NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
March 2023

Toripalimab with chemotherapy for previously untreated recurrent or metastatic nasopharyngeal carcinoma

Company/Developer	Shanghai Junshi Bioscience Co Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 30993	NICE TSID: 11857	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Toripalimab is in clinical development for the first-line treatment of recurrent/metastatic nasopharyngeal carcinoma (NPC). NPC is a rare cancer which affects the part of the throat connecting the back of the nose to the back of the mouth (the pharynx). It can be difficult to recognise, with symptoms often presenting once the cancer has reached an advanced stage. Symptoms can include nosebleeds, headaches, hearing loss and a lump in the neck that persists for more than three weeks. Surgery is not usually an option to treat NPC due to affected area being difficult to access. There are no biological agents that are used to treat NPC, with the current standard treatment in the UK being chemotherapy and/or radiotherapy.

Toripalimab is administered by injection and is a monoclonal antibody (a type of protein) designed to recognise and attach to a protein called 'programmed death-1' (PD-1), that is expressed on the surface of T cells (types of cells of the immune system). Cancer cells evade the immune system by expressing programmed death ligand-1 (PD-L1) which binds to PD-1. This prevents the immune system from recognising and attacking the cancer cells. By attaching to the PD-1 protein, toripalimab is expected to remove this suppressive effect, allowing the immune cells to recognise and kill the cancer cells. This is expected to slow down the growth of the cancer. If licensed, toripalimab would be a novel treatment option for NPC.

Proposed Indication

Toripalimab in combination with cisplatin and gemcitabine as first-line treatment for adults with recurrent or metastatic nasopharyngeal carcinoma (NPC).[1]

Technology

Description

Toripalimab is a humanized immunoglobulin G4 anti-PD-1 monoclonal antibody with potential immune checkpoint inhibitory and antineoplastic activities.[2] It blocks PD-1 interactions with its ligands, PD-L1 and PD-L2 which are expressed on the surface of T cells, and can support enhanced receptor internalisation (endocytosis function).[3] Blocking PD-1 interactions with PD-L1 and PD-L2 prevents the activation of PD-1 and its downstream signalling pathways. This may restore immune function through the activation of both T cells and T-cell-mediated immune responses against tumour cells.[3,4]

Toripalimab in combination with cisplatin and gemcitabine is in clinical development for the first-line treatment of recurrent/metastatic NPC. In phase III trial (NCT03581786), toripalimab is administered by injection at a dose of 240mg every three weeks (Q3W) before chemotherapy which is given Q3W for up to 6 cycles.[1]

Key Innovation

There are currently no biological interventions for the treatment of NPC. Currently, the only options are radiotherapy and chemotherapy.[5] Immune checkpoints inhibitors such as toripalimab have demonstrated improved benefit when combined with standard chemotherapy regimens. Clinical trials (NCT02915432, NCT03581786) have demonstrated strong safety and efficacy results for toripalimab monotherapy and have demonstrated superior clinical benefit when adding toripalimab to the standard regimen of cisplatin and gemcitabine.[6] If licensed, toripalimab would be the first biological agent used to treat NPC.

Regulatory & Development Status

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

Toripalimab is currently in phase II/III trials for several indications including:[7]

- Hepatocellular carcinoma
- Non-small cell lung cancer
- Biliary tract cancer
- Laryngeal cancer
- Digestive system carcinoma
- Primary peritoneal cancer
- Mucosal melanoma

Patient Group

Disease Area and Clinical Need

NPC is a rare type of cancer that affects the nasopharyngeal mucosal epithelium which is in the part of the throat connecting the back of the nose to the back of the mouth (the pharynx).[3,5] It can often be difficult to recognise NPC because the symptoms are similar to other, less serious conditions. Also, many people with NPC don't have any symptoms until the cancer reaches an advanced stage. Symptoms of NPC can include: a lump in the neck that does not go away after 3 weeks, hearing loss (usually only in 1 ear), tinnitus, nosebleeds, headaches, double vision and numbness in the bottom part of the face.[5] The exact cause of NPC is unknown, however there are risk factors which can increase the risk of developing this cancer. These include having a diet very high in salt-cured meats and fish, smoking, and regularly coming into contact with hardwood dust or formaldehyde. The human papilloma virus and Epstein Barr virus are also thought to be a risk factor for developing NPC.[5,8] Metastatic NPC is characterised by the cancer having spread to surrounding areas such as the lungs and recurrent cancer is when the cancer has come back, usually after a period of time during which the cancer could not be detected.[9,10]

