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Health Technology Briefing
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Alectinib adjuvant therapy for ALK-positive non-small cell lung cancer

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 24152	NICE TSID: 10490	UKPS ID: 671554

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Alectinib is in clinical development for the adjuvant treatment of patients with anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC) that have undergone complete resection. NSCLC makes up most lung cancer cases. In patients with ALK-positive NSCLC, part of the ALK gene is mutated which results in the production of an abnormal form of the ALK protein which stimulates the cancer cells to divide and grow in an uncontrolled fashion. Adjuvant therapy is the therapy that is given to the patient after surgery to remove any remaining cancer cells that have not been removed. About half of people with NSCLC experience disease recurrence following surgery. Recent treatment innovations have improved the outcomes for some patients with early-stage NSCLC; however, there are no approved ALK inhibitors for early-stage ALK-positive disease.

Alectinib is a second-generation ALK inhibitor that works by blocking the activity of ALK, thereby reducing the growth and spread of the cancer. Alectinib is indicated for the treatment of advanced ALK-positive NSCLC, and evidence suggest it could also improve outcomes in early-stage disease. Alectinib is administered orally twice a day after lung surgery. If approved, alectinib will provide a new adjuvant treatment option for ALK-positive NSCLC patients.

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.
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For the adjuvant treatment of adult patients with completely resected Stage IB to Stage IIIA anaplastic lymphoma kinase (ALK)-positive non-small cell lung cancer (NSCLC).[1]

Technology

Description

Alectinib (Alecensa, RO5424802) is an orally available anaplastic lymphoma kinase (ALK) inhibitor, a targeted therapy that blocks the activity of mutated ALK proteins. About 5% of NSCLC tumours are ALK positive.[2] In preclinical studies, inhibition of ALK tyrosine kinase activity led to blockage of downstream signalling pathways including signal transducer and activator of transcription 3 (STAT3) and phosphatidylinositol 3-kinase/protein kinase B (PI3K/AKT) and induction of tumour cell death (apoptosis).[3]

Alectinib is currently in clinical development for the adjuvant treatment of patients with completely resected ALK–positive NSCLC.[1] In the phase III trial (ALINA, NCT03456076), participants received alectinib 600 mg orally twice a day until completion of treatment period (24 months) or recurrence of disease.[1]

Key Innovation

ALK gene rearrangements are found in approximately 5% of lung adenocarcinomas and are associated with specific clinical features including a high risk of brain metastases.[4].[4] Second generation ALK inhibitor, alectinib, has been shown to be effective for a broad spectrum of ALK rearrangements and ALK mutations.[4] [4,] Adjuvant chemotherapy is recommended for patients with resected stage II-III NSCLC.[6] However, the efficacy of chemotherapy in the post-surgery setting is relatively poor and short lived.[7]

If licensed, alectinib will offer an adjuvant treatment option for patients with completely resected ALK-positive NSCLC who currently have few (well-tolerated) effective therapies available.

Regulatory & Development Status

Alectinib currently has Marketing Authorisation in the EU/UK as monotherapy for the following indications:[8]

- first-line treatment of adult patients with ALK-positive advanced NSCLC
- treatment of adult patients with ALK-positive advanced NSCLC previously treated with crizotinib.

Alectinib is in phase III clinical development for the following indications:[9]

- ALK-positive or Rearranged During Transfection (RET)-positive neoplasms.
- locally advanced, unresectable, Stage III NSCLC

Alectinib has the following regulatory designations:[10,11]

- an orphan drug in the USA in 2015 for treatment of ALK-positive NSCLC
- a breakthrough therapy by the US FDA for treatment of patients with ALK-positive metastatic NSCLC in September 2016

Patient Group

Disease Area and Clinical Need

Lung cancer starts in the windpipe (trachea), the main airway (bronchus) or the lung tissue.[12] NSCLC is the most common form of lung cancer with subtypes namely adenocarcinoma, squamous cell carcinoma and

