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Health Technology Briefing
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Nivolumab for adjuvant treatment of stage IB-IIIA non-small cell lung cancer

Company/Developer	Bristol Myers Squibb

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 31218	NICE ID: 10674	UKPS ID: 661057

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Nivolumab is in clinical development for the adjuvant treatment of stage IB-IIIA non-small cell lung cancer (NSCLC). NSCLC occurs due to tumours forming in the lung and is the most common form of lung cancer. Stage IB-IIIA disease comprises of a range of tumours from 3cm to larger than 7cm in size and have little or no spread to areas of the body close to the lung. NSCLC at early stages may not present symptoms, however patients may also have a cough that changes or gets worse, breathlessness, chest or shoulder pain and may be coughing up blood. Surgery is mostly used to treat NSCLC, and the aim of adjuvant treatment (treatment following a surgical procedure) is to reduce the risk of disease recurrence.

Nivolumab is a type of protein (monoclonal antibody) administered by intravenous (IV) infusion to increase the ability of the immune system to kill cancer cells. Nivolumab is already an established treatment in more advanced NSCLC stages and has shown potential activity in clinical trials for adjuvant treatment in other cancer types. If licensed, nivolumab could provide an additional adjuvant therapy for adults with stage IB-IIIA NSCLC.

Proposed Indication

Adjuvant treatment of adults with stage IB-IIIA NSCLC[1]

Technology

Description

Nivolumab (Opdivo) is a human immunoglobulin G4 (IgG4) monoclonal antibody (HuMAb), which binds to the programmed death-1 (PD-1) receptor and blocks its interaction with PD-L1 and PD-L2. The PD-1 receptor is a negative regulator of T-cell activity that has been shown to be involved in the control of T-cell immune responses. Engagement of PD-1 with ligands PD-L1 and PD-L2, which are expressed in antigen presenting cells and may be expressed by tumours or other cells in the tumour microenvironment, results in inhibition of T-cell proliferation and cytokine secretion. Nivolumab potentiates T-cell responses, including anti-tumour responses, through blockade of PD-1 binding to PD-L1 and PD-L2 ligands.[2]

Nivolumab is currently in phase III clinical development for the adjuvant treatment of adults with stage IB-IIIA NSCLC. In the phase III clinical trial (ANVIL, NCT02595944), participants received nivolumab via intravenous (IV) infusion over 30 minutes on day 1, at an unspecified dose. Cycles repeated every 4 weeks for up to 1 year in the absence of disease progression or unacceptable toxicity.[1]

Key Innovation

Surgical resection of tumours is the main treatment approach for patients with early stages of NSCLC (stage I, II and IIIA). However, rates of disease relapse remain high, despite complete surgical excision. The success of PD-1 inhibition (such as Nivolumab) in advanced NSCLC, means that there is potential to include this treatment type in earlier stages of disease.[3] There have been promising preliminary results released demonstrating the potential of PD-1 inhibitors in neoadjuvant settings with an adjuvant component to treat NSCLC.[4] Additionally, nivolumab has shown benefit as an adjuvant treatment option in other cancer types.[5] There are currently no PD-1 inhibitors recommended for adjuvant treatment of NSCLC.[6]

If licensed, nivolumab could provide an additional adjuvant therapy for adults with stage IB-IIIA NSCLC.

Regulatory & Development Status

Nivolumab has a Marketing Authorisation in the UK for the following NSCLC indications:[2]

- In combination with ipilimumab and 2 cycles of platinum-based chemotherapy for the first-line treatment of metastatic NSCLC in adults whose tumours have no sensitising EGFR mutation or ALK translocation
- As monotherapy for the treatment of locally advanced or metastatic NSCLC after prior chemotherapy in adults

Additionally, nivolumab as a monotherapy or in combination with various other medicinal products has a Marketing Authorisation in the UK for the following indications:[2]

- Melanoma
- Renal cell carcinoma (RCC)
- Malignant pleural mesothelioma (MPM)
- Classical Hodgkin lymphoma (cHL)
- Squamous cell cancer of the head and neck (SCCHN)
- Urothelial carcinoma
- Colorectal cancer (CRC)
- Oesophageal squamous cell carcinoma (OSCC)

