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Newcastle University

Health Technology Briefing
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Atezolizumab with platinum-based chemotherapy and bevacizumab for epithelial ovarian cancer or fallopian tube cancer or primary peritoneal cancer

Company/Developer	Roche Products Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 13559	NICE ID: 10701	UKPS ID: 661889

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

Atezolizumab in combination with bevacizumab and chemotherapy is currently in clinical development for the treatment of patients with epithelial ovarian cancer or primary peritoneal or fallopian tube cancer. Epithelial ovarian cancers are the most common type of ovarian cancer. Primary peritoneal cancer and fallopian tube cancer are similar to epithelial ovarian cancer. All three types show signs of pain and swelling in the abdominal area. Other signs and symptoms include frequent urge to urinate, trouble eating, bloating or constipation. The optimal treatment strategy for women with platinum sensitive ovarian cancer has yet to be determined.

Atezolizumab is a type of protein known as a monoclonal antibody which is designed to attach to a protein called PD-L1, which is present on many cancer cells. It administered intravenously and acts by attaching to PD-L1 which switches off immune cells that normally attack cancer cells. By attaching to PD-L1, atezolizumab reduces the effects of PD-L1 therefore increasing the immune system's ability to attack cancer cells which consequently slows down disease progression. Atezolizumab administered in combination with bevacizumab and chemotherapy will offer an additional treatment option for patients with epithelial ovarian cancer, primary peritoneal or fallopian tube cancer.

Proposed Indication

For the treatment of female adult patients with platinum sensitive epithelial ovarian cancer, peritoneal or fallopian tube cancer.[1]

Technology

Description

Atezolizumab, is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody, a type of protein designed to attach to a protein called PD-L1, which is present on many cancer cells.[2,3] 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 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 treatment of female adults with platinum sensitive ovarian cancer, primary peritoneal or fallopian tube cancer (ATALANTE; NCT02891824). Atezolizumab is administered intravenously at either 1200mg every three week (q3wk) or 800mg every 4 week (q4wk) for 6 cycles each. Atezolizumab is administered in combination with chemotherapy and bevacizumab.[1]

Key Innovation

There is evidence that anti-VEGF therapy (such as bevacizumab) and immunotherapy (such as atezolizumab) have synergistic effects when both administered to patients.[4] Treatment options for patients with ovarian cancer are noncurative. There are not currently any PD-1 inhibitors recommended for the second line treatment of ovarian cancer. If approved, atezolizumab in combination with bevacizumab and chemotherapy would be a novel treatment option for this patient group.[5]

Regulatory & Development Status

Atezolizumab currently had Marketing Authorisation in the EU/UK for the following indications:[2,3]

- Non-small-cell lung carcinoma
- Urologic neoplasms
- Breast neoplasms
- Small cell lung carcinoma
- Hepatocellular carcinoma

Atezolizumab is currently in phase II and III trials for the treatment of several indications including the following:[6]

- Small cell lung carcinoma
- Non-Small-cell lung carcinoma
- Follicular lymphoma

Patient Group

Disease Area and Clinical Need

Epithelial ovarian cancer (EOC) is the most common type of ovarian cancer which can be further classified into different subtypes: serous carcinoma, endometrioid carcinoma, clear-cell carcinoma, mucinous carcinoma, and undifferentiated or unclassified carcinoma. Other types of ovarian cancer include fallopian tube cancer (FTC) and primary peritoneal cancer (PPC). EOC accounts for approximately 90% of all cases of ovarian cancers in the UK.[7] Primary peritoneal cancer is a rare cancer of the peritoneum and fallopian tube cancer starts in the fallopian tubes which connect the ovaries to the womb.[8] Factors that can increase the risk of ovarian cancer includes age - most ovarian cancers develop after menopause- obesity, a family history of ovarian cancer, hereditary conditions (e.g., BRCA1 and BRCA2 mutations), fertility treatment, smoking and diet.[9] Signs and symptoms of ovarian, fallopian tube, or peritoneal cancer include pain or swelling in the abdomen, sudden or frequent urge to urinate, trouble eating or feeling full, lump in the pelvic area and gastrointestinal problems, such as gas, bloating, or constipation.[10]

In females in the UK, ovarian cancer is the 6th most common cancer, with around 7,500 new cases every year. Ovarian cancer accounts for 4% of all new cancer cases in females in the UK. Incidence rates for ovarian cancer are projected to rise by 15% in the UK between 2014 and 2035, to 32 cases per 100,000 females by 2035. More than 71.7% of women diagnosed with ovarian cancer in England survive their disease for one year or more (2013-2017), and more than 42.6% of women diagnosed with ovarian cancer in England survive their disease for five years or more (2013-2017).[11] In England in 2020-2021 there were 34,677 finished consultant episodes (FCEs), and 32,289 hospital admissions with a primary diagnosis of malignant neoplasm of ovary and fallopian tube (ICD-10 code C56-C57), resulting in 41,888 FCE bed days.[12]

Recommended Treatment Options

NICE recommends bevacizumab in combination with gemcitabine and carboplatin as a treatment option for treating the first recurrence of platinum-sensitive advanced ovarian cancer.[5,13]

Clinical Trial Information

Trial	**ATALANTE;** NCT02891824; A Randomized, Double-blinded, Phase III Study of Atezolizumab Versus Placebo in Patients With Late Relapse of Epithelial Ovarian, Fallopian Tube, or Peritoneal Cancer Treated by Platinum-based Chemotherapy and Bevacizumab **Phase III –** Active, not recruiting **Location(s):** 6 EU countries and Israel **Primary completion date:** October 2021
Trial Design	Randomised, parallel assignment, triple-masked
Population	N=614 (actual); subjects aged 18 to 95 years with histologically confirmed progressive non-mucinous epithelial ovarian cancer, primary peritoneal adenocarcinoma and / or fallopian-tube adenocarcinoma

Intervention(s)	1200mg of atezolizumab administrated intravenously x 6 cycles q3wk or 800mg x 6 cycles q4wkduring treatment with chemotherapy and bevacizumab, followed by atezolizumab 1200mg q3wk until progression
Comparator(s)	Placebo 1200 mg x 6 cycles q3wk or 800mg x 6 cycles q4wk during treatment with chemotherapy and bevacizumab, followed by placebo 1200mg q3wk until progression
Outcome(s)	Efficacy: Progression free survival, where the date of progression is based on investigator assessment using the RECIST version 1.1 [Time frame: An average of 19 months] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Atezolizumab is already marketed in the UK; a 60mg vial (1200mg/20ml) costs £3,807.69 and a 60mg vial (840mg/14ml) costs £2,665.38.[14]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance. Bevacizumab in combination with gemcitabine and carboplatin for treating the first recurrence of platinum-sensitive advanced ovarian cancer (TA285). May 2013.
- NICE clinical guidance. Ovarian cancer: recognition and initial management (CG122). April 2011.
- NICE quality standard. Ovarian cancer (QS18). May 2012.

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Complex Gynaecology – Specialist Gynaecological Cancers. E10/S/f.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Chemotherapy (Adult). B15/S/a.

Other Guidance

- National Comprehensive Cancer Network. Ovarian Cancer, Version 2.2020, NCCN Clinical Practice Guidelines in Oncology. February 2021.[15]
- Scottish Intercollegiate Guidelines Network. SIGN 135 - Management of epithelial ovarian cancer. October 2018.[16]
- British Gynaecological Cancer Society. British Gynaecological Cancer Society (BGCS) Epithelial Ovarian / Fallopian Tube / Primary Peritoneal Cancer Guidelines: Recommendations for Practice. 2017.[17]

Additional Information

References

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