Innovation Observatory

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Veliparib in addition to carboplatin and paclitaxel for epithelial ovarian, fallopian tube, or primary peritoneal cancer

NIHRIO ID	11351	**NICE ID**	9120
Developer/Company	AbbVie	**UKPS ID**	N/A

Licensing and market availability plans	Veliparib in addition to carboplatin and paclitaxel is currently in phase III trials for epithelial ovarian, fallopian tube or primary peritoneal cancer.

SUMMARY

Veliparib as an oral formulation, in addition to chemotherapy drugs carboplatin and paclitaxel, is in clinical development for epithelial ovarian, fallopian tube or primary peritoneal cancer. Ovarian cancer includes a group of tumours that arise from diverse types of tissue contained in the ovary. The most common type of ovarian cancer arises from epithelial cells (the outside layer of cells) on the surface of the ovary, and can often spread from the ovary to any surface within the abdominal cavity including the fallopian tubes and peritoneal cavity. Fallopian tube cancer and primary peritoneal cancer are histologically equivalent diseases to epithelial ovarian cancer.

Veliparib acts by targeting specific enzymes involved in the repair of damaged DNA that helps the body to kill cancer cells while allowing ordinary cells to survive. Veliparib is expected to be used in combination with other cytotoxic (cell-killing) cancer medicines that cause DNA damage, such as chemotherapy, where it is expected to enhance their activity by preventing DNA repair. If licensed, veliparib in addition to carboplatin and paclitaxel will offer an additional treatment option for women with stage III or IV epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.

PROPOSED INDICATION

Previously untreated, newly diagnosed stage III or IV high grade serous epithelial ovarian, fallopian tube or primary peritoneal cancer in women aged 18 years and older.[1]

TECHNOLOGY

DESCRIPTION

Veliparib (ABT-888; NSC 737664) is a PARP inhibitor. PARP is poly(ADP-ribose) polymerase, an enzyme that enables cells to repair their DNA. Veliparib inhibits PARP-1 and PARP-2, preventing the DNA repair process in cancer cells, leading to their death and potentially making them more susceptible to chemotherapy while allowing ordinary cells to survive.[2]

Veliparib in addition to carboplatin and paclitaxel for previously untreated adult patients and veliparib monotherapy as a maintenance treatment is in clinical development for patients with epithelial ovarian, fallopian tube or primary peritoneal and veliparib monotherapy. In the phase III clinical trial (NCT02470585), veliparib is administered as a capsule in addition to intravenous infusion of carboplatin and paclitaxel for six 21-day cycles followed by veliparib maintenance therapy for up to 30 additional 21-day cycles. The exact dosage has not been provided in the clinical trial registry.[1]

INNOVATION AND/OR ADVANTAGES

The combination of paclitaxel and carboplatin (intravenous) is used to treat ovarian cancer.[3] Veliparib targets the cancer cells directly while allowing ordinary cells to survive and may provide an additional route to treatment. It is expected to be used in combination with other cytotoxic (cell-killing) cancer medicines that cause DNA damage, such as chemotherapy, where it is expected to enhance their activity by preventing DNA repair.[2]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Veliparib does not currently have Marketing Authorisation in the EU/UK for any indication.
It is also in phase III clinical trials for the following indications:[4]

- Advanced or metastatic squamous non-small cell lung cancer
- Non-squamous non-small cell lung cancer
- HER2-negative metastatic or locally advanced unresectable BRCA-associated breast cancer
- Early-stage triple negative breast cancer

Veliparib is a designated orphan drug in the EU in December 2010 for the treatment of ovarian cancer.[2]

Veliparib is a designated orphan drug in the US in September 2009 for the treatment of epithelial ovarian cancer in combination with DNA-damaging agents.[5]

PATIENT GROUP

DISEASE BACKGROUND

Ovarian cancer, or cancer of the ovaries, is one of the most common types of cancer in women. It mainly affects post-menopausal women, but it can sometimes affect younger women. The symptoms are not always easy to recognise because they are similar to other common conditions, including feeling constantly bloated, discomfort in the stomach or pelvis region, and needing to urinate more often.

