Health Technology Briefing
June 2022

Atezolizumab with chemotherapy for treating recurrent triple-negative breast cancer

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 21688	NICE ID: 10519	UKPS ID: 658177

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Atezolizumab with chemotherapy is currently in clinical development for the treatment of early relapsing, recurrent triple-negative breast cancer (TNBC). TNBC is an uncommon form kind of breast cancer where the tumour cells do not have any of the receptors that are commonly found in breast cancer. TNBC is often more aggressive and harder to treat compared to other types of breast cancer. The prognosis for these patients is extremely poor so there is a need to develop additional treatment options.

Atezolizumab is a 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 licenced, atezolizumab with chemotherapy via IV infusion will provide expanded treatment options for patients with early relapsing, recurrent TNBC who currently have limited treatment options available.

Proposed Indication

Atezolizumab plus chemotherapy for patients with early relapsing recurrent (inoperable locally advanced or metastatic) triple-negative breast cancer.[1]

Technology

Description

Atezolizumab (Tecentriq) 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 anti-tumour immune response without inducing antibody-dependent cellular cytotoxicity.[2] 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 anti-tumour immune response in the tumour microenvironment. Atezolizumab spares the PD-L2/PD-1 interaction allowing PD-L2/PD-1 mediated inhibitory signals to persist.[2] 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 with chemotherapy is currently in clinical development for the treatment of inoperable recurrent TNBC. In the phase III clinical trial IMpassion132 (NCT03371017), patients are given 1200 mg of atezolizumab by IV (intravenous) infusion with chemotherapy. The chemotherapy regimen consists of gemcitabine 1000 mg/m^2, followed by carboplatin target area under the curve (AUC) 2 mg/ml/min, both administered by IV infusion on days 1 and 8 of each 3-week treatment cycle, or with capecitabine 1000 mg/m2, twice daily, orally on days 1 to 14, followed by a 7-day rest period in each 3-week treatment cycle.[1]

Key Innovation

TNBC is one of the most difficult forms of breast cancer to treat due to the lack of oestrogen (ER), progesterone (PR) or human epidermal growth factor 2 (HER-2) receptors that are targets of treatment in other forms of breast cancer.[3,4] The mainstay treatment option for these patients has been chemotherapy, usually with a taxane, however, this is associated with side effects including: increased risk of infection; hair loss; sickness; nausea; and fatigue.[5] Atezolizumab was the first immunotherapy medicinal product approved that specifically targets the TNBC phenotype.[6] Atezolizumab with nab-paclitaxel is recommended by NICE for the first-line treatment of PD-L1+, advanced TNBC patients and has demonstrated to substantially improve outcomes compared with taxane chemotherapy alone.[3]

If licenced, atezolizumab with chemotherapy will provide an additional, non-taxane treatment option for patients with early relapsing, recurrent TNBC who currently have limited treatment options available, thus expanding the patient population eligible for this immunotherapy medicinal product.[3,7]

Regulatory & Development Status

Atezolizumab has Marketing Authorisation in the EU/UK as a monotherapy for the following indications:[2]

- 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 ≥ 5%
- Adult patients with Stage II to IIIA (7th edition of the UICC/AJCC-staging system) non-small cell lung cancer (NSCLC) whose tumours have PD-L1 expression on ≥ 50% of tumour cells (TC) and whose disease has not progressed following platinum-based adjuvant chemotherapy
- First-line treatment of adult patients with metastatic NSCLC whose tumours have a PD-L1 expression ≥ 50% TC or ≥ 10% tumour-infiltrating immune cells (IC) and who do not have EGFR mutant or ALK-positive NSCLC
- Adult patients with locally advanced or metastatic NSCLC after prior chemotherapy.

Atezolizumab has Marketing Authorisation in the EU/UK as part of a combination therapy for the following indications:[2]

- In combination with bevacizumab, paclitaxel and carboplatin for the first-line treatment of adult patients with metastatic, non-squamous non-small cell lung cancer
- In combination with nab-paclitaxel and carboplatin for the first-line treatment of adult patients with metastatic non-squamous NSCLC who do not have EGFR mutant or ALK-positive NSCLC
- In combination with carboplatin and etoposide for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC)
- In combination with nab-paclitaxel for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer (TNBC) whose tumours have PD-L1 expression ≥ 1% and who have not received prior chemotherapy for metastatic disease
- In combination with bevacizumab for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy

Atezolizumab is currently in phase II/III clinical development for a large number of indications, including:[8]

- Squamous cell carcinoma of head and neck
- Gastrointestinal cancer
- Gynecological cancer
- Haematological cancer
- Genitourinary cancer
- Neuroendocrine cancer
- Early triple negative breast cancer

