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Newcastle University

Health Technology Briefing
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Durvalumab with bevacizumab and chemotherapy for treating advanced ovarian cancers

Company/Developer	AstraZeneca UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 26996	NICE TSID: 11844	UKPS ID: 668769

Licensing and Market Availability Plans

Currently in phase III clinical trials.

Summary

Durvalumab in combination with bevacizumab and chemotherapy is currently in clinical development for the treatment of patients with newly diagnosed, advanced ovarian cancer, primary peritoneal cancer, and/or fallopian tube cancer. Primary peritoneal cancer, fallopian tube cancer and epithelial ovarian cancer arise from the same type of tissue and thus exhibit many similar symptoms. These include pain and swelling in the abdominal area, constipation, and frequent urge to urinate. In advanced ovarian cancer, recurrence after chemotherapy is over 70% in the first two years with few therapeutic options.

Durvalumab is a type of protein known as a monoclonal antibody which is designed to attach to programmed cell death ligand-1 (PD-L1), which is a protein present on many cancer cells that prevents immune cells attacking cancer cells. Durvalumab is administered intravenously and acts by attaching to PD-L1, which reduces the effects of PD-L1 therefore increasing the immune system's ability to attack the cancer cells, and consequently slowing down and potentially even preventing disease progression in some patients. If licensed, durvalumab in combination with bevacizumab will offer an additional treatment and maintenance treatment option for newly diagnosed, advanced ovarian cancer.

Proposed Indication

Durvalumab in combination with standard of care platinum-based chemotherapy and bevacizumab followed by maintenance durvalumab and bevacizumab or durvalumab, bevacizumab and olaparib in patients with newly diagnosed, histologically confirmed, advanced (stage III-IV) ovarian, primary peritoneal cancer and/or fallopian-tube cancer that are candidates for cytoreductive surgery.[1]

Technology

Description

Durvalumab (Imfinzi, MEDI4736) is a fully human, immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that selectively blocks the interaction of PD-L1 with PD-1 and CD80 (B7.1). Durvalumab does not induce antibody dependent cell-mediated cytotoxicity (ADCC). Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation.[2]

Durvalumab in combination with bevacizumab is currently in development for female patients with newly diagnosed, advanced (stage III-IV) high grade epithelial ovarian cancer including high grade serious, high grade endometroid, clear cell ovarian cancer or carcinosarcoma, primary peritoneal cancer and/or fallopian-tube cancer. In phase III trial (NCT03737643), durvalumab is administered intravenously at 1120mg every three weeks for a total of 15 months maintenance treatment, and bevacizumab is administered intravenously at 15mg/kg for a total of 15 months maintenance treatment. Olaparib is included as part of a combination regimen in the study with dosing at 300mg oral tablets taken twice daily for 24 months maintenance treatment.[1,3]

Key Innovation

In advanced ovarian cancer, prognosis is poor as the recurrence rate after chemotherapy is over 70% in the first two years with few therapeutic options. There is evidence that anti-vascular endothelial growth factor (VEGF) therapy (such as bevacizumab) and immunotherapy (such as durvalumab) have synergistic effects when both administered to patients. Combining immunotherapy with drugs targeting different pathways represents potentially effective associations and may enhance efficacy and overcome cancer resistance.[4]

If licensed, durvalumab in combination with bevacizumab will offer an additional treatment option for advanced ovarian cancer in patients who have received chemotherapy and are candidates for cytoreductive surgery.

Regulatory & Development Status

Durvalumab currently has Marketing Authorisation in the UK and EU for the following indications:[2]

- For the treatment of locally advanced, unresectable non-small cell lung cancer (NSCLC) in adults whose tumours express PD-L1 on ≥ 1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy.
- In combination with etoposide and either carboplatin or cisplatin for the first-line treatment of adults with extensive-stage small cell lung cancer (ES-SCLC).

Durvalumab and bevacizumab in combination currently do not have Marketing Authorisation for any indication in the UK/EU.

Durvalumab is currently in phase II and III trials for the treatment of several indications including the following:[5]

- Renal cell cancer
- Bladder cancer
- Biliary tract cancer

Durvalumab and bevacizumab in combination are currently in phase II/III trials for the following indications:[6]

- Hepatocellular carcinoma
- Breast cancer
- Small-cell lung cancer
- Gastric cancers

