Health Technology Briefing
September 2024

Dostarlimab and docetaxel for treating advanced non-small-cell lung cancer after progression on anti-PD-L1 therapy and chemotherapy

Company/Developer	GlaxoSmithKline UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 38992	NICE ID: Not Available	UKPS ID: 668449

Licensing and Market Availability Plans

Currently in phase II/III clinical development.

Summary

Dostarlimab in combination with docetaxel is in clinical development for the treatment of advanced non-small cell lung cancer (NSCLC) in patients who have progressed on prior anti-PD(L)-1 therapy and chemotherapy. NSCLC is the most common type of lung cancer. Advanced cancer means it has spread around the body from where it started making it harder to treat and increasing rates of mortality. Symptoms include a cough, repeated chest infections, breathlessness, unexplained pain, weight loss or tiredness. Immunotherapy is one of the leading treatments for NSCLC, but it does not help many patients due to resistance, either from the start or developing later.

Dostarlimab is a monoclonal antibody immunotherapy that is administered intravenously (into the vein). It works by blocking a protein called PD-1 on certain cells of the immune system thereby increasing the body's ability to kill the cancer cells. Docetaxel is commonly used in cancer treatments as it prevents cells from dividing and multiplying. If licensed, dostarlimab in combination with docetaxel could provide an additional treatment option for patients with advanced NSCLC who have progressed on prior treatment with anti-PD-L1 therapy and chemotherapy.

Proposed Indication

For the treatment of adult patients with advanced non-small cell lung cancer (NSCLC) who have progressed on prior anti- programmed death-ligand1 (PD-L1) therapy and chemotherapy.[1]

Technology

Description

Dostarlimab (Jemperli) is a monoclonal antibody, a protein that has been designed to block programmed death receptor-1 (PD-1) on certain cells of the immune system. Some cancers can make PD-1 ligands (PD-L1 and PD-L2), proteins that combine with PD-1 to switch off the activity of the immune cells, preventing them from attacking the cancer. By blocking PD-1, dostarlimab stops the cancer switching off these immune cells, thereby increasing the immune system's ability to kill the cancer cells.[2]

The COSTAR Lung clinical trial (NCT04655976) evaluates the efficacy and safety dostarlimab plus docetaxel, in adult patients with advanced or metastatic NSCLC who have received ≤2 prior lines of therapy that include an anti-PD-1/PD-L1 therapy plus platinum-based chemotherapy only.[1,3]

Key Innovation

Immunotherapy is one of the leading systemic therapies in NSCLC patients, but it is not effective in an important proportion of them due to primary or secondary resistance mechanisms.[4] One scientific concept is to avoid resistance or to provide salvage second-line treatments in the form of dual immunologic checkpoint blockade, so immunotherapy not only blocks a single molecule with specific antibodies but acts on two different immune checkpoint targets.[4] Immunomodulation checkpoints usually adopted by healthy cells and by tumours might cause an imbalance between host surveillance and tumour progression. Checkpoint antibody inhibitors, like anti-PD-1/PD-L1, are unique inhibitors that reduce tumour growth by modulating the interaction between immune cells and tumour cells. These checkpoint inhibitors are swiftly emerging as a highly promising strategy for treating cancer because they produce impressive antitumour responses while having a limited number of adverse effects.[5]

Dostarlimab, a medicinal product that interferes with the PD-1/PD-L1 pathway, eliminates a crucial inhibitory response of an immune system and, as a result, has the potential to cause severe or deadly immune-mediated adverse effects. As cancer immunotherapy, dostarlimab enhances the antitumour immune response of the body.[5] If licensed, dostarlimab in combination with docetaxel will offer an additional treatment option of NSCLC patients whose cancer has progressed following anti-PD-L1 therapy and chemotherapy.

Regulatory & Development Status

Dostarlimab currently has Marketing Authorisation in the UK as a:[6]

- Combination treatment with platinum-containing chemotherapy for adults with mismatch repair deficient (dMMR)/microsatellite instability-high (MSI-H) primary advanced or recurrent endometrial cancer and who are candidates for systemic therapy.
- Monotherapy for adults with dMMR/ MSI-H recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen.

