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# HEALTH TECHNOLOGY BRIEFING
# OCTOBER 2021

# Tislelizumab for advanced non-small cell lung cancer after platinum based chemotherapy

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| **NIHRIO ID** | 28866 | **NICE ID** | 10706 |
| **Developer/Company** | Novartis Pharmaceuticals UK Ltd | **UKPS ID** | 662853 |

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| **Licensing and market availability plans** | Currently in phase III clinical development. |

## SUMMARY


Tislelizumab is in clinical development to treat patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) who have previously been treated with platinum-based chemotherapy. NSCLC makes up the majority of lung cancers in the UK. Metastatic NSCLC is when the cancer has spread beyond the lung that was initially affected, most often to the liver, adrenal glands, bones, and the brain. Most patients with NSCLC are diagnosed at the advanced/metastatic stage where curative treatment with surgery is unsuitable.

Tislelizumab is a drug, administered intravenously, that has been designed to recognise and block a target called PD-1 found on certain cells of the immune system. Some cancers make a protein that attaches to PD-1 and switches off the immune cells' ability to attack the cancer. By blocking PD-1, tislelizumab stops the cancer switching off these immune cells, thereby increasing the immune system's ability to kill the cancer cells. If licenced, tislelizumab will provide an additional second or third-line treatment option for adult patients with locally advanced or metastatic (Stage IIIB or IV) NSCLC who have progressed on a prior platinum-containing regimen.

# PROPOSED INDICATION

Treatment of adult patients with locally advanced or metastatic (Stage IIIB or IV) non-small cell lung cancer (NSCLC) who have progressed on a prior platinum-containing regimen.[1]

# TECHNOLOGY

## DESCRIPTION

Tislelizumab is a humanised IgG4 anti-programmed death-1 (PD-1) monoclonal antibody specifically designed to minimise binding to FcγR on macrophages.[2] Specifically, anti-PD-1 antibodies that bind FcγRs may mediate crosslinking between PD-1-positive T-cells and FcγR-positive macrophages, which could induce macrophages to phagocytose active PD-1-positive T-cells and possibly diminish cytolytic destruction of tumour cells. As an antagonist to PD-L1/PD-L2 mediated cell signalling, tislelizumab leads to increased cytokine production and restoration of T-cell activation, resulting in immune-mediated tumour cell death.[3]

In the phase III trial (NCT03358875), tislelizumab is administered as a 200g IV injection once every 3 weeks (Q3W).[1]

## INNOVATION AND/OR ADVANTAGES

NSCLC accounts for most lung cancers worldwide and has a poor prognosis at later stages; PD-1 and programmed death-ligand 1 (PD-L1) inhibitors have provided promising new treatment approaches for these patients.[3]

Tislelizumab has higher affinity to PD-1 than other antibodies targeting PD-1, potentially due to its differential PD-1 binding orientation. Tislelizumab demonstrated encouraging efficacy results, long duration of response, and a manageable safety profile in advanced NSCLC.[3]

## DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

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

Tislelizumab monotherapy is also in Phase II clinical development for relapsed or refractory mature T- and NK- neoplasms, microsatellite instability-high or a mismatch repair deficient solid tumors, locally advanced or metastatic urothelial bladder cancer and relapsed or refractory classical hodgkin lymphoma and in phase III in NSCLC, hepatocellular carcinoma and advanced esophageal cancer (ESCC).

Tislelizumab in combination with chemotherapy or chemoradiotherapy is in Phase III clinical development for the treatment of advanced ESCC, locally advanced, unresectable NSCLC, inoperable, locally advanced or metastatic gastric, or gastroesophageal junction carcinoma, untreated extensive-stage small cell lung cancer, urothelial carcinoma and recurrent or metastatic nasopharyngeal cancer. It is also in Phase II clinical trials for muscle-invasive bladder carcinoma, head and neck cancer and HER2-negative breast cancer.[4]

# PATIENT GROUP

## DISEASE BACKGROUND

Lung cancer is classified into two main types: small-cell lung cancer (SCLC) or NSCLC. NSCLC comprises approximately 80 to 85% of lung cancers in the UK. There are three common types of NSCLC: adenocarcinoma (the most common type which starts in the mucus making glands 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) and large cell carcinoma (cancer cells which appear large and round under the microscope).[5] Metastatic cancer has spread, either to both lungs, the chest or beyond.[6]

Tobacco smoking remains the main cause of lung cancer and the geographical and temporal patterns of the disease largely reflect tobacco consumption during the previous decades. Both smoking prevention and smoking cessation can lead to a reduction in a large fraction of lung cancers. In countries with active tobacco control measures, the incidence of lung cancer has begun to decline in men and is reaching a plateau for women. An increase in the proportion of NSCLC in never-smokers has been observed, especially in Asian countries. These new epidemiological data have resulted in 'non-smoking-associated lung cancer' being considered a distinct disease entity, where specific molecular and genetic tumour characteristics have been identified.[7]

Several other factors have been described as lung cancer risk factors including; exposure to radiation, certain chemicals (e.g., asbestos, silica and diesel engine exhaust fumes) and previous lung disease (e.g., tuberculosis and chronic obstructive pulmonary disease). Other factors include family history of lung cancer and certain genetic mutations.[8]

