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Imfinzi plus chemotherapy approved in the US for mismatch repair deficient advanced or recurrent endometrial cancer

Approval based on DUO-E trial results, which showed Imfinzi reduced the risk of disease progression or death by 58% vs. chemotherapy

AstraZeneca's *Imfinzi* (durvalumab) in combination with carboplatin and paclitaxel followed by *Imfinzi* monotherapy has been approved in the US as treatment for adult patients with primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR).[1]

The approval by the Food and Drug Administration (FDA) was based on the results of a prespecified exploratory subgroup analysis by MMR status in the DUO-E Phase III trial. Results from DUO-E were published in the *Journal of Clinical Oncology*.

In the trial, *Imfinzi* plus carboplatin and paclitaxel followed by *Imfinzi* monotherapy (*Imfinzi* arm) reduced the risk of disease progression or death by 58% in patients with dMMR endometrial cancer versus chemotherapy alone (hazard ratio 0.42; 95% confidence interval 0.22-0.80).[2]

In the US, endometrial cancer is the fourth most common cancer in women, with more than 66,000 patients diagnosed and almost 12,000 deaths in 2022.[3,4] Patients diagnosed at an early stage of disease have a five-year survival rate of approximately 80-90%, but there is a significant need for new treatment options for people with advanced disease, where the survival rate falls to less than 20%.[5,6]

Shannon N. Westin, Professor of Gynecologic Oncology and Reproductive Medicine at The University of Texas MD Anderson Cancer Center, and principal investigator of the trial, said, "With the incidence and mortality of endometrial cancer expected to continue to increase significantly in the coming decades, it is more important than ever that we bring new treatment options to patients at the earliest possible moment in their care. This approval underlines clear evidence that durvalumab plus chemotherapy followed by durvalumab monotherapy delivers important clinical benefits for patients with mismatch repair deficient endometrial cancer."

Dave Fredrickson, Executive Vice President, Oncology Business Unit, AstraZeneca, said: "There have been limited advances in the treatment of endometrial cancer in the last few decades, and continued innovation is critical as the burden of this cancer is expected to grow in the future. Immunotherapy in combination with chemotherapy is emerging as a new standard of care in this setting, and the approval of *Imfinzi* offers an important new option for patients with mismatch repair deficient disease."

The safety and tolerability profile of the *Imfinzi* and chemotherapy regimen was generally manageable, well tolerated and broadly consistent with prior clinical trials with no new safety signals.[1,2]

The *Lynparza* (olaparib) and *Imfinzi* arm, which investigated *Imfinzi* plus chemotherapy followed by *Imfinzi* plus *Lynparza* as maintenance therapy, also met the primary endpoint of progression-free survival (PFS). The trial continues to assess OS as a key secondary endpoint for both arms. Regulatory applications for both *Imfinzi* as well as *Imfinzi* and *Lynparza* regimens are currently under review in the EU, Japan and several other countries based on the DUO-E results.

Notes

Endometrial cancer
Endometrial cancer is a highly heterogeneous disease that originates in the tissue lining of the uterus and is most common in women who have already been through menopause, with the average age at diagnosis being over 60 years old.[7-10] It is the sixth most common cancer in women worldwide.[11,12] Incidence and mortality of endometrial cancer are expected to increase by approximately 61% and 87% respectively (from 420,400 cases and 97,700 deaths in 2022 to 676,300 cases and 183,100 deaths) in 2050.[13]

The majority of patients with endometrial cancer are diagnosed at an early stage of disease, where the cancer is

confined to the uterus.[9,10] They are typically treated with surgery and/or radiation, and the five-year survival rate is high (approximately 80-90%).[5,6] Patients with advanced disease (Stage III-IV) usually have a much poorer prognosis, with the five-year survival rate falling to less than 20%.[5,6] Immunotherapy combined with chemotherapy is emerging as a new standard of care for advanced endometrial cancer, particularly for patients with dMMR disease, who make up approximately 20-30% of all patients with this type of cancer.[6,14,15,16] There remains a high unmet need for treatments for the remaining 70-80% of endometrial cancer patients with pMMR disease.[15,16]

DUO-E
The DUO-E trial (GOG 3041/ENGOT-EN10) is a three-arm, randomised, double-blind, placebo-controlled, multicentre Phase III trial of 1st-line *Imfinzi* (durvalumab) plus platinum-based chemotherapy (carboplatin and paclitaxel) followed by either *Imfinzi* monotherapy or *Imfinzi* plus *Lynparza* (olaparib) as maintenance therapy versus platinum-based chemotherapy alone as a treatment for patients with newly diagnosed advanced or recurrent endometrial cancer.

