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AstraZeneca PLC
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# FDA Advisory Committee reviewed *Imfinzi* for treatment of resectable non-small cell lung cancer based on AEGEAN Phase III trial results

The Food and Drug Administration's (FDA) Oncologic Drugs Advisory Committee (ODAC) acknowledged that AstraZeneca's *Imfinzi* (durvalumab) met the primary endpoint of event-free survival (EFS) in the treatment of resectable non-small cell lung cancer (NSCLC) based on the AEGEAN Phase III trial results with an overall tolerable safety profile. In the trial, adult patients with resectable early-stage (IIA-IIIB) NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements were treated with *Imfinzi* in combination with neoadjuvant chemotherapy before surgery and as adjuvant monotherapy after surgery. The discussion noted that while the contribution by phase of neoadjuvant and adjuvant components of the perioperative regimen could not be clearly assigned based on the trial design, this is an important potential regimen for patients.

The FDA accepted the supplemental Biologics License Application (sBLA) in September 2023 for *Imfinzi* in this indication based on positive results from the pivotal AEGEAN trial, which were published in *The New England Journal of Medicine* in October 2023.

John V. Heymach, MD, PhD, Professor and Chair Thoracic/Head and Neck Medical Oncology, The University of Texas MD Anderson Cancer Center in Houston, Texas, said: "The majority of patients with resectable lung cancer face recurrence of their disease even after surgery and neoadjuvant chemotherapy. The Committee acknowledged the potential to address this urgent unmet need with durvalumab both before and after surgery, which can significantly increase the time patients live without progression and recurrence events in this curative-intent setting."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "The Committee's discussion of the AEGEAN data highlighted the significant benefit delivered by this *Imfinzi*-based regimen for patients with resectable lung cancer. We are committed to working closely with the FDA to bring this novel immunotherapy option to patients that offers a flexible chemotherapy backbone."

Results from a planned interim analysis of EFS from the AEGEAN trial showed a statistically significant and clinically meaningful 32% reduction in the risk of recurrence, progression events or death versus chemotherapy alone in patients treated with the *Imfinzi*-based regimen before and after surgery (32% data maturity; EFS hazard ratio of 0.68; 95% confidence interval [CI] 0.53-0.88; p=0.003902). In a final analysis of pathologic complete response (pCR), treatment with *Imfinzi* plus neoadjuvant chemotherapy before surgery resulted in a pCR rate of 17.2% versus 4.3% for patients treated with neoadjuvant chemotherapy alone (difference in pCR 13.0%; 95% CI 8.7-17.6).

*Imfinzi* was generally well tolerated, and no new safety signals were observed in the neoadjuvant and adjuvant settings. Further, adding *Imfinzi* to neoadjuvant chemotherapy was consistent with the known profile for this combination and did not compromise patients' ability to complete surgery versus chemotherapy alone.

The ODAC provides the FDA with independent, expert advice and recommendations on marketed and investigational medicines for use in the treatment of cancer. The FDA will consider the feedback as it reviews the submission and is not bound by the Committee's recommendation.

*Imfinzi* is approved in Switzerland and the UK for the treatment of adults with resectable NSCLC in Stage II and III without known EGFR mutations or ALK rearrangements, based on the AEGEAN results. Regulatory applications for *Imfinzi* in this setting are also currently under review in the EU, China and several other countries.

*Imfinzi* is the only approved immunotherapy and the global standard of care in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease has not progressed after chemoradiotherapy based on the PACIFIC Phase III trial.

Notes

**Lung cancer**

Each year, there are an estimated 2.4 million people diagnosed with lung cancer globally.[1] Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-fifth of all cancer deaths.[1-2] Lung cancer is broadly split into NSCLC and small cell lung cancer (SCLC), with 80-85% of patients diagnosed with NSCLC.[3-4]

The majority of NSCLC patients are diagnosed with advanced disease while approximately 25-30% present with resectable disease at diagnosis.[5-6] Early-stage lung cancer diagnoses are often only made when the cancer is found on imaging for an unrelated condition.[7-8]

