

Health Technology Briefing

May 2024

Osmertinib neoadjuvant for treating EGFR mutation positive resectable non-squamous non-small cell lung cancer

Company/Developer

AstraZeneca UK Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 38343

NICE ID: Not Available

UKPS ID: 670217

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Osimertinib is in phase III clinical development as a neoadjuvant treatment for epidermal growth factor receptor mutation (EGFRm) positive, resectable (stage II -IIIB), non-squamous, non-small cell lung cancer (NSCLC). Lung cancer is one of the most common and serious types of cancer and NSCLC is the most common type of lung cancer. A neoadjuvant treatment is administered before the main treatment. Resectable cancer means that the cancer can be removed by surgery, which means the cancer is normally in earlier stages. A proportion of patients with NSCLC have mutations to the protein epidermal growth factor receptor (EGFR) which controls cell growth. A treatment that lowers the risk of recurrence in this cancer is needed.

Osimertinib is an orally administered type of cancer medicine called a tyrosine kinase inhibitor. It blocks the activity of EGFR, which normally controls growth and division of cells. In lung cancer cells, EGFR is often overactive, causing uncontrolled growth of cancer cells. By blocking EGFR, osimertinib helps to reduce the growth and spread of the cancer. Osimertinib is already approved for advanced NSCLC and if licensed for the early-stage disease, it will offer an additional treatment option for patients with EGFR-positive NSCLC.

Proposed Indication

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The neoadjuvant treatment of patients with EGFR mutation positive (EGFRm+), resectable (stage II -IIIB), non-squamous, NSCLC.¹

Technology

Description

Osimertinib (Tagrisso) is a Tyrosine Kinase Inhibitor (TKI). It is an irreversible inhibitor of EGFRs harbouring sensitising-mutations (EGFRm) and TKI-resistance mutation T790M.² Osimertinib blocks the activity of EGFR, which normally controls growth and division of cells. In lung cancer cells, EGFR is often overactive, causing uncontrolled growth of cancer cells. By blocking EGFR, osimertinib helps to reduce the growth and spread of the cancer.³

Osimertinib is currently in phase III clinical development (NCT04351555, NeoADAURA) for the neoadjuvant treatment of patients with EGFRm+, resectable non-squamous NSCLC. In this study, osimertinib is given alongside platinum-based chemotherapy (pemetrexed/carboplatin or pemetrexed/cisplatin) at a dose of 80mg orally once daily and also as a monotherapy at the same dosage.¹

Key Innovation

Currently, adjuvant chemotherapy is recommended for patients with resected stage II or III NSCLC who have not received neoadjuvant chemotherapy. However, clinical outcomes associated with adjuvant chemotherapy, including in resected EGFRm NSCLC, remain suboptimal with high recurrence rates. As an advantage over adjuvant treatment, neoadjuvant treatment in resectable NSCLC has the potential to downstage the tumour and provide earlier elimination of micrometastatic disease, thereby potentially reducing the risk of disease recurrence. Furthermore, neoadjuvant NSCLC treatment data have shown that achieving a pathological complete response (pCR) is prognostic for survival.⁴

If licensed, osimertinib will provide a neoadjuvant treatment option for patients with EGFRm+, resectable, non-squamous NSCLC.

Regulatory & Development Status

Osimertinib currently has Marketing Authorisation in the EU/UK for the following indications:²

- Adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIa NSCLC whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions or exon 21 (L858R) substitution mutations.
- First line treatment of adult patients with locally advanced or metastatic NSCLC with activating EGFR mutations
- Treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC.

Osimertinib is also in phase II and III clinical development as a monotherapy or in combination for multiple NSCLC indications with different subgroups and mutations.⁵