Patient Group

Disease Area and Clinical Need

Breast cancer occurs when abnormal cells in the breast (particularly those that line the milk ducts), begin to grow and divide in an uncontrolled way and eventually form a growth (tumour).[9] TNBC is a rare form of breast cancer (accounting for 15% of breast cancers) where the tumour cells do not have receptors for the hormones oestrogen and progesterone, or the HER2 protein.[10] Some women with triple negative breast cancer also have a BRCA1 gene fault. BRCA1 is one of the gene faults that can increase the risk of breast cancer within families. Although men can have TNBC, this is very rare as most men have oestrogen receptors in their cancer cells.[10] Recurrent cancer refers to cancer that has recurred (come back), usually after a period of time during which the cancer could not be detected. The cancer may come back to the same place as the original (primary) tumour or to another place in the body.[11] Established risk factors of breast cancer include age, early onset of menstruation, late menopause, older age at first completed pregnancy, and a family history.[12] The symptoms of triple negative breast cancer include: a new lump or

thickening in your breast or armpit, a change in size, shape or feel of your breast, skin changes in the breast, etc.[10]

Breast cancer is the most common cancer in the UK, accounting for 15% of all new cancer cases (2016-18).[13] The age standardised incidence rate of breast cancer in England is 319 and 46,479 per 100,000 amongst males and females respectively.[14] In England (2020-21), there were 202,340 finished consultant episodes (FCEs) and 199,226 admissions for malignant neoplasm of breast (ICD-10 code C50), which resulted in 172,062 day cases and 47,613 FCE bed days.[15] Based on estimates that around 15% of breast cancer cases are the TNBC subtype, it can be approximated that there were approximately 30,351 FCEs and 29,884 admissions specifically for TNBC, which results in approximately 25,810 day cases and 7,142 FCE bed days.[10] For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates for all stages of breast cancer were 95.8% and 85% (age-standardised) respectively. For stage 4 breast cancer, 1-year survival rate of 66% and 5-year survival rate of 26.2% was reported.[16]

Recommended Treatment Options

Chemotherapy is the main treatment for advanced TNBC, and NICE currently recommends:

- Atezolizumab with nab-paclitaxel for treating triple-negative, unresectable, locally advanced or metastatic breast cancer in adults whose tumours express PD-L1 at a level of 1% or more and who have not had previous chemotherapy for metastatic disease.[17]

Clinical Trial Information

Trial	**IMpassion132**, NCT03371017, EudraCT 2016-005119-42, A Phase III, Randomised, Double-Blind, Placebo-Controlled, Multicentre Study Of The Efficacy And Safety Of Atezolizumab Plus Chemotherapy For Patients With Early Relapsing Recurrent (Inoperable Locally Advanced Or Metastatic) Triple-Negative Breast Cancer **Phase III:** Recruiting **Location(s):** 8 EU countries, UK, US and other countries **Primary completion date:** January 2023
Trial Design	Randomised, parallel assignment, quadruple masking
Population	N=572; 18 years and older; histologically confirmed TNBC that is either locally recurrent, inoperable and cannot be treated with curative intent or is metastatic; documented disease progression occurring within 12 months from the last treatment with curative intent; prior treatment (of early breast cancer) with an anthracycline and taxane; have not received prior chemotherapy or targeted systemic therapy for their locally advanced inoperable or metastatic recurrence (prior radiation therapy for recurrent disease is permitted)
Intervention(s)	• Atezolizumab 1200mg by IV infusion • Chemotherapy (gemcitabine, capecitabine, carboplatin)
Comparator(s)	• Placebo by IV infusion • Chemotherapy (gemcitabine, capecitabine, carboplatin)
Outcome(s)	Primary outcomes: • Overall survival (OS) in population with PD-L1+ tumour status [time frame: baseline to end of study (approximately 58 months)]

	• OS in modified intent-to-treat (mITT) population [time frame: baseline to end of study (approximately 58 months)] See trial record for full list of outcomes.
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The estimated cost of atezolizumab 60 mg per 1 ml is £2665.38 for 840mg/14ml concentrate and £3807.69 for 1200mg/20ml concentrate solution for infusion vials.[18]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Pembrolizumab for previously treated metastatic triple negative breast cancer (ID1246). Expected date of issue to be confirmed.
- NICE technology appraisal in development. Sacituzumab govitecan for treating unresectable locally advanced or metastatic triple-negative breast cancer after 2 or more therapies (ID3942). Expected August 2022.
- NICE technology appraisal in development. Pembrolizumab in combination with chemotherapy for neoadjuvant treatment of triple negative breast cancer (ID1500). Expected November 2022.
- NICE clinical guideline. Advanced breast cancer: diagnosis and treatment (CG81). February 2009.
- NICE quality standard. Breast cancer (QS12). September 2011.

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

- ESO-ESMO ABC 5 Clinical Practice. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). 2020.[19]
- Breast Cancer, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. 2020.[20]

Additional Information

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