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Imfinzi-based perioperative regimen approved in the EU for resectable non-small cell lung cancer

Approval based on AEGEAN Phase III trial results which showed a 32% reduction in the risk of recurrence, progression or death vs. neoadjuvant chemotherapy alone

AstraZeneca's *Imfinzi* (durvalumab) in combination with chemotherapy has been approved in the European Union (EU) for the treatment of adults with resectable non-small cell lung cancer (NSCLC) at high risk of recurrence and no epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements. In this regimen, patients are treated with *Imfinzi* in combination with neoadjuvant chemotherapy before surgery and as adjuvant monotherapy after surgery.

The approval by the European Commission follows the positive opinion of the Committee for Medicinal Products for Human Use and is based on results from the pivotal AEGEAN trial, which were published in *The New England Journal of Medicine*.

Each year in Europe, there are more than 450,000 people diagnosed with lung cancer.[1] Around 25-30% of all patients with NSCLC, the most common form of lung cancer, are diagnosed at an early stage to have surgery with curative intent.[2-3] However, the majority of patients with resectable disease will develop recurrence and only 36-46% of patients with Stage II disease will survive for five years.[4-5] This decreases to 24% for patients with Stage IIIA disease and 9% for patients with Stage IIIB disease, reflecting a high unmet medical need.[4]

Professor Martin Reck, Head of the Department of Thoracic Oncology at the Lung Clinic Grosshansdorf, Germany, member of the AEGEAN Steering Committee and investigator in the trial, said: "Today's approval provides an important new treatment option that should become a backbone combination approach for patients in Europe with resectable non-small cell lung cancer, who have historically faced high rates of recurrence and a poor prognosis. When added to neoadjuvant chemotherapy, perioperative durvalumab meaningfully improved outcomes in this curative-intent setting, significantly extending the time patients lived without their cancer returning."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Today's approval marks an important step towards improving outcomes for patients in Europe with resectable non-small cell lung cancer, enabling more patients to access this important immunotherapy-based regimen. This new indication builds on the established role of *Imfinzi* in unresectable disease and underscores our commitment to transforming care in the early stages of lung cancer where there is the greatest potential for cure."

Results from a planned interim analysis of event-free survival (EFS) showed a statistically significant and clinically meaningful 32% reduction in the risk of recurrence, progression events or death versus neoadjuvant chemotherapy alone in patients treated with the *Imfinzi*-based perioperative regimen (32% data maturity; EFS hazard ratio [HR] 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).

Additionally, interim overall survival (OS) results presented at the 2024 World Conference on Lung Cancer showed a favourable trend with the *Imfinzi*-based perioperative regimen (35% data maturity; median OS: not reached [NR] versus 53.2 months; HR=0.89; 95% CI 0.70-1.14). The OS data were not tested for statistical significance at this interim analysis and will continue to be assessed as a key secondary endpoint at final analysis.

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.

Imfinzi is approved in the US, China and several other countries in this setting based on the AEGEAN results. Regulatory applications are currently under review in Japan and additional countries in this indication.

Imfinzi is the global standard of care based on OS in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease as not progressed after chemoradiotherapy (CRT) based on the PACIFIC Phase III trial.

Notes

Lung cancer

Lung cancer is the leading cause of cancer death among both men and women, accounting for about one-fifth of all cancer deaths.[6-7] Lung cancer is broadly split into NSCLC and small cell lung cancer (SCLC), with 80-85% of patients diagnosed with NSCLC.[8-9] An estimated 28,000 people are treated for resectable NSCLC across the five major European countries each year.[10]

Early-stage lung cancer diagnoses are often only made when the cancer is found on imaging for an unrelated condition.[11-12] The majority of patients with resectable disease eventually develop recurrence

despite complete tumour resection and adjuvant chemotherapy.[v]

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, 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 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.

In addition to its indications in resectable, early-stage (IIA-IIIB) NSCLC and unresectable, Stage III NSCLC, *Imfinzi* is also approved for use in combination with a short course of *Imjudo* (tremelimumab) and chemotherapy for the treatment of metastatic NSCLC. *Imfinzi* is also approved for limited-stage SCLC in patients whose disease has not progressed following concurrent platinum-based CRT; and in combination with chemotherapy (etoposide and either carboplatin or cisplatin) for the treatment of extensive-stage SCLC.

Imfinzi is also 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.

In March 2025, perioperative *Imfinzi* added to standard-of-care chemotherapy met the primary endpoint of EFS in the MATTERHORN Phase III trial in resectable gastric and gastroesophageal junction cancers.

Imfinzi is also approved as a perioperative treatment in combination with neoadjuvant chemotherapy for muscle-invasive bladder cancer in the US.

Imfinzi in combination with chemotherapy followed by *Imfinzi* monotherapy is approved as a 1st-line treatment for primary advanced or recurrent endometrial cancer (mismatch repair deficient disease only in US and EU). *Imfinzi* in combination with chemotherapy followed by *Lynparza* (olaparib) and *Imfinzi* is approved for patients with mismatch repair proficient advanced or recurrent endometrial cancer in EU and Japan.

Since the first approval in May 2017, more than 374,000 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 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 *Datroway* (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.

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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