

Health Technology Briefing March 2023

Atezolizumab with paclitaxel and carboplatin for previously untreated advanced endometrial cancer

Company/Developer Roche Products Ltd

New Active Substance Significant Licence Extension (SLE)

NIHRIO ID: 33207

NICE TSID: 10710

UKPS ID: 661857

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Atezolizumab in addition to paclitaxel and carboplatin is in clinical development for recurrent or primary advanced endometrial cancer (EC). EC (uterine cancer) is cancer of the lining of the womb. Recurrent cancer is cancer that has come back after treatment. Advanced cancer is cancer that cannot normally be cured or controlled. EC is characterised by abnormal vaginal bleeding (after the menopause, between periods) and can also cause symptoms such as pain during sex and lower abdominal (tummy) pain. Typically, advanced EC is treated by using a combination of surgery, radiotherapy and/or chemotherapy. Prognosis of advanced/recurrent EC is poor and treatment options are limited, and there is a need for additional targeted treatment options to improve outcomes for this patient population.

Atezolizumab is a type of immunotherapy (therapy that targets the immune system) that is administered intravenously (IV) and attaches to a protein called PD-L1. PD-L1 is present on many cancer cells and switches off immune cells that attack cancer cells. Atezolizumab reduces the effects of PD-L1, which increases the immune system's ability to attack cancer cells and thereby slows down progression of the disease. If licensed, atezolizumab with carboplatin and paclitaxel, would offer an additional treatment option for patients with advanced/recurrent EC.

Proposed Indication

First line treatment for women over 18 years old with advanced/recurrent endometrial cancer (EC).¹

Technology

Description

Atezolizumab (Tecentriq, MPDL3280A) is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that directly binds to programmed death-ligand 1 (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

Atezolizumab (with paclitaxel and carboplatin) is in clinical development for the treatment of adult women over 18 years old with advanced/recurrent EC. In the phase III clinical trial (AtTend; NCT03603184), patients are administered paclitaxel 175 mg/m² and carboplatin area under the curve (AUC) 5 or 6 every 21 days for 6-8 cycles or until progression of disease; in addition to atezolizumab administered as IV infusion at a fixed dose of 1200 mg, every 21 days until objective radiological disease progression.¹

Key Innovation

Prognosis of advanced/recurrent EC is poor, with a median survival of 12-15 months for patients with measurable disease. Treatment options are limited, with primary management being chemotherapy with carboplatin and paclitaxel. Ultra- and hyper-mutated EC have shown peri-tumoural T cell infiltration and high expression of PD-1 and PD-L1 proteins, suggesting that immune regulation may enhance specific T cell responses and result in improved anti-tumour immunity. Preliminary data in EC patients have shown tumour control activity of the PD-L1 targeting agent atezolizumab.³

If licensed, atezolizumab with paclitaxel and carboplatin will offer an additional treatment option for women with previously untreated EC who currently have limited effective therapies available.

Regulatory & Development Status

Atezolizumab monotherapy currently has Marketing Authorisation in the EU/UK for the following indications:⁴

- Early stage and metastatic non-small cell lung cancer (NSCLC)
- Metastatic urothelial cancer
- Metastatic triple negative breast cancer
- Extensive stage small cell lung cancer
- Hepatocellular carcinoma

Atezolizumab, as a combination therapy, currently has Marketing Authorisation in the EU/UK for the following indications:⁴

- Atezolizumab, in combination with bevacizumab, paclitaxel and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous NSCLC.
- Atezolizumab, in combination with nab-paclitaxel and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous NSCLC who do not have EGFR mutant or ALK-positive NSCLC.
- Atezolizumab, in combination with carboplatin and etoposide, is indicated for the first-line treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC).
- Atezolizumab in combination with nab-paclitaxel is indicated for the treatment of adult patients with unresectable locally advanced or metastatic triple-negative breast cancer
- Atezolizumab, in combination with bevacizumab, is indicated for the treatment of adult patients with advanced or unresectable hepatocellular carcinoma who have not received prior systemic therapy.

