survival rates were 45.4% and 21% respectively.[15]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the following:

- For people with relapsed SCLC in whom chemotherapy is suitable, NICE recommends treatment with an anthracycline-containing regimen or further treatment with a platinum-based regimen to a maximum of 6 cycles.[16]
- Topotecan for the treatment of relapsed SCLC when re-treatment with the first-line regimen is not considered appropriate and the combination of cyclophosphamide, doxorubicin and vincristine is contraindicated.[17]

Clinical Trial Information

Trial	**DeLLphi-304,** NCT05740566; A Randomized, Open-label, Phase 3 Study of Tarlatamab Compared With Standard of Care in Subjects With Relapsed Small Cell Lung Cancer After Platinum-based First-line Chemotherapy **Phase III** – Active, not recruiting **Locations:** Fifteen EU countries, UK, USA, Canada and other countries **Primary completion date:** July 2027
Trial Design	Randomised, parallel assignment, open label
Population	N=509 (actual); subjects with relapsed SCLC after platinum-based first-line chemotherapy; 18 years and older.
Intervention(s)	Tarlatamab (IV infusion)
Comparator(s)	Local standard of care (Lurbinectedin, Topotecan, Amrubicin)
Outcome(s)	Primary outcome measure: • Overall survival [time frame: up to approximately 4 years] See trial record for full list of other outcomes.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

Results (efficacy)	-
Results (safety)	-

Trial	**DeLLphi-309,** NCT06745323; A Phase 2, Open-label, Randomized, Multicenter Study of Tarlatamab Dosing Regimens in Subjects With Small Cell Lung Cancer **Phase II** – Recruiting **Location:** USA and Switzerland **Primary completion date:** November 2026
Trial Design	Randomised, parallel assignment, open label
Population	N=240 (estimated); subjects with progressed or relapsed SCLC following 1 platinum-based regimen; aged 18 to 99 years old.
Intervention(s)	Tarlatamab (IV infusion): • Treatment arm A: dose 1 • Treatment arm B: dose 2 • Treatment arm C: dose 3
Comparator(s)	No comparator
Outcome(s)	Primary outcome measures: • Proportion of participants with confirmed objective response to tarlatamab [time frame: approximately 52 months] • Proportion of participants with complete response to tarlatamab [time frame: approximately 52 months] • Proportion of participants with partial response to tarlatamab [time frame: approximately 52 months] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of tarlatamab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Lurbinectedin for treating advanced small-cell lung cancer on or after platinum-based chemotherapy [ID3872]. Expected publication date: to be confirmed.
- NICE technology appraisal in development. Tarlatamab for previously treated advanced small-cell lung cancer [ID6364]. Expected publication date: 06 August 2025.
- NICE technology appraisal guidance. Topotecan for the treatment of relapsed small-cell lung cancer [TA184]. November 2009.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2024.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

- NICE quality standards. Lung cancer in adults (QS17). December 2019.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a

Other Guidance

- National Comprehensive Cancer Network (NCCN). Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. 2021.[18]
- European Society for Medical Oncology (ESMO). Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2021.[19]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2020.[20]

Additional Information

References

1 ClinicalTrials.gov. *Study Comparing Tarlatamab With Standard of Care Chemotherapy in Relapsed Small Cell Lung Cancer (DeLLphi-304). Trial ID: NCT05740566*. 2023. Status: Active, not recruiting. Available from: https://clinicaltrials.gov/study/NCT05740566#study-plan [Accessed 17 March 2025].

2 Electronic Medicines Compendium (EMC). *IMDYLLTRA 1 mg Powder for solution for infusion*. 2025. Available from: https://www.medicines.org.uk/emc/product/100374/smpc [Accessed 17 March 2023].

3 ClinicalTrials.gov. *A Phase 2, Open-label, Randomized, Multicenter Study of Tarlatamab Dosing Regimens in Subjects With SCLC (DeLLphi-309). Trial ID: NCT06745323*. 2024. Status: Not yet recruiting. Available from: https://clinicaltrials.gov/study/NCT06745323 [Accessed 17 March 2023].

