Health Technology Briefing
January 2022

Durvalumab add-on therapy for previously untreated locally advanced cervical cancer

Company/Developer	AstraZeneca UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 27194	NICE ID: 10747	UKPS ID: 663175

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Durvalumab is in clinical development as an add-on treatment of female adults with previously untreated, locally advanced cervical cancer. Durvalumab will be added to the current treatment of concurrent chemotherapy and radiation therapy (cCRT). Cervical cancer arises when abnormal cells lining the cervix begin to grow uncontrollably and create tumours. Cervical cancer may not present symptoms, however the most common symptoms seen are unusual vaginal bleeding, pain during sex, vaginal discharge and pain in the pelvis. Increasing age and Human Papilloma Virus (HPV) infection are risk factors for the development of cervical cancer. Locally advanced cervical cancer means that the tumour is within the cervix (more than 4cm) or it has grown into the tissues around the cervix, but has not spread to other organs. cCRT is the only treatment currently recommended for previously untreated cervical cancer patients.

Durvalumab is a type of protein (monoclonal antibody) administered by intravenous (IV) infusion to increase the ability of the immune system to kill cancer cells. Medicinal products with similar mechanism of action have shown beneficial treatment outcomes in cervical cancer patients previously. It is thought that adding durvalumab to cCRT may create an environment where the immune system is more able to kill cancer cells, compared to when patients are treated with cCRT alone. If licensed, durvalumab could provide a further pharmacological treatment option for previously untreated cervical cancer patients.

Proposed Indication

Add-on, first line treatment of female adults with locally advanced cervical cancer[1]

Technology

Description

Durvalumab (Imfinzi, MEDI4736) is a human immunoglobulin G1 kappa (IgG1κ) monoclonal antibody that selectively blocks the interaction of programmed cell death ligand-1 (PD-L1) and CD80. Expression of PD-L1 protein is an adaptive immune response that helps tumours evade detection by the immune system. Selective blockade of PD-L1/PD-1 and PD-L1/CD80 interactions enhances antitumour immune responses and increases T-cell activation.[2]

Durvalumab is currently in phase III clinical development for the add-on, first line treatment of female adults with locally advanced, metastatic cervical cancer.[1,a] In the phase III clinical trial (CALLA, NCT03830866), patients were administered durvalumab 1500mg via intravenous (IV) infusion in addition to concurrent chemotherapy and radiation therapy (cCRT) followed by durvalumab monotherapy every 4 weeks for up to 24 months.[1,3]

Key Innovation

Immunotherapy with anti-PD-L1 interventions has shown activity in the second line treatment of advanced cervical cancer. It is thought that the addition of immunotherapy to the first line standard of care cCRT may produce an environment which is more immunogenic. This may lead to initiation of DNA breaks, cell death phagocytosis and antigen presentation and may therefore improve anti-tumour surveillance by the immune system and enhance anti-tumour activity.[4] If approved, durvalumab would provide a novel treatment approach for first line cervical cancer patients.

Regulatory & Development Status

Durvalumab has a Marketing Authorisation in the UK for the monotherapy treatment of locally advanced, unresectable NSCLC in adults whose tumours express PD-L1 on ≥1% of tumour cells and whose disease has not progressed following platinum-based chemoradiation therapy. It is also approved 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).[2]

Durvalumab as a monotherapy and in addition to various other medicinal products is being developed for numerous indications including bladder, lung and renal cancers in phase II and phase III clinical trials.[5]

Patient Group

Disease Area and Clinical Need

Cervical cancer arises when abnormal cells in the lining of the cervix begin to grow in an uncontrolled way and tumours are created.[6] Cervical cancers can be split in to two main forms, according to the type of cell that has become cancerous: squamous cell carcinomas (the most common form) and adenocarcinomas.[7] Cervical cancer can often not present symptoms. The most common symptoms which may present include unusual vaginal bleeding, pain or discomfort during sex, vaginal discharge and pelvic pain.[8] Increasing age, HPV infection, smoking, contraceptive pill use and a family history of cervical cancer are risk factors for cervical cancer.[9]

In 2016-18, there were an average of 3,197 cases of cervical cancer each year in the UK.[10] In 2017 in England, the age-standardised incidence rates for cervical cancer was 9.4 per 100,000 and there were 674 reported deaths from cervical cancer.[11] In England in 2020-21 there were 7,586 hospital admissions and 8,091 finished consultant episodes (FCEs) for malignant neoplasm of cervix uteri (ICD-10 code C53) which resulted in 4,719 day cases and 11,296 FCE bed days.[12] The 1-year and 5-year age-standardised survival rates for cervical cancer patients (all stages) diagnosed between 2013 and 2017, followed up to 2018, in England were 81.1% and 61.4% respectively.[13]

Recommended Treatment Options

The only treatment recommended by NICE for locally advanced (Stage IIB-IVA), previously untreated cervical cancer is concurrent chemotherapy and radiation therapy (cCRT).[14]

Clinical Trial Information

Trial	**CALLA**, NCT03830866, 2018-002872-42; A Phase III, Randomized, Multi-Center, Double-Blind, Global Study to Determine the Efficacy and Safety of Durvalumab in Combination With and Following Chemoradiotherapy Compared to Chemoradiotherapy Alone for Treatment in Women With Locally Advanced Cervical Cancer **Phase III –** Active, not recruiting **Locations:** 2 EU, USA and other countries **Primary completion date:** October 2022
Trial Design	Randomized, parallel assignment, quadruple masking
Population	N=770; female adults aged 18 years and older with cervical adenocarcionoma or squamous carcinoma; FIGO stages IB2 to IIB node positive or IIA-IVA any node; no prior chemotherapy or radiotherapy for cervical cancer
Intervention(s)	Durvalumab (IV) + cCRT – participants received durvalumab via IV infusion at an unspecified dose in addition to cCRT followed by durvalumab monotherapy for up to 24 months
Comparator(s)	Placebo (IV) + cCRT – participants received IV placebo in addition to cCRT an unspecified dose and schedule
Outcome(s)	**Primary outcome measures:** The efficacy of durvalumab + standard of care cCRT compared to placebo + soc cCRT in terms of progression-free survival (PFS) [Time frame: Estimated to be from the time of randomization up to 4.5 years] See trial record for a full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

Durvalumab is already marketed in the UK for various indications; a 120mg/2.4ml concentrate for solution for infusion vial costs £592.00 and a 500mg/10ml concentrate for solution for infusion vial costs £2466.00.[15]

Relevant Guidance

NICE Guidance

- NICE technology appraisal. Topotecan for the treatment of recurrent and stage IVB cervical cancer (TA183). October 2009.
- NICE interventional procedure guidance. High dose rate brachytherapy for carcinoma of the cervix (IPG160). March 2006.

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.
- NHS England. 2013/14 NHS Standard Contract for Cancer: Radiotherapy (All Ages). B01/S/a.

Other Guidance

- National Institute for Health and Care Excellence. CKS: Cervical cancer and HPV. 2021.[14]
- Reed N, Balega J, Barwick T, Buckley L, Burton K et al. British Gynaecological Cancer Society (BGCS) Cervical Cancer Guidelines: Recommendations for Practice. 2020.[16]

Additional Information

References

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