

Health Technology Briefing November 2022

Atezolizumab with cabozantinib for treating metastatic non-small-cell lung cancer after platinum-containing chemotherapy and one programmed death-ligand 1 checkpoint inhibitor

Company/Developer

Ipsen Ltd

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 30213

NICE ID: 11812

UKPS ID: 664577

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Atezolizumab in combination with cabozantinib is in development for the treatment of metastatic non-small-cell lung cancer (NSCLC). NSCLC is the most common type of lung cancer in the UK. It causes symptoms such as a persistent cough, coughing up blood, recurrent or long chest infections, unexplained breathlessness and wheezing, and hoarseness. Metastatic NSCLC is when the cancer starts in the lungs and then spreads to other areas of the body. Current treatment options for NSCLC patient who have progressed after treatment are limited.

Atezolizumab is an antibody, which binds to a protein called programmed death-ligand 1 (PDL-1) to stop it from working. PDL-1 is common in cancer cells and prevents immune cells from attacking the cancer. By binding to PDL-1 atezolizumab increases the immune response against cancer cells. Atezolizumab is administered by intravenous (in the vein) infusion once every 21 days. Cabozantinib inhibits a protein called tyrosine kinase, a protein that promotes cancer cell growth and division, to reduce the growth and spread of cancer. It is administered orally once daily. Together they may have enhanced effectiveness against NSCLC and provide an additional treatment option for patients with metastatic NSCLC.

Proposed Indication

For the treatment of patients with metastatic non-small-cell lung cancer (NSCLC), with no sensitising epidermal growth factor receptor (EGFR) mutation or anaplastic lymphoma kinase (ALK) translocation, who have progressed following treatment with platinum-containing chemotherapy and anti-programmed death-ligand 1/programmed cell death ligand 1 (anti-PD-L1/PD-1) antibody, administered concurrently or sequentially.¹

Technology

Description

Atezolizumab (Tecentriq) is a monoclonal antibody that binds to a protein called PD-L1, which is present on many cancer cells. PD-L1 switches off immune cells that would otherwise attack cancer cells. By attaching to PD-L1, atezolizumab reduces its effects and so increases the immune system's ability to attack cancer cells and thereby slows down progression of the disease.²

Cabozantinib (Cabometyx) is a tyrosine kinase inhibitor meaning it blocks the activity of enzymes known as tyrosine kinases. These enzymes can be found in certain receptors in cancer cells, where they are involved in activating processes that include cell division and the growth of new blood vessels to supply the cancer. By blocking the activity of these enzymes in cancer cells, cabozantinib reduces the growth and spread of the cancer.³ Cabozantinib also promotes the immune response and may enhance the efficacy of PD-L1/PD-1 inhibitors.⁴

The combination of atezolizumab and cabozantinib is in development for the treatment of metastatic NSCLC that has progressed following treatment with platinum-containing chemotherapy and an anti-PD-L1/PD-1 antibody. In the phase III clinical trial (CONTACT-01, NCT04471428) atezolizumab is administered on day 1 of each 21-day cycle as 1200mg intravenous (IV) infusion and 40mg oral cabozantinib is administered days 1-21 of each cycle.¹

Key Innovation

There is an unmet need for metastatic NSCLC therapies that have higher clinical activity, as current monotherapies have modest clinical activity. Cabozantinib promotes the immune response and may enhance the efficacy of PD-L1/PD-1 inhibitors, such as atezolizumab.⁴

Regulatory & Development Status

Atezolizumab has marketing authorisation in the UK for:⁵

- Urothelial carcinoma
- NSCLC
- Small Cell Lung Cancer (SCLC)
- Breast cancer
- Hepatocellular carcinoma

Cabozantinib has marketing authorisation in the UK for:^{3,6}

- Progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma
- Advanced renal cell carcinoma (as monotherapy)
- Hepatocellular carcinoma
- Advanced renal cell carcinoma (in combination with nivolumab)

- Locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory to or not eligible for radioactive iodine (RAI) who have progressed during or after prior systemic therapy

Atezolizumab in combination with cabozantinib is in phase II/III clinical development for neuroendocrine tumours, anaplastic thyroid cancer and oesophageal cancer, amongst other conditions⁷

