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Newcastle University

Health Technology Briefing
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Atezolizumab-tiragolumab for locally advanced, recurrent, or metastatic PD-L1 selected solid tumours

Company/Developer	Roche Products Ltd

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 37233	NICE ID: Not available	UKPS ID: 671522

Licensing and Market Availability Plans

Currently in clinical development.

Summary

Atezolizumab-tiragolumab is currently in clinical development for treating adults with Programmed death ligand 1 (PD-L1)-selected solid tumours whose disease is locally advanced, recurrent or metastatic. Cancer is a condition where cells in a specific part of the body grow and reproduce uncontrollably. These cancerous cells can invade and destroy healthy tissue, including organs. One in every two people will develop cancer in their lifetime. PD-1 is a protein that normally acts as an "off switch," helping to stop immune cells from attacking other cells in the body. It does this by attaching to PD-L1, a protein found on some normal (and cancer) cells. PD-L1-select tumours have high amounts of PD-L1 so they can turn T cells off so they can't attack the cancer cells. This allows cancer cells to evade immune attack.

Atezolizumab is an immunotherapy drug that helps the body's immune system track down and fight cancer. It works by blocking PD-L1 and is part of a group of drugs that help extend the amount of time a person can live with cancer or live without their cancer getting worse. Tiragolumab is a type of targeted drug therapy that may increase anti-tumour responses when combined with other immunotherapies. If licensed, atezolizumab-tiragolumab may give a new treatment option to patients with locally advanced, recurrent or metastatic PD-L1 solid tumours.

Proposed Indication

Treating adults with histologically confirmed PD-L1-selected solid tumours whose disease is locally advanced, recurrent or metastatic.[1]

Technology

Description

Programmed death-ligand 1 (PD-L1) may be expressed on tumour cells and/or tumour-infiltrating immune cells and can contribute to the inhibition of the antitumour immune response in the tumour microenvironment. Binding of PD-L1 to the PD-1 and B7.1 receptors found on T-cells and antigen presenting cells suppresses cytotoxic T-cell activity, T-cell proliferation and cytokine production.[2]

Atezolizumab is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to PD-L1 and provides a dual blockade of the PD-1 and B7.1 receptors, releasing PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the antitumour immune response without inducing antibody-dependent cellular cytotoxicity. Atezolizumab spares the PD-L2/PD-1 interaction allowing PD-L2/PD-1 mediated inhibitory signals to persist.[2]

Tiragolumab is a monoclonal antibody designed to bind with TIGIT, a protein receptor on immune cells. Tiragolumab works as an immune amplifier, by potentially enhancing the body's immune response. By binding to TIGIT, tiragolumab blocks its interaction with a protein called poliovirus receptor (PVR, or CD155) that can suppress the body's immune response. Blockade of TIGIT and PD-L1 may synergistically enable the re-activation of T cells and enhance NK cell anti-tumour activity.[3]

Atezolizumab-tiragolumab as a fixed dose combination (FDC) is currently in phase II clinical development for treating adults aged 18 and over with PD-L1-selected solid tumours whose disease is locally advanced, recurrent, or metastatic (SKYSCRAPER-11, NCT05661578). Participants will receive 600 mg tiragolumab and 1200 mg atezolizumab as an intravenous, FDC on day one of each 21-day cycle until disease progression, loss of clinical benefit or unacceptable toxicity.[1]

Key Innovation

Cancer can be difficult to treat if it spreads to other organs in the body However, a new type of medicines that helps the body's natural defence mechanism (immune system) to attack the cancerous cells (immunotherapies) have shown encouraging results for the treatment of cancer.[4] Over the past decade, immune checkpoint inhibitors (ICIs) have emerged as a revolutionary cancer treatment modality, offering long-lasting responses and survival benefits for a substantial number of cancer patients. However, the response rates to ICIs vary significantly among individuals and cancer types, with a notable proportion of patients exhibiting resistance or showing no response. Therefore, dual ICI combination therapy has been proposed as a potential strategy to address these challenges.[5] This is the first time that the combination of atezolizumab and tiragolumab will be administered to patients in one bottle. This combination is being explored to try and simplify the administration of the two drugs and reduce the time that patients spend in the clinic.[4] In the CITYSCAPE study, atezolizumab-tiragolumab showed a clinically meaningful improvement in objective response rate and progression-free survival compared with placebo plus atezolizumab in patients with chemotherapy-naive, PD-L1-positive, recurrent or metastatic NSCLC. Atezolizumab-tiragolumab was well tolerated, with a safety profile generally similar to that of atezolizumab alone.[6] This suggests that, if licensed, atezolizumab-tiragolumab in an FDC will provide another treatment option for people with advanced, recurrent or metastatic PD-L1-selected solid tumours.

Regulatory & Development Status

Atezolizumab-tiragolumab FDC does not currently have marketing authorisation in the EU/UK for any indication.

Tiragolumab does not currently have marketing authorisation in the EU/UK for any indication.

Atezolizumab has EU/UK authorisation for the following indications:[2]

- urothelial carcinoma;
- early-stage non-small cell lung cancer (NSCLC);
- metastatic NSCLC;
- small cell lung cancer (SCLC);
- triple negative breast cancer; and
- hepatocellular carcinoma.