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large cell carcinoma.[13] ALK (anaplastic lymphoma kinase) belongs to a family of proteins called receptor tyrosine kinases (RTKs), which are involved in the growth of cells and the development of new blood vessels that supply them. In patients with ALK-positive NSCLC, an abnormal form of ALK is produced that stimulates the cancer cells to divide and grow in an uncontrolled fashion.[14] ALK-positive lung cancer represents about 4% of lung cancer and generally appears in adenocarcinoma NSCLC. Patients who are ALK-positive tend to be younger than the average lung cancer patient, about half of ALK-positive lung cancer patients are diagnosed before the age of 50, whereas most lung cancer patients are diagnosed at the age of 70 years old. They also tend not to have a smoking history.[16] The most common symptoms of lung cancer include cough, breathlessness, coughing up phlegm with blood, pain in the chest or shoulder, recurrent chest infections, loss of appetite, weight loss and fatigue.[17]

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (2016-2018). Incidence rates for lung cancer in the UK are highest in people aged 85 to 89 (2016-2018).[18] Around 80 to 85% of lung cancers are NSCLC.[13] Lung cancer is the most common cause of cancer death in the UK, accounting for 21% of all cancer deaths (2017-2019); the mortality rates are projected to fall by 9% in the UK between 2023-2025 and 2038-2040.[19] In England (2021-2022), there were 39,783 finished consultant episodes (FCE) and 31,305 admissions for Malignant neoplasm: Bronchus or lung, unspecified (ICD-10 code C34.90) which resulted in 71,851 FCD bed days and 24,189 day cases.[20]

Recommended Treatment Options

There is currently no therapy recommended by NICE for the adjuvant treatment of ALK-positive NSCLC stage IB to stage IIIA.

Clinical Trial Information

Trial	**ALINA**; NCT03456076; 2017-004331-37 A Phase III, Open-Label, Randomized Study to Evaluate the Efficacy and Safety of Adjuvant Alectinib Versus Adjuvant Platinum-Based Chemotherapy in Patients With Completely Resected Stage IB (Tumours Equal to or Larger Than 4cm) to Stage IIIA Anaplastic Lymphoma Kinase Positive Non-Small Cell Lung Cancer **Phase 3:** Active, not recruiting. **Location(s):** 11 EU countries, UK, USA and other countries **Primary completion date:** April 2024
Trial Design	Randomised, parallel assignment, open label
Population	N=257 (actual); aged 18 years and older; all sexes; patients with complete resection of histologically confirmed Stage IB to Stage IIIA NSCLC and documented ALK-positive disease
Intervention(s)	Alectinib at 600 mg orally twice daily taken with food for 24 months
Comparator(s)	Platinum-based chemotherapy regimens for 4 cycles
Outcome(s)	Primary outcome measure: Disease-free Survival (DFS), as assessed by the Investigator [Time Frame: From the date of randomization until the first DFS event, up to approximately 5 years]

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	See trial record for full list of other outcomes.
Results (efficacy)	Recent results from a pre-specified interim analysis shows alectinib demonstrated a statistically significant and clinically meaningful improvement in DFS as adjuvant therapy in people with completely resected Stage IB (tumour ≥ 4 cm) to IIIA (UICC/AJCC 7th edition) ALK-positive NSCLC. Overall survival (OS) data were immature at the time of this analysis.[22]
Results (safety)	No unexpected safety findings were observed.[22]

Estimated Cost

Alectinib is already marketed in the UK for the treatment of NSCLC; a pack of 224 x 150mg capsules cost £5,032 (list price).[23]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance in development. Treatments for non-small-cell lung cancer (GID-TA11289). Expected September 2024.
- NICE technology appraisal guidance. Ceritinib for untreated ALK-positive non-small-cell lung cancer (TA500). January 2018.
- NICE clinical guideline. Lung cancer: diagnosis and management (NG122). July 2023
- NICE quality standard. Lung cancer in adults (QS17). March 2012. Updated December 2019.

NHS England (Policy/Commissioning) Guidance

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

Other Guidance

- American Society of Clinical Oncology (ASCO). Management of Stage III Non–Small-Cell Lung Cancer: ASCO Guideline Rapid Recommendation Update. 2023.[24]
- National Comprehensive Cancer Network (NCCN) Guidelines Insights: Non–Small Cell Lung Cancer, Version 2. 2021.[25]
- European Society for Medical Oncology (ESMO). Early and locally advanced non-small-cell lung cancer: an update of the ESMO Clinical Practice Guidelines focusing on diagnosis, staging and systemic and local therapy. eUpdate 2021.[26]

Additional Information

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