Health Technology Briefing
June 2022

Tislelizumab with etoposide and carboplatin or cisplatin for treating small-cell lung cancer

Company/Developer	Novartis Pharmaceuticals UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 31394	NICE TSID: 10693	UKPS ID: 665442

Licensing and Market Availability Plans

Currently in phase II/III trials.

Summary

Tislelizumab in combination with chemotherapy is currently in clinical development for the first-line treatment of extensive stage small-cell lung cancer (SCLC). Extensive stage SCLC is when cancer cells form in the tissues of the lung and spread beyond the lung to other places in the body. Symptoms include chest discomfort or pain, a cough that does not go away or gets worse, trouble breathing and wheezing. Smoking is the biggest risk factor. Standard first-line treatment includes therapy with anti-programme death-1 (PD-1) antibodies combined with chemotherapy, which helps immune cells target cancer cells and destroy them. Despite this, extensive stage SCLC is a challenging disease to treat, and resistance eventually develops relatively quickly in most patients.

Tislelizumab targets PD-1 and is specifically designed to minimise binding to PD-1 receptor on immune cells (macrophages), to increase immune cell killing of cancer cells. Tislelizumab has been shown to have higher affinity (binding) to PD-1 than other anti-PD-1 antibodies, such as pembrolizumab and nivolumab. Tislelizumab plus chemotherapy has demonstrated encouraging anti-tumour activity and was generally well tolerated in a phase II clinical trial. It will be administered as an intravenous (IV) infusion in combination with IV etoposide and IV cisplatin or carboplatin. If approved, this combination will add an alternative treatment option for first-line treatment of extensive stage SCLC.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was available to comment.

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Proposed Indication

First-line treatment of untreated extensive-stage small cell lung cancer (SCLC).[1]

Technology

Description

Tislelizumab (BGB-A317) is a humanised IgG4 anti–programme death-1 (anti-PD-1) monoclonal antibody specifically designed to minimise binding to Fcγ receptor (FcγR) on macrophages. In pre-clinical studies, binding to FcγR on macrophages has been shown to compromise the anti-tumour activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells. It was also designed to bind to PD-1, a cell surface receptor that plays an important role in allowing tumour cells to evade the immune system. Many types of cancer cells have hijacked the programme death-ligand 1 (PD-L1) expression system that normally exists in healthy cells. By expressing PD-L1, cancer cells can interact with PD-1 expressing cytotoxic T-lymphocytes (CTLs) and protect themselves from being killed by these CTLs. Tislelizumab can potentially restore the ability of CTLs to kill cancer cells by binding to PD-1, without activating the receptor, thereby preventing PD-L1 from engaging PD-1.[2]

Tislelizumab in combination with etoposide and carboplatin or cisplatin is currently in development for the first-line treatment of untreated extensive-stage small-cell lung cancer. In the phase III clinical trial (NCT04005716), 200mg tislelizumab will be administered as an intravenous (IV) infusion once every 3 weeks (Q3W), in combination with 100mg/m^2 etoposide IV days 1-3 of each 21-day cycle, and 75mg/m^2 cisplatin IV Q3W or carboplatin area under the plasma or serum concentration-time curve (AUC) 5 IV Q3W, for 4 cycles.[1]

Key Innovation

Extensive-stage SCLC is a therapeutically challenging disease. After more than two decades without clinical progress, the addition of anti-PD-1 antibodies to platinum-based chemotherapy has demonstrated sustained overall survival benefit and represents the current standard of care in the first-line setting. Despite this benefit, resistance emerges relatively rapidly in virtually all patients.[3]

Tislelizumab has shown higher affinity to PD-1 than other anti-PD-1 antibodies, pembrolizumab and nivolumab with an approximately 100- and 50-fold slower off-rate, respectively. Moreover, tislelizumab has a different binding orientation to PD-1 compared with pembrolizumab and nivolumab.[4]

Tislelizumab plus chemotherapy has demonstrated encouraging antitumour activity and was generally well tolerated in a previous phase II clinical trial (NCT03432598).[4] If licensed, tislelizumab in combination with chemotherapy will offer an additional first-line treatment option for patients with extensive-stage SCLC.