The four main stages of ovarian cancer are:[6]

- stage I – the cancer only affects one or both of the ovaries
- stage II – the cancer has spread from the ovary and into the pelvis or womb
- stage III – the cancer has spread to the lining of the stomach, the surface of the bowel or the lymph glands in the pelvis or stomach
- stage IV – the cancer has spread to other parts of the body, such as the liver or lungs

The exact cause of ovarian cancer is unknown but risk factors include a family history of breast cancer, being over 50 years of age, hormone replacement therapy (although any increase in risk is likely to be small), endometriosis and being overweight.[7] Most (90%) ovarian cancers are epithelial, that is, they originate on the surface layer of the ovary.[8]

Fallopian tube cancer is rare - around 1% of the female reproductive system cancers occur in the fallopian tubes. Symptoms can be similar to those of ovarian cancer, and can also include vaginal bleeding unrelated to menstruation and a watery vaginal discharge that may contain blood.[9]

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.[10]

Women who undergo treatment for or survive ovarian cancer are at risk of several complications that may persist for a long time and negatively impact the quality of life. These include the early onset of menopausal symptoms and gynaecological problems leading to sexual dysfunction. These in turn can lead to psychological symptoms in addition to those caused by a distortion of body image after hysterectomy and abdominal scarring.[11]

CLINICAL NEED AND BURDEN OF DISEASE

Ovarian cancer is the 6th most common cancer in women in the UK.[12] It is a life-threatening disease that is associated with poor long-term survival.[2] Just over half (53%) of ovarian cancer cases in the UK each year are diagnosed in women aged 65 and over.[13]

In England in 2016, there were 5,895 new cases of ovarian cancer (ICD-10 C56), and the incidence was 21.1 per 100,000.[14] Fallopian tube cancer is rarer than this, making up 1 in 100 female reproductive cancers and research suggests primary peritoneal cancer affects 7 to 15 in 100 women with advanced ovarian cancer.[9,10]

According to HES data for England, there were 36,667 admissions in 2016-17 for primary diagnosis of malignant neoplasm of ovary (ICD-10 C56) of which 27,763 were day cases, and 39,380 finished consultant episodes. The corresponding figures for fallopian tube neoplasms (ICD-10 C57.0) were 2,210, 1,805 and 2,294 respectively, and for peritoneal neoplasms (ICD-10 C48.2) 4,154, 3,409 and 4,402 respectively.[15]

In the UK, age-standardised mortality rate was 12.9 per 100,000. In England and Wales, five year survival is 46%, and one year survival is 73% (2010 data).[12]

PATIENT TREATMENT PATHWAY

PATIENT PATHWAY

A woman should be referred for urgent assessment from primary care if physical examination identifies ascites and/or a pelvic or abdominal mass (which is not obviously uterine fibroids). Tests should be carried out if a woman (especially if 50 or over) reports having any of the following symptoms, among others, on a persistent or frequent basis – particularly more than 12 times per month:[16,17]

- persistent abdominal distension (women often refer to this as 'bloating')
- feeling full (early satiety) and/or loss of appetite
- pelvic or abdominal pain
- increased urinary urgency and/or frequency

Additional screening for ovarian cancer may include CA125 serum testing. In secondary care, CT scans, x-ray, biopsies, or laparoscopies may be needed to confirm or rule out ovarian cancer.[6]

Treatment for ovarian cancer is dependent on stage of disease, general health, and current fertility. Most patients undergo a combination of surgery and chemotherapy. The aim of treatment is to cure the cancer if possible. If the cancer is too advanced to be cured, treatment aims to relieve symptoms and control the cancer for as long as possible.[18]

If performing surgery for women with ovarian cancer, whether before chemotherapy or after neoadjuvant chemotherapy, the objective should be complete resection of all macroscopic disease.[16] Surgery usually involves removing: both ovaries and the fallopian tubes, the womb (hysterectomy), and/or a layer of fatty tissue in the stomach known as the omentum. Chemotherapy or targeted radiation may also be used in addition to surgery to kill, shrink, and prevent re-growth of cancer cells.[18]

CURRENT TREATMENT OPTIONS

The following are recommended first-line pharmacological treatment options for women (18 years and older) who have epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer or borderline ovarian cancer (stage II-IV):

- It is recommended that paclitaxel in combination with a platinum-based compound or platinum-based therapy alone (cisplatin or carboplatin) are offered as alternatives for first-line chemotherapy (usually following surgery) in the treatment of ovarian cancer.
- The choice of treatment for first-line chemotherapy for ovarian cancer should be made after discussion between the responsible clinician and the patient about the risks and benefits of the options available. In choosing between treatment with a platinum-based compound alone or paclitaxel in combination with a platinum-based compound, this discussion should cover the side-effect profiles of the alternative therapies, the stage of the woman's disease, the extent of surgical treatment of the tumour, and disease-related performance status.
- Bevacizumab in combination with paclitaxel and carboplatin is not recommended for first-line treatment of advanced ovarian cancer (International Federation of Gynaecology and Obstetrics [FIGO] stages IIIB, IIIC and IV epithelial ovarian, fallopian tube or primary peritoneal cancer). People currently receiving bevacizumab for first-line treatment of advanced ovarian cancer should be able to continue treatment until they and their clinicians consider it appropriate to stop.[17]