- Oesophageal or gastro-oesophageal junction cancer (OC or GEJC)

Nivolumab as a monotherapy and in addition to various other medicinal products is being developed for numerous indications in phase II and phase III clinical trials.[7]

Patient Group

Disease Area and Clinical Need

NSCLC is a form of lung cancer which accounts for approximately 80-85% of all lung cancers diagnosed in the UK. NSCLC occurs due to tumours forming in the lung. Common tumour histology may be adenocarcinoma, squamous cell cancer or large cell carcinoma.[8] Stage IB-IIIA NSCLC refers to a range of stages of disease where the cancer may be of varying size and in different areas of the body. The tumour may be between 3cm and 4cm in size (Stage IB), up to 5cm in size with or without lymph node involvement (stage II) or either up to 5cm and larger than 7cm in size with more than one tumour in the same lobe of the lung or tumours that have spread to various areas close to the lungs such as the diaphragm and oesophagus (Stage IIIA).[9-11] Lung cancer can be asymptomatic in early stages, however some of the most common symptoms which may present include a cough or a change in a cough, breathlessness, coughing up sputum with blood in it and chest or shoulder pain.[12]

In 2016-18 there were an average of 48,549 new cases of lung cancer in the UK.[13] It can be estimated that approximately 38,839-41,266 of these cases were NSCLC. In 2013-14, 16% of NSCLC patients in England had surgery to remove their tumour, with the proportion of patients increasing for those with earlier stage disease.[14] In England in 2020-21 there were 27,754 hospital admissions and 35,679 finished consultant episodes (FCE) for unspecified malignant neoplasm of bronchus and lung (ICD-10 C34.9).[15] Only 10% of patients diagnosed with lung cancer survived for 10 or more years between 2013-2017 in England. However, a diagnosis of an earlier stage of disease improves one and five year survival chances.[16]

Recommended Treatment Options

The only currently NICE recommended adjuvant treatment for patients with resected NSCLC is a cisplatin-based combination chemotherapy regimen.[6]

Clinical Trial Information

Trial	**ANVIL, NCT02595944; NCI-2015-01916, EA5142, s16-02074;** Adjuvant Nivolumab in Resected Lung Cancers (ANVIL) – A Randomised Phase III Study of Nivolumab After Surgical Resection and Adjuvant Chemotherapy in Non-Small Cell Lung Cancers **Phase III** – Active, not recruiting **Location:** USA **Primary completion date:** July 2024
Trial Design	Randomised, parallel assignment, open label
Population	N=903 (planned); adults aged 18 years and older; Patients who have undergone a complete surgical resection of stage IB, II or IIIA NSCLC and received no prior treatment with an immune checkpoint inhibitor
Intervention(s)	Nivolumab (IV) on day 1 - cycles repeat every 4 weeks for 1 year

Comparator(s)	No comparator
Outcome(s)	Primary outcome measures: • Disease-free survival (DFS) [Time Frame: Time from randomization to the earliest event defined as disease recurrence, any new lung cancer (even in the opposite lung), or death from any cause at any known point in time, assessed up to 10 years] • Overall survival (OS) [Time Frame: Time from randomization to death from any cause, assessed up to 10 years] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Nivolumab is already marketed in the UK for various indications; a 100mg/10ml vial costs £1097.00, a 240mg/24ml vial costs £2633.00 and a 40mg/4ml vial costs £439.00.[17]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Pembrolizumab for adjuvant treatment of resected non-small-cell lung cancer (GID-TA10784). Expected publication date TBC.
- NICE technology appraisal. Atezolizumab with chemotherapy for neoadjuvant and adjuvant treatment of resectable non-small-cell lung cancer (GID-TA10777). Expected publication date TBC.
- NICE technology appraisal. Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer (GID-TA10751). Expected publication date July 2022.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.
- 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

- Ettinger DS, Wood DE, Aisner DL, Akerley W, Bauman J et al. Non-Small Cell Lung Cancer, Version 5.2017, NCCN Clinical Practice Guidelines in Oncology. April 2017.[18]
- Eberhardt WEE, Ruysscher DD, Weder W, Le Pechoux C, De Leyn P et al. 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer. August 2015.[19]

Additional Information

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