Health Technology Briefing
August 2023

Tarlatamab for relapsed/refractory small-cell lung cancer

Company/Developer	Amgen Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 34208	NICE TSID: N/A	UKPS ID: N/A

Licensing and Market Availability Plans

Currently in Phase II/III clinical trials.

Summary

Tarlatamab is in clinical development for the treatment of adults with refractory (unresponsive to treatment) or relapsed small cell lung cancer (SCLC) who have progressed or recurred following one platinum-based (chemotherapy) regimen and at least a prior line of therapy. 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 nearly 70% of people with SCLC having metastatic disease at the time of diagnosis. Despite being both a chemo- and radiation-sensitive malignancy, SCLC recurrence occurs in most cases and negatively impacts patients' prognosis. The disease has lacked effective treatments with no therapies specifically approved to treat patients in the third line setting.

Tarlatamab is a type of protein that binds both to a specific target on SCLC cancer cells called delta-like ligand 3 (DDL3) 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, tarlatamab will offer an additional treatment option for recurrent small cell lung cancer (SCLC).

Proposed Indication

For the treatment of adults with refractory or relapsed small cell lung cancer (SCLC) who have progressed or recurred following one platinum-based regimen and at least a prior line of therapy.[1]

Technology

Description

Tarlatamab (AMG 757) is an investigational potential first-in-class half-life extended (HLE) bispecific T-cell engager (BiTE) immuno-oncology therapy that is uniquely designed to target delta-like ligand 3 (DLL3) cells in neuroendocrine cancers, such as small cell lung cancer (SCLC). [2,3] It binds to delta-like ligand 3 (DLL3) on target SCLC cells and CD3 on T cells, forming a cytolytic synapse inducing T cell activation and expansion and T cell-dependent killing of tumour cells.[4] DLL3 is highly upregulated on the cell surface of neuroendocrine tumours and rarely expressed on non-malignant cells, making it a novel target for investigating a BiTE immuno-oncology molecule such as tartalamab.[3,5,6]

Tarlatamab is in development for relapsed/refractory SCLC that has progressed or recurred following one platinum-based regimen and at least one line of therapy.[1] In the ongoing phase II and III trials (NCT05740566, NCT05060016), tarlatamab is administered as an intravenous (IV) infusion at an unspecified dose during the treatment period.[1,7]

Key Innovation

SCLC is an aggressive disease with still limited therapeutic options. Despite being both a chemo- and radiation-sensitive malignancy, SCLC recurrence occurs in most cases and negatively impacts patients' prognosis.[5,6] Relapsed SCLC is said to be incurable and available treatments are provided with palliative intent.[8] The disease has also lacked effective treatments with no therapies specifically approved to treat patients in the third-line setting; the prognosis of patients is poor, as there is a median overall survival of < 6 months.[8,9] Investigations of SCLC molecular abnormalities uncovered that the delta-like protein 3 (DLL3), a Notch inhibitory ligand whose expression is directly related to the key neuroendocrine transcription factor ASCL1, was found to be expressed in ~85% of SCLCs, while it exhibits minimal to absent surface expression in normal lungs. DLL3 thus represents an appealing novel biomarker as well as a potential target in SCLC treatment.[5,6,10]

Tarlatamab is an HLE BiTE immuno-oncology therapy designed to bind DLL3 on target cancer cells and CD3 on T cells, forming a cytolytic synapse inducing T cell activation and expansion and T cell-dependent killing of tumour cells.[4] Phase I trial results for tarlatamab demonstrated significant anti-tumour activity and response durability in heavily pre-treated patients with overall survival of about 13.2 months.[4,9,11] The five-year age-standardized net survival rate for stage 4 lung cancer in males in the UK is 3.2% and unfortunately, treatment options are still very limited.[12,13] Therefore, if licensed, tarlatamab will offer an additional treatment option for recurrent SCLC.

Regulatory & Development Status

Tarlatamab does not currently have marketing authorisation in the EU/UK for any indication.

