NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
February 2024

Retifanlimab with chemotherapy for previously untreated metastatic non-small-cell lung cancer

Company/Developer	Incyte Corp

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 29268	NICE ID: Not Available	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Retifanlimab is currently in clinical development for previously untreated metastatic non-small-cell lung cancer (NSCLC). NSCLC is the most common lung cancer. There are three main types: adenocarcinoma, squamous cell carcinoma and large-cell lung cancer. Stage IV NSCLC is also called metastatic (the most advanced stage) lung cancer. Smoking tobacco is the cause of most lung cancers and the biggest risk factor. NSCLC is most common in the older population. The main symptoms include a new or prolonged cough, breathlessness, coughing up blood and an ache in the shoulder and chest. Although metastatic NSCLC is considered inoperable and incurable, there are some management options available such as: chemotherapy, immunotherapy and radiation therapy.

Retifanlimab is a monoclonal antibody (a type of protein) that binds to the programmed death receptor-1 (PD-1) (a checkpoint protein involved in the body's natural immune response). This binding action blocks PD-1 interaction with its ligands, which are binding sites on the surface of cancer cells. In normal circumstances, the interaction of PD-1 and its ligands would maintain the body's natural immune tolerance. However, in cancerous cases, this binding interaction weakens the body's anti-tumour response. By blocking the PD-1/ligand pathway, retifanlimab boosts T-cell activity and therefore the immune response. Retifanlimab is administered intravenously and if licensed will offer an additional treatment option for patients diagnosed with metastatic NSCLC.

Proposed Indication

First-line treatment of metastatic non-small-cell lung cancer (NSCLC).[1]

Technology

Description

Retifanlimab (INCMGA00012) is a humanised, hinge-stabilised, immunoglobulin G4κ monoclonal antibody.[2] The PD-1 and its ligands (PD-L1 and PD-L2) are stimulating molecules of the immune checkpoint pathway with a primary function of dampening the effector phase of activated T-cells in peripheral tissues, which limits the inflammatory response.[3] Retifanlimab binds to PD-1, preventing the interaction between PD-1 and its ligands, which is essential to sustain/restore T-cell anti-tumour function.[2]

Retifanlimab and chemotherapy is in clinical development for the first-line treatment of patients with metastatic NSCLC. In the phase III clinical trial (POD1UM-304; NCT04205812), patients are administered retifanlimab 375 mg intravenously every 3 weeks on day 1 of each cycle for up to 35 cycles.[1,4]

Key Innovation

Metastatic NSCLC cannot usually be cured, but treatment might control the disease, alleviate symptoms and improve patient quality of life.[5] Checkpoint inhibitors have significantly the improved outcomes for patients with metastatic NSCLC and are approved as first-line treatment as monotherapy as well as in combination with platinum-based chemotherapy.[4] In the POD1UM-101 phase 1 study (NCT03059823), retifanlimab demonstrated clinical activity and a safety profile similar to other currently approved anti PD-1 antibodies in patients with advanced stage NSCLC.[4,6] Therefore, if licensed, retifanlimab will offer an additional treatment option for patients with metastatic NSCLC.

Regulatory & Development Status

Retifanlimab does not currently have marketing authorisation in the EU/UK for any indication.

Retifanlimab is in phase II/III clinical development for the following indications:[7]

- Anal carcinoma
- Head and neck cancer
- Urothelial cancer
- Melanoma
- Renal cell carcinoma
- Merkel cell carcinoma
- Sarcoma
- Gastric adenocarcinoma
- Pancreatic adenocarcinoma
- Endometrial cancer
- Breast cancer
- Pleural mesothelioma

Patient Group

Disease Area and Clinical Need

The most common type of lung cancer is NSCLC which accounts for around 80-85 out of 100 lung cancers.[8] There are three main types of NSCLC, including adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Adenocarcinoma is the most common type and starts in the mucus-making gland cells in the lining of the airways. Squamous cell cancer develops in the flat cells that cover the surface of the airways and tends to grow near the centre of the lung. Large cell carcinoma cancer cells appear larger than a typical cell under the microscope.[8] Metastatic (also known as stage IV) means that the cancer has grown into nearby structures and lymph nodes.[9] The most common symptoms of lung cancer are a new or prolonged cough, breathlessness, coughing up phlegm with blood, shoulder and chest aches, recurrent chest infections and appetite loss.[10] The largest risk factor of lung cancer is smoking tobacco. Other risk factors include exposure to chemicals such as asbestos, silica and diesel exhaust, as well as air pollution, previous lung disease and family history.[11]

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (2016-18). The age standardised incidence rate of lung cancer in England is 18,662 in females and 20,678 in males per 100,000 population.[12] In England (2022-23) there were 122,866 finished consultant episodes (FCEs) and 104,232 hospital admissions for NSCLC (ICD-10 code C34), which resulted in 80,131 day cases and 217,569 FCE bed days. In England between 2013 and 2018, the predicted 10-year net survival for lung cancer for both men and women was 7.6% and 11.3% respectively.[13]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following monotherapy treatment options for metastatic NSCLC as first line treatment:[14,15]

- Pembrolizumab
- Atezolizumab

NICE currently recommends the following combination treatment options for metastatic NSCLC as first line treatment: [16,17,18]

- Pembrolizumab with pemetrexed and platinum chemotherapy
- Pembrolizumab with carboplatin and paclitaxel
- Pemetrexed in combination with cisplatin

Clinical Trial Information

Trial	**POD1UM-304,** NCT04205812; A Randomized, Double Blind, Phase 3 Study of Platinum-Based Chemotherapy with or without INCMGA00012 in First-Line Metastatic Squamous and Nonsquamous Non-Small Cell Lung Cancer **Phase III** – active **Location(s)**: Five EU countries, USA and other countries **Primary completion date**: June 2024
Trial Design	Randomised, parallel assignment, double-masking
Population	N = 583 (actual); subjects with histologically or cytologically confirmed stage IV NSCLC (either nonsquamous or squamous) who have received no prior systemic treatment for the advanced/metastatic NSCLC; aged 18 years and older.

Intervention(s)	Patients receive 375 mg retifanlimab administered intravenously every three weeks on day 1 of each cycle for up to 35 cycles.[4]
Comparator(s)	• Patients will receive placebo plus chemotherapy (nonsquamous NSCLC). Placebo with pemetrexed plus cisplatin or carboplatin followed by placebo plus pemetrexed until progression. • Patients will receive retifanlimab plus chemotherapy (squamous NSCLC) retifanlimab with carboplatin + paclitaxel OR nab-paclitaxel followed by INCMGA00012 until progression.
Outcome(s)	Primary outcome: overall survival, defined as the time from randomisation until death due to any cause [time frame: up to approximately 4.5 years]. See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of retifanlimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (TA770). February 2022.
- NICE technology appraisal. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (TA705). June 2021.
- NICE technology appraisal. Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer (TA683). March 2021.
- NICE technology appraisal. Pembrolizumab for untreated PD-L1-positive metastatic non-small-cell lung cancer (TA531). July 2018.
- NICE Guideline. Lung cancer: diagnosis and management (NG122). 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

- The European Society for Medical Oncology. Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. September 2020.[19]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2019.[20]
- London Cancer Alliance. LCA Lung Cancer Clinical Guidelines. March 2016.[21]
- Scottish Intercollegiate Guidelines Network. SIGN 137 – Management of lung cancer. February
- 2014.[22]

Additional Information

Incyte Corp 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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