Health Technology Briefing
September 2022

Subcutaneous atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 29403	NICE ID: 11801	UKPS ID: 665698

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Subcutaneous (SC) atezolizumab is in development for the treatment of patients with metastatic or locally advanced non-small-cell lung cancer (NSCLC) who have previously received treatment. NSCLC is the most common type of cancer found in the lungs and is often caused by things such as smoking. Advanced or metastatic NSCLC means that the cancer has spread to other parts of the body, making it harder to treat. Existing treatment options for previously treated NSCLC are all administered via intravenous (IV) infusion, which means patients often spend hours receiving treatment in hospitals.

SC atezolizumab is a drug that has been developed to destroy cancer cells and stop them from spreading through the body. SC administration reduces the burden of treatment for patients as they receive the medicine faster, while keeping the same safety and effectiveness. IV administration often causes additional side effects for patients, such as infections at the infusion site, which is not seen with SC. If licensed SC atezolizumab will offer an additional treatment option for patients with previously treated locally advanced or metastatic NSCLC.

Proposed Indication

Treatment of patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) who have not been exposed to cancer immunotherapy but have failed prior platinum-based therapies.[1]

Technology

Description

Atezolizumab (Tecentriq) is a humanised IgG1 monoclonal anti-programmed death-ligand 1 (PD-L1) antibody. It negatively regulates the cytotoxic T-lymphocyte activation, suppressing T-cell migration, proliferation, and secretion of cytotoxic mediators leading to inhibited tumour cell killing.[2] Atezolizumab is currently only licensed for intravenous (IV) use.[3]

Subcutaneous (SC) atezolizumab is in clinical development for the treatment of patients with advanced or metastatic NSCLC who have failed platinum-based therapies. In the phase III clinical trial (NCT03735121), atezolizumab will be administered subcutaneously at 1800mg or 1200mg.[1,4]

Key Innovation

SC atezolizumab is in development to improve treatment options, reduce burden, and increase efficiency for patients and practitioners. It has been found to have comparable efficacy and safety profile as the already licensed IV formulation.[4] SC delivery gives a shorter administration time than IV, and results in less infusion related adverse events. This can increase quality of life and treatment adherence.[5] If licensed, SC atezolizumab will offer an additional treatment option for previously treated metastatic or advanced NSCLC patients.

Regulatory & Development Status

SC atezolizumab does not have Marketing Authorisation in the EU/UK. IV atezolizumab currently has Marketing Authorisation in the EU/UK for:[3]

- Urothelial carcinoma
- Early-stage NSCLC
- Metastatic NSCLC
- Small cell lung cancer (SCLC)
- Breast cancer
- Hepatocellular carcinoma

SC atezolizumab is also in phase III/ II clinical development for early-stage NSCLC.[6]

Patient Group

Disease Area and Clinical Need

Lung cancers can be broadly grouped into SCLC and NSCLC, with NSCLC accounting for 80-85% of lung cancer diagnoses in the UK. NSCLC can then be further categorised into adenocarcinoma, squamous cell carcinoma and large cell carcinoma- these are often grouped together as they all respond to treatments in a similar way.[7] 79% of lung cancers diagnosed in 2015 were deemed preventable, with lifestyle factors such as smoking and occupational hazards (inhalation of chemicals such as asbestos) being the leading causes (72% and 13% respectively). Age, gender, and genetics also show influence on prevalence with

most cases diagnosed in those aged 85-89, males, and those with a family history (2016-18 data). Medical conditions such as chronic obstructive pulmonary disease (COPD) and pneumonia also increase the likelihood of development.[8,9] In the earlier stages of the disease there are often no signs or symptoms, but as the disease progresses symptoms can include a persistent cough, recurrent chest infections, breathlessness, chest and shoulder pain, and fatigue.[10]