In the UK, about 260 people are diagnosed with NPC each year. About three times as many men as women are affected by NPC, with the average age at diagnosis being 50. In England, almost 75% of people diagnosed with NPC will live for at least 1 year after diagnosis, with almost 50% living for 5 years or more after diagnosis.[5] In England 2021-22, there were 1,615 finished consultant episodes (FCE) and 1,475 admissions for malignant neoplasm of the nasopharynx (ICD-10 code C11), which resulted in 1,042 day cases and 2,635 FCE bed days.[11]

Recommended Treatment Options

Advanced NPCs are often treated with a combination of chemotherapy and radiotherapy. They are often curable if the cancer hasn't spread beyond the head and neck region. Surgery is not usually used to treat NPC as it is difficult to access the affected area.[5] NICE guidance states people with locally advanced (stage II and above) NPC should be offered intensity-modulated radiation therapy with concomitant chemotherapy. Adjuvant or neo-adjuvant chemotherapy for people with locally advanced (stage II and above) NPC should be considered.[12]

Clinical Trial Information

Trial	**JUPITER-02;** NCT03581786; A Phase III, Randomized, Placebo Controlled, Multicenter, Double-Blind Study Comparing Toripalimab Injection (JS001) Combined With Chemotherapy Versus Placebo Combined With Chemotherapy for Recurrent or Metastatic Nasopharyngeal Cancer **Phase III** – active, not recruiting **Location(s):** China **Primary completion date:** May 2020
Trial Design	Randomised, placebo-controlled, double-blind, parallel assignment
Population	N=289 (actual); patients aged 18 to 75 years old with histologically/cytologically confirmed recurrent or metastatic NPC and no previous chemotherapy
Intervention(s)	Toripalimab 240mg IV injection + gemcitabine 1000mg/m^2 IV + cisplatin 80mg/m^2 IV
Comparator(s)	Placebo IV injection + gemcitabine 1000mg/m^2 IV + cisplatin 80mg/m^2 IV
Outcome(s)	**Primary outcome measures:**

	• IRC-assessed progression-free survival (PFS) according to RECIST v1.1 [time frame: up to 2 years]: To evaluate the efficacy of JS001 plus chemotherapy compared with placebo plus chemotherapy, as measured by IRC-assessed PFS according to RECIST v1.1 in all patients. See trial record for full list of other outcomes.
Results (efficacy)	At the prespecified interim PFS analysis, a significant improvement in PFS was detected in the toripalimab arm compared to the placebo arm: median PFS of 11.7 versus 8.0 months, hazard ratio (HR) = 0.52 (95% confidence interval (CI): 0.36–0.74), P = 0.0003. An improvement in PFS was observed across key subgroups, including PD-L1 expression. As of 18 February 2021, a 40% reduction in risk of death was observed in the toripalimab arm compared to the placebo arm (HR = 0.603 (95% CI: 0.364–0.997)).[13]
Results (safety)	The incidence of grade ≥3 adverse events (AEs) (89.0 versus 89.5%), AEs leading to discontinuation of toripalimab/placebo (7.5 versus 4.9%) and fatal AEs (2.7 versus 2.8%) was similar between the two arms; however, immune-related AEs (irAEs) (39.7 versus 18.9%) and grade ≥3 irAEs (7.5 versus 0.7%) were more frequent in the toripalimab arm.[13]
Clinical Trial Information	
Trial	NCT03474640; A Phase 1, Multicenter, Open-label Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of TAB001 in Subjects With Advanced Malignancies **Phase I** – active, not recruiting **Location(s):** USA **Primary completion date:** August 2022
Trial Design	Non-randomised, open label, sequential assignment
Population	N=198 (actual); patients aged 18 years and older with histologically or cytologically documented, incurable, or metastatic solid tumour that has progressed on, or been intolerant to, all standard systemic therapy options
Intervention(s)	Toripalimab 80mg, 240mg or 480mg IV infusion
Comparator(s)	No comparator
Outcome(s)	**Primary outcome measures:** • Number of participants with treatment-related adverse events as assessed by CTCAE v4.0 [time frame: through day 90 of last dose]. See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-
Clinical Trial Information	
Trial	NCT02915432; A Multi-Center, Open Label Phase Ib/II Clinical Study to Evaluate JS001 in Patients With Advanced Gastric Adenocarcinoma, Esophageal

