Health Technology Briefing
November 2022

Osimertinib maintenance therapy for treating stage III unresectable EGFR mutation positive non-small-cell lung cancer after definitive platinum-based chemoradiation therapy

Company/Developer	AstraZeneca

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 26769	NICE ID: 10460	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Osimertinib is in development for the treatment of stage III, unresectable EGFR mutation positive non-small cell lung cancer (NSCLC) following definitive chemoradiation therapy. NSCLC is the most common form of lung cancer. Stage III lung cancer means the cancer is in more than one lobe of the lung, or it has spread to lymph nodes or nearby structures in the chest. EGFR is a protein on cells that helps them grow. A mutation in the gene for EGFR can make it grow too much, which can cause cancer. Smoking tobacco is the cause of most lung cancers and the biggest risk factor. Other risk factors include second-hand smoke, exposure to workplace carcinogens, radiation exposure, environmental pollution, and family history of lung cancer. There are currently no approved treatment options for the maintenance treatment of stage III, unresectable EGFR mutation positive NSCLC following chemoradiation therapy

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. If licensed, osimertinib will provide an additional maintenance treatment option for patients with stage III unresectable EGFR mutation positive NSCLC following definitive chemoradiotherapy.

Proposed Indication

Maintenance therapy for locally advanced (stage III), unresectable epidermal growth factor receptor (EGFR) mutation positive non-small cell lung cancer (NSCLC) whose disease has not progressed following definitive platinum-based chemoradiation therapy.[1]

Technology

Description

Osimertinib (Tagrisso) is a tyrosine kinase inhibitor (TKI). It is an irreversible inhibitor of epidermal growth factor receptors (EGFRs) harbouring sensitising-mutations and TKI-resistance mutation T790M.[2] Upon oral administration, osimertinib mesylate selectively and covalently binds to and inhibits the activity of the mutant forms of EGFR, including the T790M EGFR mutant form, thereby preventing EGFR-mediated signalling. This may both induce cell death and inhibit tumour growth in EGFR-overexpressing tumour cells. EGFR, a receptor tyrosine kinase overexpressed or mutated in many types of cancers, plays a key role in tumour cell proliferation and tumour vascularisation.[3]

Osimertinib is currently in clinical development for the treatment of stage III unresectable EGFR mutation positive NSCLC following definitive chemoradiotherapy. In the phase III clinical trial (LAURA, NCT03521154) patients are given osimertinib 80mg or 40mg orally once daily.[1]

Key Innovation

It is estimated that EGFR mutations are present in approximately 34% of patients with stage III NSCLC. Although there are limited outcome data for patients with EGFR mutation positive NSCLC receiving platinum-based chemoradiotherapy, there is evidence to suggest that following chemoradiotherapy patients with EGFR mutation positive NSCLC have superior local, but inferior distant control, including central nervous system (CNS) metastases, versus those with EGFR wild-type NSCLC. This highlights the need for targeted therapy with CNS activity for these patients. Trial results indicate that EGFR-TKIs may be efficacious for this patient population, and the third-generation EGFR-TKI osimertinib as maintenance therapy post-chemoradiotherapy could provide therapeutic benefits in this setting.[4]

If licensed, osimertinib will provide an additional maintenance treatment option for patients with stage III unresectable EGFR mutation positive NSCLC following definitive chemoradiotherapy.

Regulatory & Development Status

Osimertinib monotherapy has Marketing Authorisation in the EU/UK for:[2]

- the adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.
- the first-line treatment of adult patients with locally advanced or metastatic NSCLC with activating EGFR mutations.
- the treatment of adult patients with locally advanced or metastatic EGFR T790M mutation-positive NSCLC.

Osimertinib as a monotherapy and in combination with other therapies is also in phase II/III clinical development for the treatment of various other lines of NSCLC and for NSCLC with brain metastases.[5]

Osimertinib has been awarded an orphan drug designation by the FDA in April 2014 for the treatment of EGFR mutation-positive NSCLC.[6]

Patient Group

Disease Area and Clinical Need

NSCLC is the most common form of lung cancer. Around 80 to 85% of lung cancer cases in the UK are NSCLC. The three main types are adenocarcinoma, squamous cell carcinoma, and large cell carcinoma.[7] Smoking tobacco is the cause of most lung cancers and the biggest risk factor. Other risk factors include second-hand smoke, exposure to workplace chemicals, radiation exposure, air pollution and family history of lung cancer.[8] Symptoms of lung cancer include a cough, repeated chest infections, breathlessness, unexplained pain, weight loss or tiredness. However, lung cancer may not always have symptoms early on. Sometimes it is found by chance when a person is having tests for another condition.[9] Stage III lung cancer means the cancer is in more than one lobe of the lung, or it has spread to lymph nodes or nearby structures in the chest.[10] EGFR is a protein on cells that helps them grow. A mutation in the gene for EGFR can make it grow too much, which can cause cancer.[11]

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (2016-18).[12] The age standardised incidence rate of lung cancer in England is 88.4 and 67.4 per 100,000 amongst males and females respectively.[13] In England (2021-22), there were 119,396 finished consultant episodes (FCEs) and 99,551 admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34), which resulted in 75,969 day cases and 206,640 FCE bed days.[14] In England (2017), there were 38,888 patients diagnosed with malignant neoplasm of bronchus and lung and 28,170 deaths registered where malignant neoplasm of bronchus and lung was the underlying cause.[15] In England, there were 7,564 newly diagnosed cases of stage III lung cancer.[16] For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates for stage III lung cancer were 48.7% and 12.6% respectively.[17]

Recommended Treatment Options

There are currently no medicinal products approved for the treatment of EGFR-TK positive NSCLC patients following chemoradiotherapy.[18]

Clinical Trial Information

Trial	**LAURA, NCT03521154, 2018-001061-16;** A Phase III, Randomized, Double-blind, Placebo-controlled, Multicenter, International Study of Osimertinib as Maintenance Therapy in Patients With Locally Advanced, Unresectable EGFR Mutation-positive Non-Small Cell Lung Cancer (Stage III) Whose Disease Has Not Progressed Following Definitive Platinum-based Chemoradiation Therapy **Phase III** – Active, not recruiting **Locations:** 2 EU countries, USA and other countries **Primary completion date:** July 2023
Trial Design	Randomised, parallel assignment, double-blind, placebo controlled
Population	N=216 (actual); patients with histologically documented NSCLC of predominantly non-squamous pathology who present with locally advanced, unresectable (Stage III) disease; the tumour harbours one of the two common EGFR mutations known to be associated with EGFR-TKI sensitivity (Ex19del, L858R), either alone or in combination with other EGFR mutations; aged 18 and older
Intervention(s)	Osimertinib (oral) 80mg or 40mg

Comparator(s)	Placebo (oral)
Outcome(s)	**Primary outcome:** • Progression-free survival (PFS) [Time frame: approximately 13 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Osimertinib is already marketed in the UK; a pack of 30 x 80mg or 40mg tablets costs £5,770.[19]

Relevant Guidance

NICE Guidance

- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019. Last updated September 2022.
- NICE quality standard. Lung cancer in adults (QS17). 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.[20]
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2019.[21]
- Scottish Intercollegiate Guideline Network (SIGN). Management of lung cancer. 2014.[22]

Additional Information

AstraZeneca 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.

References

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