Lung cancer is the 3rd most common cancer in the UK, accounting for 13% of all new cancer cases (28,549) and 21% of cancer deaths (35,137) (2016-18). The one-year survival rate in England is 40.6%, dropping to 16.2% over five years, and 9.5% over ten years (2013-17).[8] In England (2020-21), there were 103,856 finished consultant episodes (FCE) for malignant neoplasm of the bronchus and lung (ICD-10 code: C34), with 86,043 hospital admissions that resulted in 62,688 day cases and 170,030 FCE bed days.[11] In England between 2013 and 2017, the age-standardised net lung cancer survival for stage III (locally advanced) was 48.7% at one year and 12.6% at five years, and for stage IV (metastatic) was 19.3% at one year and 2.9% for five years.[12] In 2020, there were 28,730 registrations of deaths in England and Wales for malignant neoplasms of the trachea, bronchus and lung in England (ICD-10 code C34).[13]

Recommended Treatment Options

Treatment of metastatic NSCLC aims to control the cancer for as long as possible and help with symptoms, and may include chemotherapy, targeted cancer drugs, immunotherapy, radiotherapy, or symptom control treatments.[14] NICE recommended treatments for previously treated locally advanced or metastatic NSCLC include durvalumab, atezolizumab, ramucirumab, erlotinib and gefitinib, nintedanib and pemetrexed.[15]

Clinical Trial Information

Trial	NCT03735121, 2018-002328-18; A Randomized, Multicenter, Phase Ib/III Study to Investigate the Pharmacokinetics, Efficacy, and Safety of Atezolizumab Subcutaneous Compared With Atezolizumab Intravenous in Patients With Previously Treated Locally Advanced or Metastatic Non-Small Cell Lung Cancer **Phase III –** Active, not recruiting **Location(s):** 8 EU countries, UK, USA and other countries **Primary completion date:** April 2022
Trial Design	Randomised, sequential assignment, open label
Population	N= 438 patients with previously treated locally advanced or metastatic NSCLC; aged 18 years and older.
Intervention(s)	SC atezolizumab in combination with rHuPH20, followed by atezolizumab alone in some cohorts for part one. Part two consists of atezolizumab alone or in combination with rHuPH20.
Comparator(s)	No comparator used
Outcome(s)	Primary outcome measures: • Observed concentration of atezolizumab in serum at cycle 1 in part 1 [Time frame: predose of cycle 2. Cycle length is 14 or 21 days] • Observed concentration of atezolizumab in serum at cycle 1 in part 2 [Time frame: predose of cycle 2. Cycle length is 14 or 21 days] • Area under the concentration-time curve from time zero to 21 days (AUC_{0-21}) of atezolizumab in Part 2 {Time frame: at cycle 1. Cycle length is 21 days]

	See trial record for full list of other outcomes
Results (efficacy)	SC atezolizumab 1800 mg every 3 weeks and 1200 mg every 2 weeks provided similar serum trough concentration (C_{trough}) and area under the curve values in cycle 1 to the corresponding IV atezolizumab reference.[4]
Results (safety)	SC atezolizumab was well tolerated and exhibited a safety profile consistent with the established IV formulation.[4]

Estimated Cost

The hospital indicative price of 1200mg/20ml atezolizumab concentrate for IV infusion is £3,807.69.[16]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Durvalumab for maintenance treatment of unresectable non-small-cell lung cancer after platinum-based chemoradiation (TA798). June 2022.
- NICE technology appraisal. Atezolizumab for treating locally advanced or metastatic non-small-cell lung cancer after chemotherapy (TA520). May 2018.
- NICE technology appraisal. Pemetrexed for the maintenance treatment of non-small-cell lung cancer (TA190). August 2017.
- NICE technology appraisal. Ramucirumab for previously treated locally advanced or metastatic non-small-cell lung cancer (TA403). August 2016.
- NICE technology appraisal. Erlotinib and gefitinib for treating non-small cell lung cancer that has progressed after prior chemotherapy (TA374). December 2015.
- NICE technology appraisal. 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.
- NICE interventional procedure guidance. Microwave ablation for primary or metastatic cancer in the lung (IPG716). February 2022.

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

- National comprehensive cancer network (NCCN). Guidelines Insights: Non–Small Cell Lung Cancer. 2021.[17]
- European society for medical oncology (ESMO). Metastatic Non-Small-Cell Lung Cancer: Clinical Practice Guidelines for diagnosis, treatment, and follow-up. 2018.[18]
- Healthcare Improvement Scotland. SIGN 137: Management of lung cancer. 2014.[19]

Additional Information

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