	Squamous Cell Carcinoma, Nasopharyngeal Carcinoma and Head and Neck Squamous Cell Carcinoma **Phase I/II** – active, not recruiting **Location(s):** China **Primary completion date:** February 2020
Trial Design	Non-randomised, open label, factorial assignment
Population	N=401 (actual); patients aged 18 to 75 years old with histologically or cytologically confirmed advanced and/or metastatic gastric adenocarcinoma, oesophageal squamous cell carcinoma, NPC, or head and neck squamous cell carcinoma
Intervention(s)	Toripalimab injection administered at a dose of 240mg or 360mg in combination with chemotherapy, or toripalimab monotherapy at a dose of 3mg/kg
Comparator(s)	No comparator
Outcome(s)	**Primary outcome measures:** • Objective response rate (ORR) evaluated based on Response Evaluation Criteria in Solid Tumours (RECIST 1.1) [time frame: up to 1.5 approximately years]: To preliminarily evaluate the anti-tumour activity of toripalimab injection in treating advanced gastric adenocarcinoma, oesophageal squamous cell carcinoma, NPC, and head and neck squamous cell carcinoma. See trial record for full list of other outcomes.
Results (efficacy)	In cohort 2, chemotherapy-naive patients received toripalimab (360 mg d1, Q3W) plus capeOX (oxaliplatin 130 mg/m2 d1, capecitabine 1000 mg/m2 bid d1-d14, Q3W) as first-line treatment. The objective response rate was 66.7% and disease control rate was 88.9%.[14]
Results (safety)	Grade 3 or higher treatment-related adverse events was 38.9% in cohort 2.[14]

Estimated Cost

The cost of toripalimab is not yet known.

Relevant Guidance

NICE Guidance

- NICE guidance in development. Tislelizumab with chemotherapy for untreated recurrent or metastatic nasopharyngeal cancer TS ID 10687 (GID-TA11100). Expected date of issue to be confirmed.
- 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

- Spanish Society for Medical Oncology, Spanish Group for the Treatment of Head and Neck Tumours (TTCC). SEOM-TTCC clinical guideline in nasopharynx cancer. 2021.[15]
- European Society for Medical Oncology, EURACAN. Nasopharyngeal carcinoma: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2021.[16]
- Simo R, Robinson M, Lei M, Sibtain A, Hickey S. Nasopharyngeal carcinoma: United Kingdom National Multidisciplinary Guidelines. 2016.[17]

Additional Information

Shanghai Junshi Bioscience Co Ltd indicated on 24th November 2022 that they have submitted a single MAA to the MHRA to cover two indications: toripalimab in combination with cisplatin and gemcitabine for the first-line treatment of recurrent or metastatic NPC and toripalimab in combination with paclitaxel and cisplatin for the first-line treatment of unresectable, locally advanced/recurrent or metastatic ESCC. Two briefings are being submitted in March 2023 to cover the single MAA. This briefing is for NPC and the ESCC briefing will be NIHRIO ID 36077.

Shanghai Junshi Bioscience Co Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

References

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