The DUO-E trial randomised 699 patients with newly diagnosed advanced or recurrent epithelial endometrial carcinoma to receive either *Imfinzi* (1120mg) or placebo, given every three weeks in addition to standard-of-care platinum-based chemotherapy. After 4-6 cycles of chemotherapy, patients (whose disease had not progressed) then received either *Imfinzi* (1500mg) or placebo every four weeks as maintenance, plus 300mg *Lynparza* (300mg BID [2x150mg tablets, twice a day]) or placebo until disease progression.

The dual primary endpoint was PFS of each treatment arm versus standard of care. Key secondary endpoints included overall survival (OS), safety and tolerability. The trial continues to assess OS for both *Imfinzi* monotherapy and *Imfinzi* plus *Lynparza* as maintenance therapy in the overall trial population. Mismatch repair (MMR) status, recurrence status and geographic location were stratification factors. The trial was sponsored independently by AstraZeneca and conducted in 253 study locations across 22 countries including the US, Europe, South America and Asia.

For more information about the trial, please visit ClinicalTrials.gov.

Imfinzi
Imfinzi (durvalumab) is a human monoclonal antibody that binds to the PD-L1 protein and blocks the interaction of PD-L1 with the PD-1 and CD80 proteins, countering the tumour's immune-evading tactics and releasing the inhibition of immune responses.

In addition to its indications in unresectable, Stage III NSCLC and ES-SCLC, *Imfinzi* is currently approved in a number of countries in combination with a short course of tremelimumab (*Imjudo*) and chemotherapy for the treatment of metastatic NSCLC.

Imfinzi is also approved in a number of countries in combination with chemotherapy in locally advanced or metastatic biliary tract cancer and in combination with *Imjudo* in unresectable hepatocellular carcinoma (HCC). Imfinzi is also approved as a monotherapy in unresectable HCC in Japan and the EU.

Since the first approval in May 2017, more than 220,000 patients have been treated with *Imfinzi*. As part of a broad development programme, *Imfinzi* is being tested as a single treatment and in combinations with other anti-cancer treatments for patients with SCLC, NSCLC, bladder cancer, breast cancer, several gastrointestinal cancers and other solid tumours.

AstraZeneca in immuno-oncology (IO)
AstraZeneca is a pioneer in introducing the concept of immunotherapy into dedicated clinical areas of high unmet medical need. The Company has a comprehensive and diverse IO portfolio and pipeline anchored in immunotherapies designed to overcome evasion of the anti-tumour immune response and stimulate the body's immune system to attack tumours.

AstraZeneca aims to reimagine cancer care and help transform outcomes for patients with *Imfinzi* as monotherapy and in combination with *Imjudo* as well as other novel immunotherapies and modalities. The Company is also exploring next-generation immunotherapies like bispecific antibodies and therapeutics that harness different aspects of immunity to target cancer.

AstraZeneca is boldly pursuing an innovative clinical strategy to bring IO-based therapies that deliver long-term survival to new settings across a wide range of cancer types. With an extensive clinical programme, the Company also champions the use of IO treatment in earlier disease stages, where there is the greatest potential for cure.

AstraZeneca in oncology
AstraZeneca is leading a revolution in oncology with the ambition to provide cures for cancer in every form, following the science to understand cancer and all its complexities to discover, develop and deliver life-changing medicines to patients.

The Company's focus is on some of the most challenging cancers. It is through persistent innovation that AstraZeneca has built one of the most diverse portfolios and pipelines in the industry, with the potential to catalyse changes in the practice of medicine and transform the patient experience.

AstraZeneca has the vision to redefine cancer care and, one day, eliminate cancer as a cause of death.

AstraZeneca
AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Diseases, and BioPharmaceuticals, including Cardiovascular, Renal & Metabolism, and Respiratory & Immunology. Based in Cambridge, UK, AstraZeneca's innovative medicines are sold in more than 125 countries and used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on social media @AstraZeneca.

Contacts
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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