Patient Group

Disease Area and Clinical Need

NSCLC is one of two types of lung cancer, and makes up approximately 80-85% of lung cancers in the UK.⁸ Metastatic cancer is when the cancer begins in one part of the body, before spreading to other areas.⁹ NSCLC is grouped into three types: adenocarcinoma, squamous cell carcinoma and large cell lung cancer, depending on the cells involved.¹⁰ Lung cancer symptoms include persistent cough, chest infection that does not improve or repeated chest infections, unexplained breathlessness and wheezing, coughing up blood, chest or shoulder pain, and a hoarse voice. Other symptoms include loss of appetite, unexplained weight loss and tiredness.¹¹ There are a number of risk factors for developing lung cancer, including ageing, lowered immunity, air pollution and exposure to certain chemicals, however smoking is the most common cause of lung cancers.¹²

In England, 2021-22, there were 119,396 finished consultant episodes (FCE) of malignant neoplasm of bronchus and lung (ICD-10 code C34), resulting in 75,969 day cases and 206,640 FCE bed days.¹³ Based on NSCLC accounting for ~80-85% of UK lung cancers this results in an estimated 95,517-101,487 FCE, 60,775-64,574 day cases and 165,312-175,644 FCE bed days.^{8,13} There are no UK-wide survival/mortality statistics available for different stages of lung cancer however, based on survival in England for people diagnosed between 2013-17, around 5% of people with stage 4 (metastatic) lung cancer will survive for 5 years or more.^{14,15}

Recommended Treatment Options

NICE recommends the following pharmacological therapies for patients with metastatic NSCLC who have progressed following treatment:¹⁶

- Docetaxel, pembrolizumab, atezolizumab and nivolumab for squamous NSCLC (PD-L1 <50%)
- Docetaxel for squamous NSCLC (PD-L1 ≥50%)
- Pembrolizumab, atezolizumab, nivolumab and docetaxel with or without nintedanib for non-squamous NSCLC (PD-L1 <50%)
- Docetaxel with or without nintedanib for non-squamous NSCLC (PD-L1 ≥50%)

Clinical Trial Information

Trial

CONTACT-01; [NCT04471428](#); [EudraCT 2020-000100-11](#); A Phase III, Multicenter, Randomized, Open-Label, Controlled Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Atezolizumab Given in Combination With Cabozantinib Versus Docetaxel Monotherapy in Patients With Metastatic Non-Small Lung Cancer Previously Treated With an Anti-PD-L1/PD-1 Antibody and Platinum-Containing Chemotherapy
Phase III – Active, not recruiting
Location(s): 9 EU countries, UK, USA and other countries
Primary completion date: May 2022

Trial Design	Randomised, open label, parallel assignment.
Population	N=366 (actual); aged 18 years and older; metastatic NSCLC; documented radiographic disease progression during or following treatment with platinum-containing chemotherapy and anti-PD-L1/PD-1 antibody, administered concurrently or sequentially for metastatic NSCLC
Intervention(s)	40mg oral cabozantinib once daily on days 1-21 of each cycle and 1200mg IV infusion of atezolizumab on day 1 of each cycle.
Comparator(s)	Docetaxel
Outcome(s)	Primary outcome measure: Overall Survival (OS) [Time frame: Up to approximately 43 months] Overall survival (OS) after randomization, defined as the time from randomization to death from any cause. See trial record for full list of other outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Atezolizumab 1200mg/20ml concentrate for solution for infusion (1 vial) has an NHS indicative price of £3,807.69.¹⁷

Cabozantinib 40mg tablets (30 tablets) has an NHS indicative price of £5,143.00.¹⁷

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (TA520). May 2018.
- NICE technology appraisal guidance. Nintedanib for previously treated locally advanced, metastatic, or locally recurrent non-small-cell lung cancer (TA347). July 2015.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.
- NICE quality standard. Lung cancer in adults (QS17). December 2019.

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

- NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 2. 2021.¹⁸
- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. 2020 update.¹⁹
- Scottish Intercollegiate Guidelines Network. Management of lung cancer (SIGN 137). 2014.²⁰

Additional Information

References

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