The majority of patients with resectable disease eventually develop recurrence despite complete tumour resection and adjuvant chemotherapy.[9] Only 36-46% of patients with Stage II disease will survive for five years.[10] This decreases to 24% for patients with Stage IIIA disease and 9% for patients with Stage IIIB disease, reflecting a high unmet medical need.[10]

**AEGEAN**

AEGEAN is a randomised, double-blind, multi-centre, placebo-controlled global Phase III trial evaluating *Imfinzi* as perioperative treatment for patients with resectable Stage IIA-IIIB (Eighth Edition AJCC Cancer Staging Manual) NSCLC, irrespective of PD-L1 expression. Perioperative therapy includes treatment before and after surgery, also known as neoadjuvant/adjuvant therapy. In the trial, 802 patients were randomised to receive a 1500mg fixed dose of *Imfinzi* plus chemotherapy or placebo plus chemotherapy every three weeks for four cycles prior to surgery, followed by *Imfinzi* or placebo every four weeks (for up to 12 cycles) after surgery. Patients with known EGFR or ALK genomic tumour aberrations were excluded from the primary efficacy analyses.

In the AEGEAN trial, the primary endpoints were pCR, defined as no viable tumour in the resection specimen (including lymph nodes) following neoadjuvant therapy, and EFS, defined as the time from randomisation to an event like tumour recurrence, progression precluding definitive surgery, or death. Key secondary endpoints were major pathologic response, defined as residual viable tumour of less than or equal to 10% in the resected primary tumour following neoadjuvant therapy, disease-free survival, overall survival (OS), safety and quality of life. The final pathologic response analyses were performed after all patients had the opportunity for surgery and pathology assessment per the trial protocol. The trial enrolled participants from 264 centres in more than 25 countries and regions including in the US, Canada, Europe, South America and Asia.

***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.

*Imfinzi* is the only approved immunotherapy and the global standard of care in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease has not progressed after chemoradiotherapy. *Imfinzi* is also approved for the treatment of extensive-stage SCLC and in combination with a short course of *Imjudo* (tremelimumab) and chemotherapy for the treatment of metastatic NSCLC.

In limited-stage SCLC, *Imfinzi* demonstrated statistically significant and clinically meaningful improvements in the dual primary endpoints of OS and progression-free survival compared to placebo in patients who had not progressed following standard-of-care concurrent chemoradiotherapy in the ADRIATIC Phase III trial.

In addition to its indications in lung cancers, *Imfinzi* is approved in combination with chemotherapy (gemcitabine plus cisplatin) 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 and in combination with chemotherapy (carboplatin plus paclitaxel) followed by *Imfinzi* monotherapy in primary advanced or recurrent endometrial cancer that is mismatch repair deficient in the US.

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, breast cancer, bladder cancer, several gastrointestinal and gynaecologic cancers, and other solid tumours.

**AstraZeneca in lung cancer**
AstraZeneca is working to bring patients with lung cancer closer to cure through the detection and treatment of early-stage disease, while also pushing the boundaries of science to improve outcomes in the resistant and advanced settings. By defining new therapeutic targets and investigating innovative approaches, the Company aims to match medicines to the patients who can benefit most.

The Company's comprehensive portfolio includes leading lung cancer medicines and the next wave of innovations, including *Tagrisso* (osimertinib) and *Iressa* (gefitinib); *Imfinzi* and *Imjudo*; *Enhertu* (trastuzumab deruxtecan) and datopotamab deruxtecan in collaboration with Daiichi Sankyo; *Orpathys* (savolitinib) in collaboration with HUTCHMED; as well as a pipeline of potential new medicines and combinations across diverse mechanisms of action.

AstraZeneca is a founding member of the Lung Ambition Alliance, a global coalition working to accelerate innovation and deliver meaningful improvements for people with lung cancer, including and beyond treatment.

**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 strives to redefine cancer care and help transform outcomes for patients with *Imfinzi* as a monotherapy and in combination with *Imjudo* as well as other novel immunotherapies and modalities. The Company is also investigating next-generation immunotherapies like bispecific antibodies and therapeutics that harness different aspects of immunity to target cancer, including cell therapy and T cell engagers.

AstraZeneca is 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. The Company is focused on exploring novel combination approaches to help prevent treatment resistance and drive longer immune responses. 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.

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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**
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