

Health Technology Briefing August 2022

Atezolizumab for previously untreated recurrent or advanced non-small cell lung cancer unsuitable for platinum-doublet chemotherapy

Company/Developer

Roche Ltd.

New Active Substance

Significant Licence Extension (SLE)

NIHRIO ID: 28867

NICE ID: 11785

UKPS ID: 665154

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Atezolizumab is in development for the treatment of locally advanced, recurrent, or metastatic non-small cell lung cancer (NSCLC) who are deemed unsuitable for platinum-doublet chemotherapy. NSCLC is the most common form of lung cancer. Metastatic NSCLC describes tumours that have spread from the lungs to other parts of the body. Smoking tobacco is the cause of most lung cancers and the biggest risk factor. Other risk factors include second-hand smoke, exposure to workplace carcinogens, radiation exposure, environmental pollution, and family history of lung cancer. Current standard of care treatment can help to control the cancer for some time and reduce symptoms, however, sometimes NSCLC can continue to grow despite chemotherapy and immunotherapy.

Atezolizumab is an intravenously (IV) administered monoclonal antibody, a type of protein designed to attach to a protein called PD-L1, which is present on many cancer cells. PD-L1 acts to switch off immune cells that would otherwise attack cancer cells. By attaching to PD-L1 and reducing its effects, atezolizumab increases the immune system's ability to attack cancer cells and thereby slow down progression of the disease. If licensed, atezolizumab will provide an additional treatment option for patients with locally advanced, recurrent, or metastatic NSCLC who are deemed unsuitable for platinum-doublet chemotherapy.

Proposed Indication

Treatment naïve patients with locally advanced or recurrent or metastatic non-small cell lung cancer (NSCLC) who are deemed unsuitable for platinum-doublet chemotherapy.¹

Technology

Description

Atezolizumab (Tecentriq) is a monoclonal antibody and immune checkpoint inhibitor. Atezolizumab binds to programmed death-ligand 1 (PD-L1) to help immune cells kill cancer cells and is used to treat many different types of cancer that express PD-L1.² 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. Atezolizumab 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.³

Atezolizumab is currently in phase III clinical development for the first-line treatment of patients with locally advanced, recurrent, or metastatic NSCLC (NCT03191786). In this trial, participants receive atezolizumab 1200 milligrams (mg) intravenous (IV) infusion on day 1 of each 21-day cycle.¹

Key Innovation

Atezolizumab does not affect the interaction between PD-1 and its other ligand PD-L2. Keeping the PD-L2/PD-1 interaction intact may preserve a component of peripheral immune homeostasis, which is thought to reduce the risk of severe inflammatory lung toxicity.⁴ Atezolizumab has shown a clinical benefit in the first-line setting of NSCLC regardless of histology, PDL-1 expression, and EGFR or KRAS mutation status. High rates of response and tolerability have been demonstrated.⁵ Survival rates for advanced lung cancer remain poor despite currently available treatments, with only around 5% of people with stage IV lung cancer surviving for 5 years or more after diagnosis.⁶ There is therefore still an unmet need for further effective treatment options.

If licensed, atezolizumab will provide an additional treatment option for treatment naïve patients with locally advanced, recurrent, or metastatic NSCLC who are deemed unsuitable for platinum-doublet chemotherapy.

Regulatory & Development Status

Atezolizumab monotherapy has Marketing Authorisation in the EU/UK for the following indications:³

- The treatment of adult patients with locally advanced or metastatic urothelial carcinoma after prior platinum-containing chemotherapy, or who are considered cisplatin ineligible, and whose tumours have a PD-L1 expression \geq 5%
- Adjuvant treatment following complete resection for adult patients with Stage II to IIIA NSCLC whose tumours have PD-L1 expression on \geq 50% of tumour cells and whose disease has not progressed following platinum-based adjuvant chemotherapy
- The first-line treatment of adult patients with metastatic NSCLC whose tumours have a PD-L1 expression \geq 50% of tumour cells or \geq 10% tumour-infiltrating immune cells and who do not have EGFR mutant or ALK-positive NSCLC

- The treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy

Atezolizumab is also in phase II/III development for various cancer indications, including:⁷

- Cervical cancer
- Urinary tract cancer
- Gastro-intestinal cancers
- Hepatocellular carcinoma
- Small cell lung cancer
- Thymic carcinoma
- Head and neck tumours
- Solid tumours

Patient Group

Disease Area and Clinical Need

NSCLC is the most common form of lung cancer. Around 80 to 85% of lung cancer cases in the UK are NSCLC. The three main types are adenocarcinoma, squamous cell carcinoma and large cell carcinoma.⁸ Smoking tobacco is the cause of most lung cancers and the biggest risk factor. Other risk factors include second-hand smoke, exposure to workplace chemicals, radiation exposure, air pollution and family history of lung cancer.⁹ Symptoms of lung cancer include a cough, repeated chest infections, breathlessness, unexplained pain, weight loss or tiredness. However, lung cancer may not always have symptoms early on. Sometimes it is found by chance when a person is having tests for another condition.¹⁰ Locally advanced lung cancer has usually spread to nearby lymph nodes. It may also have spread to tissues and structures further from the lung, but it has not spread to other parts of the body. Metastatic lung cancer has spread further outside the lung to other parts of the body.¹¹

