# Health Technology Briefing
# April 2025

# Ceralasertib with durvalumab for treatment of previously treated non-small-cell lung cancer

| Company/Developer | AstraZeneca UK Ltd |
|---|---|

☐ New Active Substance ☒ Significant Licence Extension (SLE)

| NIHRIO ID: 35552 | NICE ID: Not available | UKPS ID: 670183 |
|---|---|---|

## Licensing and Market Availability Plans

In phase III clinical development.

## Summary

Ceralasertib with durvalumab is in clinical development for treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC), for patients whose disease has progressed following immunotherapy (treatment that helps the body's immune system fight diseases) and platinum chemotherapy (treatment using drugs containing platinum, which kills cancer cells by damaging their DNA). Metastatic NSCLC is lung cancer which has spread to other parts of the body such as the lungs, liver, and brain. Locally advanced NSCLC is lung cancer which has spread to tissues surrounding the lungs, but not distant sites in the body. Lung cancer symptoms can include persistent cough, chest infection that does not improve or repeated chest infections, unexplained breathlessness, and coughing up blood. The most common cause of lung cancers is smoking, however other risk factors include air pollution, ageing, exposure to certain chemicals and lowered immunity. Advanced NSCLC can be difficult to treat due to the tumour cells becoming resistant to certain treatment mechanisms, meaning there are limited therapies available for patients with locally advanced or metastatic NSCLC.

Ceralasertib is a protein which interferes with the repair of DNA (genetic) damage, leading to increased cell mutations and tumour cell death. Ceralasertib is administered by mouth via tablets. Durvalumab is an antibody (protein) which enhances immune system's activity against tumour cells, it is given as an intravenous infusion (into the vein). The combination of durvalumab with ceralasertib has been shown to improve progression free survival and overall survival in patients with advanced NSCLC. If licensed, durvalumab with ceralasertib could offer an effective therapeutic option for patients who have typically poor outcomes with limited therapeutic options available.

## Proposed Indication

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.

Treatment of Non Small Cell Lung Cancer (NCLC) whose disease progressed on or after prior anti Programmed Cell Death Ligand 1 (PD-L1) therapy and platinum based chemotherapy.[1]

## Technology

### Description

Ceralasertib is an orally available morpholino-pyrimidine-based inhibitor of ataxia telangiectasia and rad3 related (ATR) kinase, with potential anticancer activity. Upon administration, ceralasertib selectively inhibits ATR activity by blocking the downstream phosphorylation of the serine/threonine protein kinase CHK1. This prevents ATR-mediated signalling, and results in the inhibition of DNA damage checkpoint activation, disruption of DNA damage repair, and the induction of tumour cell apoptosis.[2] Accumulation of unrepaired DNA damage and genomic instability in tumour cells, leading to apoptosis of tumour cells.[3] Durvalumab is a fully human, immunoglobulin G1 kappa (IgG1κ ) monoclonal antibody that selectively blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1). Durvalumab does not induce antibody dependent cell-mediated cytotoxicity (ADCC). Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation.[4]

Ceralasertib with durvalumab is in a phase III clinical trial (LATIFY, NCT05450692) for the treatment for locally advanced or metastatic NSCLC following anti-PD-L1 therapy and platinum based chemotherapy.[1] Ceralasertib is administered by oral tablets followed by intravenous durvalumab.[1]

### Key Innovation

Currently, there are few options offering clinical benefit for patients with metastatic or locally advanced NSCLC following failure of standard-of-care therapies. In the phase II HUDSON trial, ceralasertib with durvalumab enhanced immunogenicity of cancer cells and improved immunotherapy efficacy.[5] Combining durvalumab with ceralasertib may amplify the antitumour immune response, and potentially lead to durable tumour control. The combination of durvalumab with ceralasertib provided longer progression free survival and overall survival compared with other treatment regimens.[6]

If licensed, ceralasertib with durvalumab will offer an additional treatment option for patients with advanced or metastatic NSCLC whose disease progressed on or after prior PD-L1 therapy and platinum based chemotherapy.

### Regulatory & Development Status

Ceralasertib does not currently have marketing authorisation in the UK/EU for any indication.
Durvalumab has Marketing Authorisation in EU/UK for the treatment of:[7]

- non-small cell lung cancer (as a monotherapy)
- small cell lung cancer (in combination)
- biliary tract cancer (in combination)
- hepatocellular carcinoma (in combination)
- endometrial cancer (as a monotherapy or in combination)

Ceralasertib with durvalumab is in phase II/III clinical development for:[8]

- gynaecological cancers
- advanced NSCLC with PD-1 immune checkpoint inhibitor resistance
- extensive stage small cell lung cancer
- solid tumours
- advanced triple negative breast cancer