4 Paz-Ares LG, Felip E, Ahn M-J, Blackhall FH, Borghaei H, Cho BC, et al. Randomized phase 3 study of tarlatamab, a DLL3-targeting bispecific T-cell engager (BiTE),compared to standard of care in patients with relapsed small cell lung cancer (DeLLphi-304). *Journal of Clinical Oncology*. 2023;41(16_suppl):TPS8611-TPS. Available from: https://doi.org/10.1200/JCO.2023.41.16_suppl.TPS8611.

5 Qin A, Kalemkerian GP. Treatment Options for Relapsed Small-Cell Lung Cancer: What Progress Have We Made? *Journal of Oncology Practice*. 2018;14(6):369-70. Available from: https://doi.org/10.1200/jop.18.00278.

6 ClinicalTrials.gov. *Search Results: Tarlatamab | Phase: 2, 3 | Sponsor/Collaborator: Amgen*. 2025. Available from: https://clinicaltrials.gov/search?intr=Tarlatamab&spons=Amgen&aggFilters=phase:2%203 [Accessed 17 March 2025].

7 European Medicines Agency (EMA). *EU/3/23/2876 - orphan designation for treatment of small cell lung cancer*. 2024. Available from: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu-3-23-2876#key-facts [Accessed 17 March 2025].

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.

8 Medicines & Healthcare products Regulatory Agency. *Decision: Orphan register*. 2025. Available from: https://www.gov.uk/government/publications/orphan-registered-medicinal-products/orphan-register [Accessed 06 May 2025].
9 Macmillan Cancer Support. *Small cell lung cancer (SCLC)*. 2020. Available from: https://www.macmillan.org.uk/cancer-information-and-support/lung-cancer/small-cell-lung-cancer [Accessed 17 March 2025].
10 Cancer Research UK. *Types of lung cancer*. 2022. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/stages-types-grades/types [Accessed 10 April 2025].
11 American Cancer Society. *What Is Lung Cancer?* 2024. Available from: https://www.cancer.org/cancer/types/lung-cancer/about/what-is.html [Accessed 17 March 2025].
12 National Cancer Institute. *Small Cell Lung Cancer Treatment (PDQ®)–Patient Version*. 2025. Available from: https://www.cancer.gov/types/lung/patient/small-cell-lung-treatment-pdq [Accessed 17 March 2025].
13 Cancer Research UK. *Lung cancer statistics*. 2025. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/lung-cancer#heading-Zero [Accessed 21 March 2025].
14 NHS Digital. *Hospital Admitted Patient Care Activity, 2023-24: Diagnosis*. 2024. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2023-24 [Accessed 21 March 2025].
15 Cancer Research UK. *One-Year and Five-Year Survival for Common Cancers*. 2023. Available from: https://crukcancerintelligence.shinyapps.io/CancerStatsDataHub/ [Accessed 21 March 2025].
16 National Institute for Health and Care Excellence. *Lung cancer: diagnosis and management* (*NG122)*. Available from: https://www.nice.org.uk/guidance/ng122/chapter/Treatment#second-line-treatment-for-small-cell-lung-cancer-that-has-relapsed-after-first-line-treatment [Accessed 22 May 2025].
17 National Institute for Health and Care Excellence. *Topotecan for the treatment of relapsed small-cell lung cancer* (*TA184)*. Available from: https://www.nice.org.uk/guidance/ta184 [Accessed 21 March 2025].
18 Ganti AKP, Loo BW, Bassetti M, Blakely C, Chiang A, D'Amico TA, et al. Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*. 2021;19(12):1441-64. Available from: https://doi.org/10.6004/jnccn.2021.0058.
19 Dingemans AMC, Früh M, Ardizzoni A, Besse B, Faivre-Finn C, Hendriks LE, et al. Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2021;32(7):839-53. Available from: https://doi.org/10.1016/j.annonc.2021.03.207.
20 NHS Northern Cancer Alliance. *Northern Cancer Alliance Lung Cancer Clinical Guidelines*. Last Update Date: 2020. Available from: https://www.northerncanceralliance.nhs.uk/wp-content/uploads/2019/05/Lung-Clinical-Guidelines-v13.2.pdf [Accessed 17 March 2025].

NB: This briefing presents independent research funded by the National Institute for Health and Care Research (NIHR). The views expressed are those of the author and not necessarily those of the NHS, the NIHR or the Department of Health.

Copyright © National Institute for Health and Care Research Innovation Observatory, The University of Newcastle upon Tyne.