Regulatory & Development Status

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

Tislelizumab is currently in phase II/III clinical trials for combination therapy for various cancer indications.[5]

Patient Group

Disease Area and Clinical Need

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SCLC is a disease in which malignant cells form in the tissues of the lung. In extensive-stage, cancer has spread beyond the lung or the area between the lungs or the lymph nodes above the collarbone to other places in the body. Smoking cigarettes, pipes, or cigars is the biggest factor for lung cancer. Other risk factors include being exposed to second-hand smoke, asbestos, arsenic, chromium, beryllium, nickel, soot or tar in the workplace, radiation exposure, air pollution, family history of lung cancer, human immunodeficiency virus (HIV) infection, taking beta-carotene supplements whilst a smoker and increasing age.[6] Symptoms of SCLC include chest discomfort or pain, a cough that does not go away or gets worse, trouble breathing, wheezing, blood in sputum, hoarseness, trouble swallowing, loss of appetite and unknown weight loss.[7]

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (2016-2018).[8] Extensive stage SCLC is a form of lung cancer accounting for 1 in 8 lung cancer cases in the UK.[9] 48,549 new cases of lung cancer were diagnosed annually on average between 2016-2018 in the UK.[8] Using these statistics, it can be estimated that an average of 6,068 cases of extensive stage SCLC are diagnosed in the UK every year.[8,9]

Recommended Treatment Options

Currently, the only treatment recommended by the National Institute for Health and Care Excellence (NICE) as first-line therapy for extensive stage SCLC is atezolizumab in combination with carboplatin and etoposide.[10]

Clinical Trial Information

Trial	NCT04005716; A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Platinum Plus Etoposide With or Without Tislelizumab (BGB-A317) in Patients With Untreated Extensive-Stage Small Cell Lung Cancer **Phase 3** – Active, not recruiting **Location(s) –** Asia **Primary completion date** – July 2022
Trial Design	Randomised, parallel assignment, quadruple-masked
Population	N = 457 (actual); histologically or cytologically confirmed extensive stage-SCLC, no prior systemic treatment for extensive stage-SCLC; aged 18 years and older.
Intervention(s)	200mg tislelizumab IV infusion Q3W, in combination with 100mg/m^2 etoposide IV days 1-3 of each 21-day cycle, and 75mg/m^2 cisplatin IV Q3W or carboplatin area under the plasma or serum concentration-time curve (AUC) 5 IV Q3W, for 4 cycles.
Comparator(s)	Placebo Q3W in combination with chemotherapy consisting of etoposide (100 mg/m^2 IV Days 1-3 of each 21-day cycle) and platinum (cisplatin 75 mg/m^2 IV Q3W or carboplatin AUC 5 IV Q3W) for 4 cycles.
Outcome(s)	**Primary outcome:** • Overall Survival (OS) [Time Frame: Baseline until death from any cause (up to approximately 51 months)] See trial record for full list of outcomes.

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Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of tislelizumab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Atezolizumab with carboplatin and etoposide for untreated extensive-stage small-cell lung cancer (TA638). July 2020.
- NICE guideline. Suspected cancer: recognition and referral (NG12). December 2021.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.
- NICE quality standard. Lung cancer in adults (QS17). December 2019.
- NICE quality standard. Suspected cancer (QS124). December 2017.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

Other Guidance

- National Comprehensive Cancer Network (NCCN). Small Cell Lung Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. December 2021.[11]
- European Society for Medical Oncology (ESMO). Small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. July 2021.[12]
- NHS Northern Cancer Alliance. Lung Cancer Clinical Guidelines. May 2019.[13]
- London Cancer Alliance. LCA Lung Cancer Clinical Guidelines. March 2016.[14]
- Scottish Intercollegiate Guidelines Network. SIGN 137 – Management of lung cancer. February 2014.[15]

Additional Information

Novartis signed a strategic collaboration agreement in 2021 to in-license tislelizumab from BeiGene, Ltd. in major markets outside of China, Under the terms of the agreement, Novartis obtain the development and commercialisation rights to tislelizumab in the United States, Canada, Mexico, the European Union, United Kingdom, Norway, Switzerland, Iceland, Liechtenstein, Russia, and Japan.[16]

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