Patient Group

Disease Area and Clinical Need

Lung cancer is classified into two main histologic types: small cell lung cancer (SCLC) or NSCLC. NSCLC comprises about 80-85% of lung cancers in the UK.⁶ A stage IIA cancer describes a tumour larger than 4 cm but 5 cm or less in size that has not spread to the nearby lymph nodes. Stage IIB lung cancer describes a tumour that is 5 cm or less in size that has spread to the lymph nodes within the lung, called the N1 lymph nodes. A stage IIB cancer can also be a tumour more than 5 cm wide that has not spread to the lymph nodes. Stage III lung cancers are classified as either stage IIIA, IIIB, or IIIC. The stage is based on the size of the tumour and which lymph nodes the cancer has spread to. Stage III cancers have not spread to other distant parts of the body.⁷ The EGFR mutation is one of the most common mutations in non-small cell lung cancer. The EGFR gene controls the production of EGFR proteins. When cancer cells test positive for the EGFR protein, it means that the EGFR gene contains a mutation and is sending faulty instructions to the cells. This mutation allows cancer to grow and spread. They respond to targeted therapies called EGFR inhibitors.⁸ Certain factors can increase the risk of developing lung cancer, including: smoking tobacco, exposure to radiation (by exposure to radon gas and previous radiotherapy treatment), exposure to certain chemicals (e.g. asbestos, silica and diesel engine exhaust fumes), previous lung disease (e.g. tuberculosis and COPD), family history of lung cancer and certain genetic mutations and lowered immunity (e.g. due to certain conditions e.g. HIV/AIDS, rheumatoid arthritis and systemic lupus erythematosus, or immunosuppressive medications).⁹ Symptoms of lung cancer include a persistent cough (which may be more painful, have a different sound or bring up coloured mucus), shortness of breath, coughing up blood, aches and pains in the chest or shoulder, loss of appetite, weight loss and fatigue.¹⁰

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2016 - 2018).¹¹ Between 2017 and 2019 in the UK, there were 34,771 deaths due to lung cancer; the age standardised mortality rate was 55.5 per 100,000.¹² In 2013-2017 in England, the 1 year survival rate for all stages of lung cancer was 40.6%, dropping to 16.2% after 5 years.¹³ 1 in 10 (9.5%) people diagnosed with lung cancer in England survive their disease for ten years or more, but lung cancer survival has not shown much improvement in the last 50 years in the UK.¹¹

In England, 2022-23, there were 122,866 finished consultant episodes (FCE) and 104,232 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34) which resulted in 217,569 FCE bed days and 80,131 day cases.¹⁴

Recommended Treatment Options

Treatment for lung cancer includes surgery, chemotherapy, radiotherapy, immunotherapy, and other targeted therapy drugs. Patients may be offered one or more different treatments depending on the stage, histology and type of lung cancer as well as their general health.¹⁵ NICE recommends nivolumab with chemotherapy as neoadjuvant treatment for resectable non-small-cell lung cancer.¹⁶

Clinical Trial Information

Trial

NeoADAURA, [NCT04351555](#), [EudraCT2020-000058-89](#), A Phase III, Randomised, Controlled, Multi-center, 3-Arm Study of Neoadjuvant Osimertinib as Monotherapy or in Combination With Chemotherapy Versus Standard of Care Chemotherapy Alone for the Treatment of Patients With Epidermal Growth Factor Receptor Mutation Positive, Resectable Non-small Cell Lung Cancer
Phase 3: Recruiting
Locations: UK, US, Canada and 7 EU countries
Primary completion date: July 2029

Trial Design	Randomised, Parallel Assignment, Double masked.
Population	N=328 (estimated). Male or female, aged 18+ with histologically or cytologically documented non-squamous NSCLC with completely resectable disease.
Intervention(s)	Osimertinib (Oral administered, 80mg daily) with or without platinum based standard of care therapy (pemetrexed/carboplatin or pemetrexed/cisplatin)
Comparator(s)	Placebo with platinum based standard of care therapy (pemetrexed/carboplatin or pemetrexed/cisplatin)
Outcome(s)	Original primary outcome measures <ul style="list-style-type: none"> Major pathological response (MPR) [Time frame: from date of randomisation to an average of 12 weeks after the first dose] <p>See trial record for secondary outcome measures.</p>
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Osimertinib currently costs £5,770 for 30mg, 40mg or 80mg tablets.¹⁷

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Nivolumab as neoadjuvant (with chemotherapy) and adjuvant (as monotherapy) treatment for resectable non-small-cell lung cancer (ID6310). Expected TBC.
- NICE technology appraisal guidance in development. Durvalumab as neoadjuvant (with chemotherapy) and adjuvant (as monotherapy) treatment for resectable non-small-cell lung cancer (ID6220). Expected TBC.
- NICE technology appraisal guidance in development. Pembrolizumab as neoadjuvant (with chemotherapy) and adjuvant (as monotherapy) treatment for resectable non-small-cell lung cancer (ID5094). Expected October 2024.
- NICE technology appraisal guidance. Nivolumab with chemotherapy for neoadjuvant treatment of resectable non-small-cell lung cancer (TA876). March 2023
- NICE clinical guideline. Lung cancer: diagnosis and management (CG121). March 2019.
- NICE quality standard. Lung cancer in adults (QS17). Updated March 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) Guidelines Insights: Non-Small Cell Lung Cancer, Version 2. 2021.¹⁸
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up 2019.¹⁹

- Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer (SIGN 137). 2014.²⁰

Additional Information

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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.