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

## Patient Group

### Disease Area and Clinical Need

NSCLC is one of two main forms of primary lung cancer, and makes up approximately 80-85% of lung cancer cases.[9] The three most common types of NSCLC are adenocarcinoma, squamous cell carcinoma and large cell lung cancer, depending on the cells involved.[10] Metastatic NSCLC (stage 4) is when the cancer spreads to other parts of the body such as the bones, lungs, brain, liver or adrenal glands.[11] Locally advanced NSCLC (Stage 3) is cancer that has spread into tissues around the lungs and may have spread into the nearby lymph nodes.[12] Lung cancer symptoms include persistent cough, chest infection that does not improve or repeated chest infections, unexplained breathlessness, and wheezing, coughing up blood, chest or shoulder pain, and a hoarse voice. Other symptoms include loss of appetite, unexplained weight loss and tiredness.[13] There are a number of risk factors for developing lung cancer including; ageing, lowered immunity, air pollution and exposure to certain chemicals, however smoking is the most common cause of lung cancers.[14]

In England, between 2023-2024 there were 125,652 finished consult episodes (FCE) of malignant neoplasm of bronchus and lung (ICD10 code C34), resulting in 81,951 day cases and 220,815 FCE bed days.[15] In the UK it is estimated that around 80 - 85% of lung cancer cases are NSCLC, this would result in an estimated 176,652-187,693 FCE bed days and 65,561-69,658 day cases.[9,15] In England, in 2022, the incidence of malignant neoplasm of bronchus and lung for females was 69.3 per 100,000 and 83.2 per 100,000 for men.[16] In England (2013 – 2017), almost 15% and 5% of people with Stage 3 and Stage 4 NSCLC respectively will survive their cancer for 5 years or more after diagnosis.[17]

### Recommended Treatment Options

There are currently no National Institute for Health and Care Excellence (NICE) recommended treatment options for individuals NCLC whose disease progressed on or after prior anti Programmed Cell Death Ligand 1 (PD-L1) Therapy and platinum based chemotherapy.

## Clinical Trial Information

| | |
|---|---|
| Trial | **LATIFY, NCT05450692; EudraCT 2022-000493-26;** A phase III, open-label, randomised, multicentre study of ceralasertib plus durvalumab versus docetaxel in patients with advanced or metastatic non-small cell lung cancer without actionable genomic alterations, and whose disease has progressed on or after prior anti-PD-(L)1 therapy and platinum-based chemotherapy: LATIFY<br>**Phase III –** Active, not recruiting<br>**Locations:** 9 EU countries, UK, and other countries<br>**Primary completion date:** August 2025 |
| Trial Design | Randomised, parallel assignment, open label |
| Population | N (actual) = 594. Patients with locally advanced or metastatic NSCLC after progression on prior anti-PD-L1 therapy and platinum-based chemotherapy: aged 18 years old and older. |
| Intervention(s) | Ceralasertib oral tablets with intravenous infusion of durvalumab in each 28-day cycle. |

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

| | |
|---|---|
| Comparator(s) | Docetaxel intravenous infusion in 21-day cycles. |
| Outcome(s) | Primary outcome: Overall Survival (OS) [Time frame: every 3 months (+/- 1 week) following objective progression of disease (PD) or treatment discontinuation (up to three years)].<br><br>See trial record for full list of other outcomes. |
| Results (efficacy) | - |
| Results (safety) | - |

## Estimated Cost

The cost of ceralasertib is not yet known.

Durvalumab is marketed in the UK for treatment of non-small cell lung cancer, the NHS indicative price for 120mg per 2.4ml-infusion vial is £592.00 and for 500mg per 10ml-infusion vial is £2466.00.[18]

## Relevant Guidance

### NICE Guidance

- NICE technology appraisal in development. Cobolimab with dostarlimab and docetaxel for treating advanced non-small-cell lung cancer after anti-PD-L1 treatment and chemotherapy (GID-TA11500). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Dostarlimab and docetaxel for treating advanced non-small-cell lung cancer after anti-PD-L1 treatment and chemotherapy (GID-TA11655). Expected date of issue to be confirmed.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2024

### 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.
- NHS England. Clinical Commissioning Policy: Stereotactic Ablative Body Radiotherapy for Non-Small-Cell Lung Cancer (Adult). B01/P/a. April 2013

### Other Guidance

- National Comprehensive Cancer Network. NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 3. 2025.[19]
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2018.[20]
- Scottish Intercollegiate Guidelines Network. Management of lung cancer (SIGN 137). 2014.[21]

## References

1 ClinicalTrials.gov. *A Phase III, Open-label, Randomised, Multicentre Study of Ceralasertib Plus Durvalumab Versus Docetaxel in Patients With Advanced or Metastatic Non-Small Cell Lung*

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

*Cancer Without Actionable Genomic Alterations, and Whose Disease Has Progressed On or After Prior Anti-PD-(L)1 Therapy and Platinum-based Chemotherapy: LATIFY. Trial ID: NCT05450692*. Status: Active, not recruiting Available from: https://clinicaltrials.gov/study/NCT05450692?term=NCT05450692&rank=1#study-overview [Accessed 18 February 2025].