Symptoms of lung cancer include a persistent cough (which may be more painful, have a different sound or bring up coloured mucus), shortness of breath, coughing up blood, aches and pains in the chest or shoulder, loss of appetite, weight loss and fatigue.[9,10]

## CLINICAL NEED AND BURDEN OF DISEASE

Primary lung cancer remains the most common malignancy, and deaths from lung cancer exceed those from any other malignancy worldwide.[7] Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases in 2017. There are around 48,000 new lung cancer cases in the UK yearly.[11] In the UK it is estimated that up to 85% of lung cancer cases are NSCLC, which would mean around 40,800 of the annual new lung cancer cases are NSCLC.[12]

In 2020/21 there were 86,043 hospital admissions with primary diagnosis malignant neoplasm of bronchus and lung (ICD-10 code C34), and 103,856 finished consultant episodes (FCEs), resulting in 170,030 FCE bed days.[13]

Survival rates for lung cancer depend on at which stage of disease the cancer is identified.[11] In England between 2013 and 2017, the age-standardised net lung cancer survival for stage IV (metastatic) was 19.3% at one year and 2.9% at five years, and for stage III it was 48.7% at one year and 12.6% at five years.[14] There are around 35,100 lung cancer deaths in the UK every year (based on data from 2016-2018). Mortality rates for lung cancer are projected to fall by 21% in the UK between 2014 and 2035.[15] In England and Wales in 2020 there were 28,730 deaths with malignant neoplasm of bronchus and lung (ICD-10 codes C34) recorded as the underlying cause.[16]

# PATIENT TREATMENT PATHWAY

## TREATMENT PATHWAY

Treatment of NSCLC depends on the stage of the cancer and the general health of the patient. The main treatment options for stage I, II and III NSCLC are surgery, chemotherapy and radiotherapy. At stage IV NSCLC, treatment aims to control the cancer for as long as possible and help with symptoms. Treatment generally include chemotherapy, targeted cancer drugs, radiotherapy, immunotherapy and symptom control treatment.[17]

## CURRENT TREATMENT OPTIONS

Current second line or further treatments for non-squamous NSCLC are:[18]

- Pemetrexed maintenance after other platinum doublet chemotherapy
- Pemetrexed maintenance
- Docetaxel +/- Nintedanib
- Atezolizumab
- Nivolumab
- Pembrolizumab

Current second line or further treatment for squamous NSCLC are:[19]

- Atezolizumab
- Nivolumab
- Pembrolizumab
- gemcitabine or vinorelbine and cisplatin or carboplatin
- Docetaxel monotherapy

## PLACE OF TECHNOLOGY

If licenced, tislelizumab will provide an additional treatment option for adult patients with locally advanced or metastatic (Stage IIIB or IV) NSCLC who have progressed on a prior platinum-containing regimen.

# CLINICAL TRIAL INFORMATION

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| **Trial** | **BGB-A317-303;** NCT03358875, 2018-000245-39**;** A Phase 3, Open-Label, Multicenter, Randomized Study to Investigate the Efficacy and Safety of BGB-A317 (Anti-PD1 Antibody) Compared With Docetaxel in Patients With Non-Small Cell Lung Cancer Who Have Progressed on a Prior Platinum-Containing Regimen<br>**Phase III** - Active, not recruiting<br>**Location(s):** 4 EU countries and other countries.<br>**Primary completion date:** December 2022 |
| **Trial design** | Randomised, parallel assignment, open label |
| **Population** | N=805, Subjects with locally advanced or metastatic (Stage IIIB or IV) NSCLC of either squamous or non-squamous histology types with disease progression during or following treatment with at least one platinum-containing regimen, but no more than 2 lines of systemic therapy; aged 18 years and older |
| **Intervention(s)** | Tislelizumab 200 mg IV once every 3 weeks |

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| **Comparator(s)** | Docetaxel 75 mg/m2 IV once every 3 weeks |
| **Outcome(s)** | Primary outcome measure:<br>- Overall survival (OS) in PD-L1+ and all participants (co-primary endpoint) [Time Frame: Up to 31 months]<br><br>See trial record for full list of other outcomes. |
| **Results (efficacy)** | - |
| **Results (safety)** | - |

# ESTIMATED COST

The cost of tislelizumab is not yet known.

# RELEVANT GUIDANCE

## NICE GUIDANCE

- 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. Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy. [TA520]. May 2018.
- NICE technology appraisal. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer. [TA403]. August 2016.
- NICE technology appraisal. Pemetrexed maintenance treatment for non-squamous non-small-cell lung cancer after pemetrexed and cisplatin [TA402]. 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. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer [TA347]. July 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 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). Non–Small Cell Lung Cancer, Version 5.2017, NCCN Clinical Practice Guidelines in Oncology. 2017.[20]
- European Society for Medical Oncology. Metastatic Non-Small-Cell Lung Cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2017.[21]
- European Society for Medical Oncology. ESMO Consensus Conference on Lung Cancer: Non-small-cell lung cancer first-line/second and further lines in advanced disease. 2014.[22]

- Scottish Intercollegiate Guidelines Network. Management of lung cancer (SIGN 137). 2014.[23]

## ADDITIONAL INFORMATION

## REFERENCES


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