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

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.
## Proposed Indication

First-line treatment of untreated extensive-stage small cell lung cancer (SCLC).<sup>1</sup>

## 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.<sup>2</sup>

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/m² etoposide IV days 1-3 of each 21-day cycle, and 75mg/m² cisplatin IV Q3W or carboplatin area under the plasma or serum concentration-time curve (AUC) 5 IV Q3W, for 4 cycles.<sup>1</sup>

### 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.<sup>3</sup>

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.<sup>4</sup>

Tislelizumab plus chemotherapy has demonstrated encouraging antitumour activity and was generally well tolerated in a previous phase II clinical trial (NCT03432598).<sup>4</sup> 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.<sup>5</sup>

## Patient Group

### Disease Area and Clinical Need
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. 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.

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (2016-2018). Extensive stage SCLC is a form of lung cancer accounting for 1 in 8 lung cancer cases in the UK. 48,549 new cases of lung cancer were diagnosed annually on average between 2016-2018 in the UK. 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.

**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.

**Clinical Trial Information**

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>NCT04005716</th>
<th>Study Design</th>
<th>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</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Asia</td>
<td>Primary completion date</td>
<td>July 2022</td>
</tr>
</tbody>
</table>

**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/m² etoposide IV days 1-3 of each 21-day cycle, and 75mg/m² 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 (100mg/m² IV Days 1-3 of each 21-day cycle) and platinum (cisplatin 75 mg/m² 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.
Estimated Cost

The cost of tislelizumab is not yet known.

Relevant Guidance

NICE Guidance


NHS England (Policy/Commissioning) Guidance


Other Guidance


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

References