Dostarlimab is currently in phase II/III clinical development for the treatment of:[7]

- Rectal cancer
- Colon cancer

- Endometrial cancer
- Ovarian cancer Head and neck cancer

Patient Group

Disease Area and Clinical Need

NSCLC is the most common type of lung cancer 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] Locally advanced cancer is cancer that has spread into tissues around the lungs and might have spread into nearby lymph nodes.[9] Metastatic (also known as advanced or stage 4) means that the cancer has spread from where it started in the lung.[10] 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.[11] The main risk factor for 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.[12]

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases (2016-18).[13] The age standardised incidence rate of lung cancer in England is 68 in females and 86.8 in males per 100,000 population (2017-19).[14] 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.[15] In England (2013-17) the one-year standardised survival rate of stage 4 lung cancer was 17.1% and 21.9% for men and women respectively, changing to 2.3% and 3.4% at 5 years.[16]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends the following treatment options for advanced NSCLC following treatment with anti-PD1 therapy with no targetable mutations include:[17]

- Docetaxel as a monotherapy for patients with squamous NSCLC and PD-L1 <50%.
- Docetaxel as a monotherapy for patients with squamous NSCLC and PD-L1 ≥50%.
- Docetaxel as a monotherapy for patients with non-squamous NSCLC and PD-L1 <50%.
- Docetaxel as a monotherapy for patients with non-squamous NSCLC and PD-L1 ≥50%.
- Docetaxel in combination with nintedanib for patients with non-squamous NSCLC and PD-L1 <50%.
- Docetaxel in combination with nintedanib for patients with non-squamous NSCLC and PD-L1 ≥50%.

Clinical Trial Information

Trial	**COSTAR Lung;** NCT04655976, 2020-003433-37**;** A Randomized, Open Label Phase 2/3 Study Comparing Cobolimab + Dostarlimab + Docetaxel To Dostarlimab + Docetaxel To Docetaxel Alone In Participants With Advanced Non-Small Cell Lung Cancer Who Have Progressed On Prior Anti-PD-(L)1 Therapy And Chemotherapy **Phase II/III -** active, not recruiting **Location(s):** Eleven EU countries, USA, UK, Canada, and other countries **Primary completion date:** November 2024
Trial Design	Randomised, parallel assignment, open label, active comparator controlled
Population	N=758; Participants with advanced non-small cell lung cancer (NSCLC) who have progressed on prior anti-PD-L1 therapy and chemotherapy, aged 18 years and older
Intervention(s)	Participants receive cobolimab with dostarlimab and docetaxel, or dostarlimab and docetaxel
Comparator(s)	Docetaxel
Outcome(s)	Primary outcome measures: - Overall survival in participants receiving cobolimab + dostarlimab + docetaxel relative to participants receiving docetaxel alone [Time frame: up to 44 months] - Overall survival in participants receiving dostarlimab + docetaxel relative to participants receiving docetaxel alone [Time frame: up to 44 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The NHS indicative cost of one vial of dostarlimab (50mg/1ml) is £5,887.33.[18]

Relevant Guidance

NICE Guidance

- NICE technology appraisal awaiting development. Plinabulin with docetaxel for previously treated advanced non-small-cell lung cancer [ID3895]. Expected date of issue to be confirmed.
- NICE technology appraisal awaiting development. Sacituzumab govitecan for treating advanced non-small-cell lung cancer after platinum-based chemotherapy and a PD-1 or PD-L1 inhibitor [ID 6375]. Expected date of issue to be confirmed.

- NICE technology appraisal awaiting development. Tislelizumab for treating advanced non-small-cell lung cancer after platinum-based chemotherapy [ID6161]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Datopotamab deruxtecan for treating advanced non-small-cell lung cancer after platinum-based chemotherapy [ID6241]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Tarlatamab for previously treated advanced small-cell lung cancer [ID6364]. Expected publication date: 11 December 2024.
- NICE technology appraisal. Nivolumab for advanced non-squamous non-small-cell lung cancer after chemotherapy [TA713]. July 2021.
- NICE technology appraisal. Nivolumab for advanced squamous non-small-cell lung cancer after chemotherapy [TA655]. October 2020.
- NICE technology appraisal. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer [TA403]. August 2016.
- NICE technology appraisal. Erlotinib and gefitinib for treating non-small-cell lung cancer that has progressed after prior chemotherapy [TA374]. December 2015.
- NICE technology appraisal. Pemetrexed for the treatment of non-small-cell lung cancer [TA124]. August 2007.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2023.
- NICE quality standard. Lung cancer in adults (QS17). December 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.[19]
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up 2019[20]
- Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer (SIGN 137). 2014[21]

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.