NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
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Amivantamab with lazertinib for previously untreated locally advanced or metastatic non-small-cell lung cancer

Company/Developer	Janssen-Cilag Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30223	NICE TSID: 11842	UKPS ID: 665953

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Amivantamab with lazertinib is in clinical development for the treatment of patients with EGFR-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC). NSCLC makes up the majority of lung cancers in the UK. In locally advanced NSCLC, the cancer has spread into tissues around the lungs, and metastatic NSCLC is when the cancer starts in the lungs and then spreads to other areas of the body. Epidermal growth factor receptor (EGFR) is a protein that is involved in processes that control cell division and survival. Changes (mutations) in EGFR causes cancer cells to divide more rapidly. More than 60% of NSCLCs express EGFR, making it an important therapeutic target for the treatment of these tumours.

Amivantamab is a monoclonal antibody (a type of protein) designed to recognise and attach to two receptors (targets) on the surface of the NSCLC cells simultaneously, blocking them from receiving messages the cancer cells need for growing and spreading. Lazertinib selectively blocks EGFR, leading to cell death in EGFR mutant-expressing cancer cells. Amivantamab is administered intravenously, and lazertinib is administered orally. If approved, amivantamab with lazertinib would offer an additional treatment option for patients with EGFR-mutated locally advanced or metastatic NSCLC.

Proposed Indication

First-line treatment of epidermal growth factor receptor (EGFR)-mutated locally advanced or metastatic Non-Small Cell Lung Cancer (NSCLC).[1]

Technology

Description

Amivantamab (Rybrevant; JNJ-61186372) is an EGFR-MET bispecific antibody with immune cell-directing activity that targets activating and resistant *EGFR* mutations and mesenchymal-epithelial transition (MET) mutations and amplifications to inhibit tumour growth.[2,3]

Lazertinib (JNJ-73841937) is a third-generation, selective inhibitor of certain forms of the EGFR with activating mutations, including the resistance mutation T790M, exon 19 deletions (Del19), and the L858R mutation, with potential antineoplastic activity. Upon administration, lazertinib specifically and irreversibly binds to and inhibits selective EGFR mutants, which prevents EGFR mutant-mediated signalling and leads to cell death in EGFR mutant-expressing tumour cells.[4]

Amivantamab and lazertinib combination therapy is in clinical development for the first-line treatment of patients with EGFR-mutated locally advanced or metastatic NSCLC. In the phase III clinical trial (MARIPOSA; NCT04487080), patients will be administered 1,050 mg of amivantamab intravenously (IV) for body weight less than 80 kg and 1,400 mg for body weight greater than or equal to 80 kg in 28-day cycles: once weekly in cycle 1 (with a split dose on days 1-2), and then every two weeks in subsequent cycles. Lazertinib will be administered 240 mg orally once daily.[1]

Key Innovation

Pro-cancerous, activating mutations in the tyrosine kinase transmembrane EGFR are common in NSCLC. Therefore, drug development to target these EGFR mutations is vital in advancing therapeutic strategies for patients with EGFR-mutated NSCLC.[5] Amivantamab is approved to treat NSCLC that is locally advanced or has spread to other parts of the body and has certain mutations (changes) in the *EGFR* gene.[6] Lazertinib may inhibit programmed cell death-1 ligand 1 (PD-L1) and inflammatory cytokines in specific cancer cells harbouring certain EGFR mutations. Compared to some other EGFR inhibitors, lazertinib may have therapeutic benefits in tumours with T790M- or L858R-mediated drug resistance. In addition, lazertinib penetrates the blood-brain barrier (BBB) and does not cause dose-limiting toxicities which occur during the use of non-selective EGFR inhibitors.[4 7]

If licensed, amivantamab with lazertinib would offer an additional treatment option for patients with EGFR-mutated locally advanced or metastatic NSCLC.

Regulatory & Development Status

Lazertinib does not currently have Marketing Authorisation in the EU/UK for any indication.