For maintenance therapy, niraparib is recommended for use within the Cancer Drugs Fund as an option for treating relapsed, platinum-sensitive high-grade serous epithelial ovarian, fallopian tube

or primary peritoneal cancer that has responded to the most recent course of platinum-based chemotherapy in adults, only if:

- they have a germline BRCA mutation and have had 2 courses of platinum-based chemotherapy or
- they do not have a germline BRCA mutation and have had 2 or more courses of platinum-based chemotherapy and
- the conditions in the managed access agreement for niraparib are followed.[19]

PLACE OF TECHNOLOGY

If licensed, veliparib in addition to carboplatin and paclitaxel will offer an additional treatment option for women with stage III or IV high grade serous epithelial ovarian cancer, fallopian tube cancer, or primary peritoneal cancer.

CLINICAL TRIAL INFORMATION

Trial	NCT02470585, EudraCT2014-005070-11; veliparib vs placebo; both in combination with carboplatin/ paclitaxel followed by veliparib vs placebo as maintenance; phase III
Sponsor	AbbVie
Status	Ongoing
Source of Information	Trial registry[1]
Location	EU (incl UK), USA, and other countries
Design	Randomised, placebo-controlled
Participants	n= 1140; aged 18-99 years; females; epithelial ovarian, fallopian tube, or primary peritoneal cancer, newly diagnosed, stage III or IV high grade serous adenocarcinoma.
Schedule	Randomised to: • Intravenous carboplatin/paclitaxel plus veliparib capsules for six 21-day cycles followed by veliparib capsules maintenance therapy for up to 30 additional 21-day cycles • Intravenous carboplatin/paclitaxel plus veliparib capsules for six 21-day cycles followed by placebo capsules maintenance therapy for up to 30 additional 21-day cycles • Intravenous carboplatin/paclitaxel plus placebo capsule for six 21-day cycles followed by placebo capsule maintenance therapy for up to 30 additional 21-day cycles
Follow-up	Active treatment for six 21 day cycles, maintenance therapy for 30 additional 21 day cycles, follow-up at 3 yrs
Primary Outcomes	Progression-free survival
Secondary Outcomes	• Overall Survival, • Disease related symptom (DRS) scores
Key Results	-
Adverse effects (AEs)	-
Expected reporting date	Study completion date reported as May 2020

ESTIMATED COST

The cost of veliparib is not yet known.

ADDITIONAL INFORMATION

AbbVie did not enter information about this technology onto the UK PharmaScan database, the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines

RELEVANT GUIDANCE

NICE GUIDANCE

- NICE technology appraisal in development. Lurbinectidin for treating advanced platinum-resistant ovarian cancer (GID-TA10313). Expected publication date: to be confirmed
- NICE technology appraisal in development. Ovarian (epithelial), fallopian and peritoneal cancer - pazopanib (maintenance) (GID-TAG444). Expected publication date: to be confirmed
- NICE technology appraisal in development. Ovarian cancer - vintafolide (with pegylated liposomal doxorubicin) (GID-TAG332). Expected publication date: to be confirmed
- NICE technology appraisal in development. Cediranib for treating relapsed platinum-sensitive ovarian, fallopian tube or primary peritoneal cancer (GID-TA10018). Expected publication date: to be confirmed
- NICE technology appraisal in development. Olaparib for maintenance treatment of ovarian, fallopian tube or peritoneal cancer that has a BRCA germline mutation after response to first-line platinum-based chemotherapy (GID-TA10257). Expected publication date: October 2019
- NICE technology appraisal. Niraparib for maintenance treatment of relapsed, platinum-sensitive ovarian, fallopian tube and peritoneal cancer (TA528). July 2018
- NICE technology appraisal. Bevacizumab in combination with paclitaxel and carboplatin for first-line treatment of advanced ovarian cancer (TA284). May 2013
- NICE clinical guideline. Ovarian cancer: recognition and initial management (CG122). April 2011
- NICE quality standard. Ovarian cancer (QS18). May 2012
- NICE interventional procedures guidance. Ultra-radical (extensive) surgery for advanced ovarian cancer (IPG470). November 2013

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

- NHS England. NHS standard contract for complex gynaecology - specialist gynaecological cancers. E10/S/f. 2013
- 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

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- National Comprehensive Cancer Network. Ovarian cancer, version 1.2016, NCCN clinical practice guidelines in oncology. 2016[23]
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