Atezolizumab with paclitaxel and carboplatin is also in phase II/III clinical development for the treatment of:⁵

- breast cancer
- NSCLC
- squamous cell carcinoma of the head and neck
- advanced solid tumors
- cancers of unknown primary site

Patient Group

Disease Area and Clinical Need

EC is cancer of the lining of the womb, also called the endometrium.⁶ The cause of EC in most women remains unknown. However, there are several risk factors that increase the chance of this cancer developing, such as increasing age, longer exposure to oestrogen (exogenous or endogenous), being overweight or obese, having diabetes, treatment with tamoxifen, endometrial hyperplasia and factors relating to menstruation including starting early, late menopause and polycystic ovary syndrome. The risk of womb cancer increases with age: almost three quarters of cases of womb cancer are in women aged 40 to 74. Most women diagnosed with womb cancer have had their menopause.⁷ The most common symptom is abnormal bleeding from the vagina (after the menopause, between periods or heavier periods) and a change to vaginal discharge. Less common symptoms include pain in the lower abdomen and pain during sex.⁸

EC is the 4th most common cancer in females in the UK, accounting for 5% of all new cancer cases. Between 2016 and 2018, in the UK there were over 9,700 new cases of EC in females. The age-standardised incidence rate of uterine cancer in females in England in 2016-2018 was 29.5.6 per 100,000 population.⁹

In England in 2021-2022, there were 18,420 finished consultant episodes (FCE) and 17,317 hospital admissions for malignant neoplasm of endometrium (ICD 10: C54.1), resulting in 27,566 FCE bed days and 9,644 day cases.¹⁰ In England (2017), there were 7,732 patients diagnosed with malignant neoplasm of corpus uteri and 1,540 deaths registered where malignant neoplasm of corpus uteri was the underlying cause. The directly age-standardised rates per 100,000 population of registrations of death was 5.4.⁸ For patients diagnosed between 2013 and 2017, followed up to 2018, the 1-year and 5-year survival rates were 83.3% and 47.8% respectively.¹¹

Recommended Treatment Options

There are currently no specific National Institute for Health and Care Excellence (NICE) treatment recommendations for previously untreated advanced endometrial cancer.

Chemotherapy recommendations for previously untreated advanced endometrial cancer include:¹²

- Carboplatin
- Paclitaxel

Endocrine therapy recommendations for previously untreated advanced endometrial cancer include:¹²

- Progestins
- Aromatase inhibitors
- Tamoxifen
- Fulvestrant

Clinical Trial Information

<p>Trial</p>	<p>AtTEnd, NCT03603184, Phase 3 Double-blind Randomized Placebo Controlled Trial of Atezolizumab in Combination With Paclitaxel and Carboplatin in Women With Advanced/Recurrent Endometrial Cancer Phase III: active, not recruiting Location: Four EU countries, UK and other countries Primary completion date: July 2022</p>
<p>Trial Design</p>	<p>Randomised, parallel assignment, double blinded</p>
<p>Population</p>	<p>N = 550 (estimated); female age 18 years and older; subjects with newly diagnosed, histologically-confirmed with residual disease after surgery either measurable or evaluable, or inoperable stage III-IV endometrial carcinoma/carcinosarcoma, after diagnostic biopsy, and naïve to first line systemic anti-cancer treatment. Recurrent EC patients if not yet treated for recurrent disease.</p>
<p>Intervention(s)</p>	<p>Paclitaxel 175 mg/m² + carboplatin AUC 5 or 6 IV administered every 21 days for 6-8 cycles or progression of disease + atezolizumab IV administered at a fixed dose of 1200 mg, every 21 days.</p>
<p>Comparator(s)</p>	<p>Paclitaxel 175 mg/m² (IV) + carboplatin AUC 5 or 6 will be administered (IV) every 21 days for 6-8 cycles or progression of disease.</p>
<p>Outcome(s)</p>	<p>Primary outcome measure:</p> <ul style="list-style-type: none"> • Overall survival [timeframe: up to two years after the last patient enrolled] • Progression free survival [timeframe: up to two years after the last patient enrolled]

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

Estimated Cost

Atezolizumab is already marketed in the UK. The NHS indicative price is:¹³

- for 1200mg/20ml concentrate for solution for infusion vials £3,807.69
- for 840mg/14ml concentrate for solution for infusion vials £2,665.38

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Lenvatinib with pembrolizumab for untreated recurrent or advanced endometrial cancer [ID3966]. Expected date of issue to be confirmed.
- NICE technology appraisal in development. Dostarlimab with carboplatin and paclitaxel for treating recurrent or advanced endometrial cancer [ID3968]. Expected date of issue to be confirmed.
- NICE guidelines. Suspected cancer: recognition and referral [NG12]. December 2021.
- NICE interventional procedure guidance. Laparoscopic hysterectomy (including laparoscopic total hysterectomy and laparoscopically assisted vaginal hysterectomy) for endometrial cancer [IPG356]. September 2010.
- NICE interventional procedure guidance. Laparoscopic techniques for hysterectomy [IPG239]. November 2007.

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.
- NHS England. 2013/14 NHS Standard Contract for Complex Gynaecology: specialist gynaecological cancers. E10/S/f.

Other Guidance

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Additional Information

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