Tarlatamab is not in phase II and III clinical development for the treatment of any other indication aside from SCLC.[14]

Tarlatamab was awarded an FDA orphan drug designation for the treatment of SCLC.[15]

Patient Group

Disease Area and Clinical Need

Lung cancer is the third most common cancer in the UK. 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. SCLC makes up about 1 in 7 lung cancers (about 15%).[16] SCLC is a particularly aggressive form of lung cancer and tends to spread faster than non-SCLC, with nearly 70% of people with SCLC having metastatic disease at the time of diagnosis.[17] Symptoms of small cell lung cancer include chest pain, lingering cough, trouble breathing, face and neck swelling, severe tiredness, loss of appetite, weight loss, etc.[18] 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.[18]

In 2017, there were 38,888 lung cancer diagnoses in England.[19] Around 48,500 people are diagnosed with lung cancer in the UK each year.[20] An estimated 64,214 people who had previously been diagnosed with lung cancer were alive in the UK at the end of 2013.[21] There were 34,771 deaths from lung cancer in the UK between 2017 and 2019.[22] For people diagnosed between 2013 and 2017, non-age-standardised 5–year survival statistics are almost 15% and 5% for stage 3 and 4 lung cancer respectively.[23] In England, 2021-22, there were 119,396 finished consultant episodes (FCE) and 99,551 admissions for a primary diagnosis of malignant neoplasm of the bronchus and lung (ICD-10 code C34) which resulted in 206,640 FCE bed days and 75,969 day cases.[24]

Recommended Treatment Options

There are no National institute for Health and Care Excellence (NICE) recommended third-line treatment options for SCLC.

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**: Recruiting **Location(s)**: USA and six other countries **Primary completion date**: July 1, 2025
Trial Design	Randomised, parallel assignment, open label
Population	N = 700 (estimated); subjects with histologically or cytologically confirmed relapsed/refractory SCLC that progressed/recurred following one platinum-based regimen; aged 18 years and older
Intervention(s)	Tarlatamab administered as an IV infusion.
Comparator(s)	Current standard of care administered per local standards
Outcome(s)	Overall Survival (OS) [-Time Frame: Up to approximately 5 years] See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Clinical Trial Information

Trial	**DeLLphi-301**; NCT05060016; 2021-002566-40; A Phase 2 Study Evaluating the Efficacy, Safety, Tolerability, and Pharmacokinetics of Tarlatamab in Subjects With Relapsed/Refractory Small Cell Lung Cancer After Two or More Prior Lines of Treatment **Phase II** – Active, not recruiting. **Location(s):** USA, United Kingdom, 11 EU countries, and other countries **Primary completion date**: Jan 2024
Trial Design	Randomised, sequential assignment, open label
Population	N = 222; subjects with histologically or cytologically confirmed refractory / relapsed SCLC who progressed or recurred following 1 platinum-based regimen and at least 1 other prior line of therapy; aged 18 years or older
Intervention(s)	Tarlatamab administered as IV infusion. Part 1: Tarlatamab Low Dose Part 1: Tarlatamab High Dose Part 2: Dose Expansion Part 3: Modified Monitoring Sub-study
Comparator(s)	None
Outcome(s)	• Part 1 only: Objective Response (OR) per Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1 by Investigator [Time Frame: Up to a maximum of 24 months] • Part 1 & 3: Number of Participants who Experience One or More Treatment-emergent Adverse Events [Time Frame: Up to a maximum of 24 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 guidance. Topotecan for the treatment of relapsed small-cell lung cancer [TA184]. November 2009.
- NICE guideline. Lung cancer: diagnosis and management (NG122). July 2023
- 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.[25]
- European Society for Medical Oncology (ESMO). Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2021.[26]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2019.[27]
- Scottish Intercollegiate Guideline Network (SIGN). Management of lung cancer. 2014.[28]

Additional Information

Amgen Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development.

As a result, the NIHR Innovation Observatory has had to obtain data from other sources.

UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit.

We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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