Patient Group

Disease Area and Clinical Need

Ovarian cancer mostly affects women over 50, but the risk is greatest in those aged between 75 and 79.[7,8] Epithelial ovarian cancer is the most common type of ovarian cancer and starts in the surface layer covering the ovary.[9] The symptoms of ovarian cancer can include bloating, discomfort in the tummy or pelvic area, feeling full quickly, needing to pee more often, unexplained tiredness, unexplained weight loss, and constipation or diarrhoea.[10] Fallopian tube cancer, is another form of ovarian cancer with similar symptoms can also include vaginal bleeding unrelated to menstruation and a watery vaginal discharge that may contain blood.[11] Peritoneal cancer is a rare cancer of the peritoneum and is similar to epithelial ovarian cancer. Again, symptoms are unclear and are similar to other conditions: painful and swollen abdomen, constipation or diarrhoea, nausea and vomiting, indigestion, bloating and loss of appetite.[12] 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., breast cancer type 1 susceptibility protein (BRCA) 1 and BRCA2 mutations), fertility treatment, smoking and diet.[13]

Around 7,500 women are diagnosed with ovarian cancer in the UK each year (2016-2018), making ovarian cancer the 6th most common cancer in women. Ovarian cancer accounts for 4% of all new cancer cases in females in the UK (2016-2018). 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).[14] In England in 2021-2022 there were 42,173 finished consultant episodes (FCEs), and 39,296 hospital admissions with a primary diagnosis of malignant neoplasm of ovary and fallopian tube (ICD-10 code C56-C57), and peritoneum (ICD-10 code C48.2) resulting in 51,634 FCE bed days.[15]

Recommended Treatment Options

The National Institute for Health and Care Excellence (NICE) recommends the following treatment options for advanced ovarian cancer:[16-18]

- Olaparib plus bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer
- Niraparib for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy

Clinical Trial Information

Trial	**DUO-O;** NCT03737643 **EudraCT;** 2017-004632-11; A Phase III Randomised, Double-Blind, Placebo-Controlled, Multicentre Study of Durvalumab in Combination With Chemotherapy and Bevacizumab, Followed by Maintenance Durvalumab, Bevacizumab and Olaparib in Newly Diagnosed Advanced Ovarian Cancer Patients **Phase III** – Recruiting **Location(s)**: USA, Canada, 12 EU counties and other countries **Primary completion date**: June 2023
Trial Design	Randomised, parallel assignment, quadruple-masked
Population	N=1374; females aged 18 and older, with histologically confirmed advanced ovarian cancer
Intervention(s)	Active Comparator: Arm 1 Platinum-based chemotherapy in combination with bevacizumab and durvalumab placebo (saline IV infusion) followed by maintenance bevacizumab, durvalumab placebo (saline IV infusion) and olaparib placebo (tablets). Experimental: Arm 2 Platinum-based chemotherapy in combination with bevacizumab and durvalumab followed by maintenance bevacizumab, durvalumab and olaparib placebo. Experimental: Arm 3 Platinum-based chemotherapy in combination with bevacizumab and durvalumab followed by maintenance bevacizumab, durvalumab and olaparib. Experimental: tBRCAm cohort Platinum-based chemotherapy in combination with bevacizumab and durvalumab followed by maintenance bevacizumab, durvalumab and olaparib. Bevacizumab is optional according to local practice.
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measures: • Progression Free Survival (PFS) - in non-tBRCA HRD positive patients defined as time from randomisation to first progression by investigator assessment using modified RECIST 1.1 or death (by any cause in the absence of progression) [Time frame: Approximately 4 years] • PFS in all non-tBRCA patients defined as time from randomisation to first progression by investigator assessment using modified RECIST 1.1 or death (by any cause in the absence of progression) [Time frame: Approximately 4 years] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Durvalumab 120mg/2.4ml costs £592.00 per vial and 500mg/10ml costs £2,466.00 per vial.[19]

Relevant Guidance

NICE Guidance

- NICE technology appraisal guidance (TA693). Olaparib plus bevacizumab for maintenance treatment of advanced ovarian, fallopian tube or primary peritoneal cancer. April 2021.
- NICE technology appraisal guidance (TA673). Niraparib for maintenance treatment of advanced ovarian, fallopian tube and peritoneal cancer after response to first-line platinum-based chemotherapy. February 2021.
- NICE clinical guideline (CG122). Ovarian cancer: recognition and initial management. April 2011.
- NICE quality standard (QS18). Ovarian Cancer. May 2012.

NH S 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
- NHS England 2018/19 Manual for Prescribed Specialised Services

Other Guidance

- British Gynaecological Cancer Society. British Gynaecological Cancer Society (BGCS) Epithelial Ovarian / Fallopian Tube / Primary Peritoneal Cancer Guidelines: Recommendations for Practice. 2017.[20]
- Scottish Intercollegiate Guidelines Network. SIGN 135 - Management of epithelial ovarian cancer. October 2018.[21]
- European Society for Medical Oncology and European Society of Gynaecological Oncology Consensus Conference Recommendations on Ovarian Cancer: Pathology and Molecular Biology, Early and Advanced Stages, Borderline Tumours and Recurrent Disease. May 2019.[22]
- National Comprehensive Cancer Network. NCCN Guidelines® Insights: Ovarian Cancer, Version 3.2022.[23]

Additional Information

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