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Newcastle University

Health Technology Briefing
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Tislelizumab in combination with Paclitaxel, Cisplatin, and Radiotherapy for Oesophageal cancer

Company/Developer	Novartis Pharmaceuticals UK Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 33458	NICE ID: 10731	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Tislelizumab is in clinical development to treat patients with localised oesophageal squamous cell carcinoma (ESCC). ESCC begins in the food pipe (oesophagus) and may spread to other parts of the body. Localised cancer is when it is still located only in the tissue or organ where it started, and has not spread to nearby lymph nodes or to other parts of the body. Symptoms include difficulty swallowing, persistent indigestion or heartburn, weight loss, pain in the throat, and chronic cough. In the UK it is more common in older people (≥75 years old) and males. There is a need for new treatment options, including immunotherapies, as ESCC progresses rapidly and has high mortality.

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 first-line treatment option for adult patients with localised ESCC.

Proposed Indication

For the treatment of adults with localised oesophageal squamous cell carcinoma (ESCC).[1]

Technology

Description

Tislelizumab (BGB-A317) is a humanised IgG4 anti–PD-1 (programmed death-1) monoclonal antibody specifically designed to minimise binding to FcγR on macrophages. Binding to FcγR on macrophages compromises the anti-tumour activity of PD-1 antibodies through activation of antibody-dependent macrophage-mediated killing of T effector cells. PD-1 is 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 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 paclitaxel, cisplatin, and radiotherapy is currently in phase III clinical development for the treatment of adult patients with localized ESCC (NCT03957590). In this trial, 200 mg of tislelizumab is administered intravenously once every 3-week cycle in combination with intravenously administered paclitaxel and cisplatin, and radiotherapy.[1]

Key Innovation

Tislelizumab, as an antagonist to PD-L1/PD-L2 mediated cell signalling, leads to increased cytokine production and restoration of T-cell activation, resulting in immune-mediated tumour cell death. Tislelizumab has a higher affinity to PD-1 than other anti-PD-1 antibodies, potentially due to its differential PD-1 binding orientation. In early clinical research, tislelizumab has demonstrated promising efficacy results, a manageable safety profile and longer duration of response.[3] There are currently no biological or immunotherapies recommended for the treatment of localised ESCC. Tislelizumab is a innovative immunotherapy for the treatment of ESCC.

Regulatory & Development Status

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

Tislelizumab is in phase II and III clinical development for the treatment of various types of cancers, some of which include:[4]

- Hepatocellular carcinoma
- Muscle-invasive bladder cancer
- Non-small cell lung cancer
- Classical Hodgkin lymphoma
- Diffuse large B-cell lymphoma

Tislelizumab was granted orphan drug designation in the EU in 2020 for the treatment of oesophageal cancer.[5]

Patient Group

Disease Area and Clinical Need

Oesophageal cancer is a type of cancer affecting the food pipe (oesophagus), the long tube that carries food from the mouth to the stomach.[6,7] Most oesophageal cancers can be categorised into two main histologic subtypes: squamous cell carcinoma (SCC) and adenocarcinoma. SCC is the most common oesophageal cancer subtype diagnosed worldwide.[8] Localized cancer is usually located only in the tissue or organ where it started, and has not spread to nearby lymph nodes or to other parts of the body.[9] The most common symptoms of oesophageal cancer include: difficulty swallowing (dysphagia), persistent indigestion or heartburn, weight loss, pain in the throat or behind the breastbone, and persistent cough.[10]

Oesophageal cancer is more common in men than women. It is also more common in older people. In the UK, on average each year around 40% of new cases are in people aged 75 years and over, whereas the condition is very rare in people aged younger than 40 years.[7] There were approximately 9,300 new cases of oesophageal cancer in the UK every year in 2016-2018.[11] Oesophageal cancer was the 7th most common cause of cancer death in the UK in 2018. The crude mortality rate in England was 11.7 per 100,000 in 2018 which accounted for 5% of cancer related deaths.[12] In the 2020 death registration in England and Wales, there were 6,952 deaths due to malignant neoplasm of the oesophagus (C15).[13] In England, in 2020-21, there were 37,125 finished consultant episodes (FCE) for malignant neoplasm of the oesophagus (ICD 10: C15), resulting in 29,505 hospital admissions and 64,565 FCE bed days.[14]

Recommended Treatment Options

Patients with resectable non-metastatic ESCC are given a choice between radical chemotherapy or chemoradiotherapy prior to surgical resection.[15] The patient may have one of these treatments or a combination. Chemotherapy combined with radiotherapy is called chemoradiotherapy. Patients might have it on its own as the main treatment, or before surgery.[16]

Clinical Trial Information

Trial	NCT03957590; A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Tislelizumab (BGB-A317) Versus Placebo in Combination with Concurrent Chemoradiotherapy in Patients with Localized Oesophageal Squamous Cell Carcinoma (ESCC) **Phase III –** Recruiting **Location(s):** China **Primary completion date:** November 2021
Trial Design	Randomised, double-blind, parallel assignment
Population	N=316 (estimated); Subjects aged 18-75 years with measurable and or unmeasurable ESCC with adequate organ function.
Intervention(s)	Tislelizumab 200mg (IV) +paclitaxel 135mg/m^2 (IV) + cisplatin 25mg/m^2 (IV) for a total of 2 cycles + radiotherapy 50.4 Gy in 28 fractions.
Comparator(s)	Placebo to match tislelizumab + paclitaxel 135mg/m^2 (IV) + cisplatin 25mg/m^2 (IV) + radiotherapy
Outcome(s)	Primary outcome measure:

	Progression-free survival (PFS) [Time Frame: From date of randomization up to 4 years, approximately] See trial record for full list of all outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of tislelizumab is not yet known.

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Nivolumab for adjuvant treatment of resected oesophageal or gastro-oesophageal junction cancer (TA746) November 2021
- NICE technology appraisal guidance. Pembrolizumab with platinum- and fluoropyrimidine-based chemotherapy for untreated advanced oesophageal and gastro-oesophageal junction cancer (TA737). October 2021.
- NICE technology appraisal guidance. Nivolumab for previously treated unresectable advanced or recurrent oesophageal cancer (TA707). June 2021.
- NICE clinical guideline. Oesophago-gastric cancer: assessment and management in adults (NG83). January 2018.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy Proposition: 18F-flourodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) as part of radical radiotherapy treatment planning for oesophageal cancer (all ages). Published date to be confirmed.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Oesophageal and Gastric (Adult). B11/S/a.
- 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

- Jaffer A. A., Thomas A. D., David J. B. et al. Esophageal and Esophagogastric Junction Cancers, Version 2.2019, NCCN Clinical Practice Guidelines in Oncology. 2019.[17]
- European Society of Medical Oncology. Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2016[18]
  Allum W.H., Blazeby J.M., Griffin S.M. et al. Guidelines for the management of oesophageal and gastric cancer. 2011.[19]

Additional Information

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