

HEALTH TECHNOLOGY BRIEFING OCTOBER 2021

Tislelizumab in combination with chemotherapy for nasopharyngeal cancer – first line

NIHRIO ID	27171	NICE ID	10687
Developer/Company	Novartis Pharmaceuticals UK Ltd	UKPS ID	663009

Licensing and market availability plans	Currently in phase III clinical trials.
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SUMMARY

Tislelizumab in combination with gemcitabine and cisplatin is in clinical development for the treatment of patients with recurrent or metastatic nasopharyngeal cancer (NPC). NPC is a rare type of cancer that affects the part of the throat connecting the back of the nose to the back of the mouth (the pharynx). It is often difficult to distinguish the symptoms of NPC from less serious conditions and many people do not have any symptoms until the cancer reaches an advanced stage. Therefore, there is a medical need for effective treatments for advanced nasopharyngeal cancer.

Tislelizumab is a protein 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, the medicine stops the cancer switching off these immune cells, thereby increasing the immune system's ability to kill the cancer cells. If licenced, tislelizumab in combination with gemcitabine and cisplatin will provide a first line treatment option for patients with recurrent or metastatic nasopharyngeal cancer.

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.

PROPOSED INDICATION

First line treatment for patients with recurrent or metastatic nasopharyngeal cancer.¹

TECHNOLOGY

DESCRIPTION

Tislelizumab (BGB-A317) is a humanized IgG4 anti-PD-1 monoclonal antibody specifically designed to minimize binding to FcγR on macrophages. Tislelizumab is 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 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, or 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

In the phase III clinical trial (NCT03924986), the following treatment regimen was administered:¹

- Tislelizumab 200mg intravenously (IV) once every 3 weeks (Q3W)
- Gemcitabine 1 g/m² IV infusion on day 1 and day 8 of each 3-week cycle, for 4 to 6 cycles
- Cisplatin 80 mg/m² IV infusion on day 1 of each 3-week cycle, for 4 to 6 cycles.

INNOVATION AND/OR ADVANTAGES

There are currently no biological interventions for the treatment of nasopharyngeal cancer. Currently, the only options are radiotherapy and chemotherapy.^{3,4} Immune checkpoints have previously demonstrated improved benefit when combined with standard chemotherapy regimens.²

Tislelizumab plus chemotherapy met its primary end point of progression-free survival (PFS) at the interim analysis of the phase 3 RATIONALE 309 trial (NCT03924986).⁵

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

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

The EMA granted for tislelizumab orphan designation for the treatment of nasopharyngeal cancer in June 2021.⁶

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 tumours, locally advanced or metastatic urothelial bladder cancer and relapsed or refractory classical Hodgkin lymphoma and in phase III in Non-Small Cell Lung Cancer (NSCLC), hepatocellular carcinoma and advanced esophageal squamous cell carcinoma (ESCC).⁷

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 and in phase II clinical trials for muscle-invasive bladder carcinoma, head and neck cancer and HER2-negative breast cancer.⁸

PATIENT GROUP

DISEASE BACKGROUND

Nasopharyngeal cancer is a rare type of cancer that affects the part of the throat connecting the back of the nose to the back of the mouth (the pharynx). It is distinguished from other types of cancer that also affect the throat, such as laryngeal cancer and oesophageal cancer.⁹ Cancer that spreads from where it started to a distant part of the body is called metastatic cancer.¹⁰ Cancer that has recurred is cancer that has come back, usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour or to another place in the body.¹¹

The exact cause of nasopharyngeal cancer is unknown. Factors can increase the risk of developing the condition include exposure to the Epstein-Barr virus (EBV), family history, diet high in salt-cured foods and occupational exposure to hardwood dust. Nasopharyngeal cancer is more common in some ethnic groups living in the UK. For example, in people of south Chinese or north African descent. It is also more common in men than women.⁹

Symptoms of nasopharyngeal cancer can include: a lump in the neck, hearing loss (usually only in 1 ear), tinnitus, a blocked or stuffy nose, and nosebleeds. It is often difficult to distinguish these symptoms from less serious conditions and many people with nasopharyngeal cancer do not have any symptoms until the cancer reaches an advanced stage.⁹