Lung cancer is the third most common cancer in the UK, accounting for 13% of all new cancer cases.¹² The age standardised incidence rate of lung cancer in England is 88.4 and 67.4 per 100,000 amongst males and females respectively.¹³ In England (2020-21), there were 103,856 finished consultant episodes (FCEs) and 86,043 hospital admissions for malignant neoplasm of bronchus and lung (ICD-10 code C34), which resulted in 62,688 day cases and 170,030 FCE bed days.¹⁴ In England (2017), there were 38,888 patients diagnosed with malignant neoplasm of bronchus and lung and 28,170 deaths where malignant neoplasm of bronchus and lung was the underlying cause.¹⁵ In England, there were 7,564 newly diagnosed cases of stage III lung cancer and 18,213 newly diagnosed cases of stage IV lung cancer.¹⁶ For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates for stage III lung cancer were 48.7% and 12.6% respectively. The 1-year and 5-year survival rates for stage IV lung cancer were 19.3% and 2.9% respectively.¹⁷

Recommended Treatment Options

Treatment for lung cancer includes surgery, chemotherapy, radiotherapy, immunotherapy, and other targeted therapy drugs. People may be offered one or more different treatments depending on the stage, histology, and type of lung cancer as well as their general health. Systemic anti-cancer treatments are increasingly used to treat advanced NSCLC.¹⁸

Recommendations by the National Institute for Health and Care Excellence (NICE) include the following systemic anti-cancer treatments for people with:¹⁹

- Squamous NSCLC with no targetable mutations and PD-L1 <50%
 - Pembrolizumab with carboplatin and paclitaxel
- Squamous NSCLC with no targetable mutations and PD-L1 ≥ 50%
 - Atezolizumab
 - Pembrolizumab
 - Pembrolizumab with carboplatin and paclitaxel
- Non-squamous NSCLC with no targetable mutations and PD-L1 <50%
 - Pemetrexed and cisplatin
 - Pemetrexed and carboplatin
 - Atezolizumab and bevacizumab, carboplatin and paclitaxel
 - Pembrolizumab and pemetrexed and platinum chemotherapy
- Non-squamous NSCLC with no targetable mutations and PD-L1 ≥ 50%
 - Pembrolizumab and pemetrexed and platinum chemotherapy
 - Pembrolizumab
 - Atezolizumab

The following treatment options are licensed in the UK for the first line treatment of advanced NSCLC:^{20,21}

- Vinorelbine
- Gemcitabine

Clinical Trial Information

Trial	<p>IPSOS, NCT03191786, 2015-004105-16; A Phase III, Open-Label, Multicenter, Randomized Study to Investigate the Efficacy and Safety of Atezolizumab Compared With Chemotherapy in Patients With Treatment Naïve Advanced or Recurrent (Stage IIIB Not Amenable for Multimodality Treatment) or Metastatic (Stage IV) Non-Small Cell Lung Cancer Who Are Deemed Unsuitable for Platinum-Containing Therapy</p> <p>Phase III – Active, not recruiting</p> <p>Location(s): 12 EU countries, UK, Canada, and other countries</p> <p>Primary completion date: April 2022</p>
Trial Design	Randomised, parallel assignment, open label
Population	N=453 (actual); histologically or cytologically confirmed diagnosis of advanced or recurrent (Stage IIIB not amenable for multimodality treatment) or metastatic (Stage IV) NSCLC; no prior systemic treatment for advanced or recurrent or metastatic NSCLC; aged 18 years and older
Intervention(s)	Atezolizumab 1200mg (IV)
Comparator(s)	Either vinorelbine (oral) or gemcitabine (IV)
Outcome(s)	<p>Primary outcome:</p> <ul style="list-style-type: none"> - Overall survival [Time frame: from randomisation up to death from any cause(up to approximately 3.5 years)]

	See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Atezolizumab is already marketed in the UK; a 1200mg/20ml concentrate for solution for infusion vial costs £3,807.69 and a 840mg/14ml concentrate for solution for infusion vial costs £2,665.38.²²

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Cemiplimab with chemotherapy for untreated advanced or metastatic non-small-cell lung cancer (GID-TA10907). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Sugemalimab with chemotherapy for untreated metastatic non-small-cell lung cancer (GID-TA10900). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Canakinumab with pembrolizumab and chemotherapy for untreated advanced non-small cell lung cancer with no EGFR or ALK mutations (GID-TA10857). Expected date of issue to be confirmed.
- NICE technology appraisal. Pembrolizumab with carboplatin and paclitaxel for untreated metastatic squamous non-small-cell lung cancer (TA770). February 2022.
- NICE technology appraisal. Nivolumab with ipilimumab and chemotherapy for untreated metastatic non-small-cell lung cancer (TA724). September 2021.
- NICE technology appraisal. Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer (TA705). June 2021.
- NICE technology appraisal. Atezolizumab in combination for treating metastatic non-squamous non-small-cell lung cancer (TA584). June 2019.
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- NICE technology appraisal. Gefitinib for the first-line treatment of locally advanced or metastatic non-small-cell lung cancer (TA192). July 2010.
- NICE technology appraisal. Pemetrexed for the first-line treatment of non-small-cell lung cancer (TA181). September 2009.
- NICE guideline. Lung cancer: diagnosis and management (NG122). March 2019.
- NICE quality standard. Lung cancer in adults (QS17). December 2012.
- NICE interventional procedures guidance. Microwave ablation for primary or metastatic cancer in the lung (IPG716). February 2022.
- NICE interventional procedures guidance. Percutaneous radiofrequency ablation for primary or secondary lung cancers (IPG372). December 2010.

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. 2021.²³

- European Society for Medical Oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2019.²⁴
- Scottish Intercollegiate Guideline Network (SIGN). Management of lung cancer. 2014.²⁵

Additional Information

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