2 National Cancer Institute *Ceralasertib*. 2025. Available from: https://www.cancer.gov/publications/dictionaries/cancer-drug/def/ceralasertib [Accessed 11 April 2025].

3 Hardaker EL, Sanseviero E, Karmokar A, Taylor D, Milo M, Michaloglou C, et al. The ATR inhibitor ceralasertib potentiates cancer checkpoint immunotherapy by regulating the tumor microenvironment. *Nature Communications*. 2024;15(1):1700. Available from: https://doi.org/10.1038/s41467-024-45996-4.

4 Electronic Medicines Compendium *Imfinzi 50 mg/mL concentrate for solution for infusion*. 2025. Available from: https://www.medicines.org.uk/emc/product/9495/smpc [Accessed 11 April 2025].

5 John V. Heymach. *Durvalumab and Ceralasertib Blaze a New Trail in NSCLC Therapy*. Available from: https://medicineinnovates.com/durvalumab-ceralasertib-blaze-trail-nsclc-therapy/#:~:text=Ceralasertib%2C%20an%20ATR%20kinase%20inhibitor%2C%20is%20posited%20to,cancer%20cells%20and%20improving%20the%20efficacy%20of%20immunotherapy. [Accessed 18 February 2025].

6 Besse B, Pons-Tostivint E, Park K, Hartl S, Forde PM, Hochmair MJ, et al. Biomarker-directed targeted therapy plus durvalumab in advanced non-small-cell lung cancer: a phase 2 umbrella trial. *Nature Medicine*. 2024;30(3):716-29. Available from: https://doi.org/10.1038/s41591-024-02808-y.

7 Electronic Medicines Compendium. *Imfinzi 50 mg/mL concentrate for solution for infusion*. 2024. Available from: https://www.medicines.org.uk/emc/product/9495#PHARMACOKINETIC_PROPS [Accessed 18 February 2025].

8 ClinicalTrials.gov *ClinicalTrials.gov: Search*. 2025. Available from: https://clinicaltrials.gov/search?intr=Ceralasertib%20%5C(AZD6738%5C)%2BDurvalumab&aggFilters=phase:2%203%204,status:act%20rec [Accessed 18 February 2025].

9 National Health Service. *Lung cancer*. 2022. Available from: https://www.nhs.uk/conditions/lung-cancer/ [Accessed 19 February 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 19 February 2025].

11 Jaime Herndon. *What to Know About Metastatic Non-Small Cell Lung Cancer*. 2023. Available from: https://www.healthline.com/health/nsclc/metastatic-non-small-cell-lung-cancer [Accessed 19 February 2025].

12 Cancer Research UK *What is metastatic lung cancer?* 2023. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/metastatic/what-is [Accessed 19 February 2025].

13 Macmillan Cancer Support. *Signs and symptoms of lung cancer*. Available from: https://www.macmillan.org.uk/cancer-information-and-support/lung-cancer/signs-and-symptoms-of-lung-cancer [Accessed 19 February 2025].

14 Macmillan Cancer Support *Causes and risk factors of lung cancer*. Available from: https://www.macmillan.org.uk/cancer-information-and-support/lung-cancer/causes-and-risk-factors-of-lung-cancer [Accessed 19 February 2025].

15 National Health Service England *Hospital Admitted Patient Care Activity, 2023-24*. 2024. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2023-24.

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

16 National Health Service England *Cancer Registration Statistics, England, 2022*. 2024. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/cancer-registration-statistics/england-2022#summary [Accessed 18 February 2025].

17 Cancer Research UK *Survival for lung cancer*. Available from: https://www.cancerresearchuk.org/about-cancer/lung-cancer/survival [Accessed 18 February 2025].

18 British National Forumulary. *Durvalumab [Specialist drug]*. Available from: https://bnf.nice.org.uk/drugs/durvalumab-specialist-drug/medicinal-forms/ [Accessed 19 February 2025].

19 Riely GJ, Wood DE, Aisner DL, Akerley W, Bauman JR, Bharat A, et al. *NCCN Clinical Practise Guidelines in Oncology (NCCN Guidelines): Non-Small Cell Lung Cancer, Version 3. 2025*. 2025. Available from: https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1450 [Accessed 18 February 2025].

20 Planchard D, Popat S, Kerr K, Novello S, Smit EF, Faivre-Finn C, et al. Metastatic non-small cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of Oncology*. 2018;29:iv192-iv237. https://www.sciencedirect.com/science/article/pii/S0923753419317107.

21 Scottish Intercollegiate Guidelines Network. *Management of lung cancer*. 2014. Available from: https://www.sign.ac.uk/our-guidelines/management-of-lung-cancer/ [Accessed 19 February 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.