CLINICAL NEED AND BURDEN OF DISEASE

Cancer of the nasopharynx is rare in Europe, with an annual crude incidence rate of 1.1 per 100,000.¹² In the UK, about 250 people are diagnosed with nasopharyngeal cancer each year.⁹

In 2020-21 there were 1,462 hospital admissions with primary diagnosis malignant neoplasm of nasopharynx (ICD-10 code C11), and 1,581 finished consultant episodes (FCEs), resulting in 2,091 FCE bed days.¹³

The outlook for nasopharyngeal cancer depends on age, general health and how advanced the condition is when diagnosed. Overall, about 50 out of every 100 people (50%) diagnosed with nasopharyngeal cancer will live for five years or more after diagnosis. Survival rates are better for younger people, but worse for older people. Around 70 out of 100 (70%) people under 45 years of age, and 35 out of 100 (35%) people aged 65 to 74, will live for five years or more after being diagnosed with nasopharyngeal cancer.¹⁴

In England and Wales in 2020 there were 143 deaths with malignant neoplasm of nasopharynx (ICD-10 code C11) recorded as the underlying cause.¹⁵

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

The optimal treatment strategy of patients with advanced nasopharyngeal cancer should be discussed in a multidisciplinary team. Radiation therapy (RT) is the mainstay of treatment and is an essential component of curative-intent treatment of non-disseminated nasopharyngeal

cancer. Stage I disease is treated by RT alone, while stage III, IVA, IVB disease are treated by RT with concurrent chemotherapy.

In metastatic NPC, palliative chemotherapy should be considered for patients with adequate performance status. Platinum combination regimens are commonly used as first-line therapy since cisplatin represents the most effective drug.¹²

CURRENT TREATMENT OPTIONS

NICE guidance states people with locally advanced (stage II and above) nasopharyngeal cancer should be offered intensity-modulated radiation therapy with concomitant chemotherapy. Adjuvant or neo-adjuvant chemotherapy for people with locally-advanced (stage II and above) nasopharyngeal cancer should be considered.¹⁶

PLACE OF TECHNOLOGY

If licenced, tislelizumab in combination with gemcitabine and cisplatin will provide a first line treatment option for patients with recurrent or metastatic nasopharyngeal cancer.

CLINICAL TRIAL INFORMATION

Trial	BGB-A317-309; NCT03924986 ; Phase 3, Double-Blind, Randomized Study to Compare the Efficacy and Safety of Tislelizumab Combined With Chemotherapy Versus Chemotherapy as First-Line Treatment for Recurrent or Metastatic Nasopharyngeal Cancer Phase III - Recruiting Location(s): China, Taiwan and Thailand Primary completion date: August 2021
Trial design	Randomised, parallel assignment, double blind.
Population	N=256 (estimated), treatment-naive for recurrent or metastatic nasopharyngeal cancer (NPC), aged between 18 to 75 years.
Intervention(s)	200mg of Tislelizumab administered intravenously every 3 weeks (Q3W) combined with 1g/m ² of gemcitabine administered as an IV infusion on day 1 and day 8 (within 30 minutes) of each 3-week cycle for 4 to 6 cycles plus 80mg/m ² of cisplatin administered on day 1 (over 4 hours) of each 3 week cycle, for 4 to 6 cycles.
Comparator(s)	Matched tislelizumab placebo combined with gemcitabine plus cisplatin.
Outcome(s)	Primary outcome(s); - Progression-free Survival [Time Frame: up to 2 years.] 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 guideline. Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over (NG36). June 2018.

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

- SEOM clinical guideline in nasopharynx cancer. 2017.¹⁷
- Nasopharyngeal carcinoma: United Kingdom National Multidisciplinary Guidelines. 2016.¹⁸
- Nasopharyngeal cancer: EHNS-ESMO-ESTRO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2012.¹²

ADDITIONAL INFORMATION

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