Amivantamab has Marketing Authorisation in the EU/UK for treatment of adult patients with locally advanced or metastatic NSCLC with activating epidermal growth factor receptor (EGFR) Exon 20 insertion mutations, whose disease has progressed on or after platinum-based chemotherapy.[8]

Patient Group

Disease Area and Clinical Need

Non-Small Cell Lung Cancer (NSCLC) is one of two main forms of primary lung cancer, and makes up approximately 80-85% of lung cancer cases.[9] NSCLC is grouped into three types, namely adenocarcinoma, squamous cell carcinoma and large cell lung cancer, depending on the cells involved.[10] Metastatic NSCLC (stage 4) is when the cancer spreading to other parts of the body such as the bones, lungs, brain, liver or adrenal glands.[11] Locally advanced NSCLC (Stage 3A) is cancer that has spread into tissues around the lungs.[12] More than 60% of NSCLCs express EGFR mutation.[13,14] 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.[15] 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.[16]

In England, 2021-22, there were 119,396 finished consultant episodes (FCE) of malignant neoplasm of bronchus and lung (ICD-10 code C34), resulting in 75,969 day cases and 206,640 FCE bed days.[17] In the UK it is estimated that around 80 - 85% of lung cancer cases are NSCLC, this would result in an estimated 95,517-101,487 FCE, 60,775-64,574 day cases and 165,312-175,644 FCE bed days.[18,19]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.[19]

Recommended Treatment Options

NICE recommends the following pharmacological therapies for adult patients with previously untreated EGFR-mutated locally advanced or metastatic NSCLC: [20,21,22,23,24]

- Osimertinib
- Dacomitinib
- Erlotinib
- Afatinib
- Gefitinib

Clinical Trial Information

Trial	**MARIPOSA; NCT04487080; 2020-000743-3;** A Phase 3, Randomized Study of Amivantamab and Lazertinib Combination Therapy Versus Osimertinib Versus Lazertinib as First-Line Treatment in Patients With EGFR-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer **Phase III** – Active, not recruiting. **Location(s):** 9 EU countries, UK, USA, Canada and other countries. **Primary completion date:** April 2024
Trial Design	Randomised, parallel assignment, triple-blind
Population	N=1074; aged 18 years and older; Subjects with newly diagnosed histologically or cytologically confirmed, locally advanced or metastatic NSCLC that is treatment naive and not amenable to curative therapy including surgical resection or chemoradiation

Intervention(s)	Amivantamab 1050mg (IV) once weekly in cycle 1, then every 2 weeks in subsequent cycles + Lazertinib 240 mg (oral) once daily
Comparator(s)	• Osimertinib 80 mg (oral) once daily + Placebo lazertinib • Lazertinib 240 mg (oral) once daily + Placebo Osimertinib
Outcome(s)	Primary outcome measure: • Progression-Free Survival (PFS) According to RECIST v1.1 by Blinded Independent Central Review (BICR) [Time Frame: Up to approximately 42 months]
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Amivantamab is already marketed in the UK; a 350 mg/7 ml vial costs £1,079.[25]

The cost of lazertinib is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Amivantamab with carboplatin and pemetrexed for untreated EGFR exon 20 insertion-positive advanced non-small-cell lung cancer [TA11023]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Cimavax for treating wild-type EGFR-positive non-small-cell lung cancer. [TA10225]. Expected date of issue to be confirmed.
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- NICE technology appraisal. Osimertinib for untreated EGFR mutation-positive non-small-cell lung cancer [TA654]. October 2020.
- NICE technology appraisal. Osimertinib for treating EGFR T790M mutation-positive advanced non-small-cell lung cancer [TA653]. October 2020.
- NICE technology appraisal. Dacomitinib for untreated EGFR mutation-positive non-small-cell lung cancer [TA595]. August 2019.
- NICE technology appraisal. Necitumumab for untreated advanced or metastatic squamous non-small-cell lung cancer [TA411]. September 2016.
- NICE technology appraisal. Afatinib for treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer [TA310]. April 2014.
- NICE technology appraisal. Erlotinib for the first-line treatment of locally advanced or metastatic EGFR-TK mutation-positive non-small-cell lung cancer [TA258]. June 2012.
- NICE technology appraisal. Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer [TA192]. July 2010.
- NICE clinical guideline. Lung cancer: diagnosis and management [NG122]. March 2019.

- NICE diagnostic guidance. EGFR-TK mutation testing in adults with locally advanced or metastatic non-small-cell lung cancer [DG9]. August 2013.

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 2. 2021.[26]
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2018. [27]
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Additional Information

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