Atezolizumab-tiragolumab (not as an FDC) is currently in phase III clinical development for multiple indications, including:[7]

- oesophageal carcinoma;
- NSCLC;
- hepatocellular carcinoma;
- SCLC; and
- recurrent/metastatic PD-L1 positive squamous cell carcinoma of the head and neck.

Atezolizumab-tiragolumab has the following regulatory designations:[3]

- A breakthrough therapy by the US FDA for PD-L1- high NSCLC in January 2021.

Patient Group

Disease Area and Clinical Need

Cancer is a condition where cells in a specific part of the body grow and reproduce uncontrollably. The cancerous cells can invade and destroy surrounding healthy tissue, including organs.[8] The main signs and symptoms of cancer are: coughing; chest pain and breathlessness; changes in bowel habits; bloating; bleeding; lumps; moles; unexplained weight loss; tummy or back pain; indigestion and heartburn; itchy or yellow skin; and feeling tired and unwell.[9] Cancer is recurrent when it returns after treatment. This may occur because the original treatment did not get rid of all the cancer cells and those left behind grew into a new tumour or some cancer cells have spread elsewhere in the body and started growing there to form a tumour.[10] Advanced cancers can be locally advanced or metastatic. Locally advanced means that cancer has grown outside the body part it started in but has not yet spread to other parts of the body, while metastatic cancers have spread from where they started to other parts of the body.[11] PD-L1 is a type 1 transmembrane protein that belongs to the B7 ligands family. Expression of PD-L1 on tumour cells promotes down-regulation and self-tolerance of the immune system from rejecting the tumour by supressing T-cell inflammatory activity through binding to the regulatory T-cell receptor, PD-1.[12]

One in two people will develop some form of cancer during their lifetime.[8] A person's risk of developing cancer depends on many factors, including age, genetics and exposure to risk factors. Smoking is the largest cause of cancer in the UK, accounting for 15% of all cancer cases. There are around 375,000 new cancer cases in the UK every year, which is around 1,000 every day (2016-2018). Together, breast, prostate, lung and bowel cancers accounted for over half (53%) of all new cancer cases in the UK in 2016-2018. Incidence rates for all cancers combined in the UK are highest in people aged 85 to 89 (2016-2018). There are around 167,000 cancer deaths in the UK every year, which is nearly 460 every day (2017-2019). Together, lung,

bowel, breast and prostate cancers accounted for almost half (45%) of all cancer deaths in the UK in 2017-2019. Around a fifth of all cancer deaths are from lung cancer.[13]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) currently recommends atezolizumab, alone or in combination with nab-paclitaxel, or pembrolizumab for the treatment of different types of PD-L1-positive cancers.[14-16]

Clinical Trial Information

Trial	**SKYSCRAPER-11,** NCT05661578, EudraCT2022-001157-23**;** A Phase II, Single-Arm, Open-Label Study Evaluating the Safety and Pharmacokinetics of the Intravenous Fixed-Dose Combination (IV FDC) of Tiragolumab and Atezolizumab in Participants With Locally Advanced, Recurrent or Metastatic Solid Tumors **Phase II:** Recruiting **Locations:** 3 EU countries, US, Canada and other countries. **Primary completion date:** February 2025
Trial Design	Single group assignment, open-label
Population	N=60 (estimated); males and females aged 18 and over with histologic documentation of locally advanced, recurrent, or metastatic malignancy; PD-L1 selected tumours, as determined by the VENTANA PD-L1 immunohistochemistry assay. No prior treatment with checkpoint inhibitor therapies.
Intervention(s)	600 mg tiragolumab and 1200 mg atezolizumab FDC (intravenously administered) on day one of each 21-day cycle until disease progression, loss of clinical benefit or unacceptable toxicity.
Comparator(s)	-
Outcome(s)	Primary outcome measure: Percentage of participants with adverse events (AEs) [Time frame: Up to approximately 24 months] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of atezolizumab-tiragolumab FDC is currently unknown.

Relevant Guidance

NICE Guidance

- NICE Technology appraisal guidance in development. Avelumab for untreated PD-L1 positive recurrent or metastatic non-small-cell lung cancer. [ID1261]. Expected publication date TBC.

- NICE Technology appraisal guidance in development. Tiragolumab with atezolizumab for untreated PD-L1-positive advanced non-small-cell-lung cancer. [ID5122]. Expected publication date TBC.
- NICE Technology appraisal guidance. Atezolizumab for untreated PD-L1-positive advanced urothelial cancer when cisplatin is unsuitable. [TA739]. Published October 2021.
- NICE Technology appraisal guidance. Atezolizumab with nab-paclitaxel for untreated PD-L1-positive, locally advanced or metastatic, triple-negative breast cancer. [TA639]. Published July 2020.
- NICE Technology appraisal guidance. Pembrolizumab for untreated PD-L1-positive metastatic non-small cell lung cancer. [TA531]. Published July 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

- Hendriks LE, Kerr KM, Menis J, Veronesi G, Reck M, et al. Non-oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. 2023.[17]
- Lordick F, Carneiro F, Cascinu S, Vogel A, Smyth EC, et al. Gastric cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. 2022.[18]
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Additional Information

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