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Imfinzi-based perioperative regimen recommended for approval in the EU by CHMP for resectable non-small cell lung cancer

Recommendation based on AEGEAN Phase III trial results which showed Imfinzi reduced the risk of recurrence, progression or death by 32% vs. neoadjuvant chemotherapy alone

AstraZeneca's *Imfinzi* (durvalumab) in combination with chemotherapy has been recommended for approval 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 Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) based its positive opinion on results from the pivotal AEGEAN trial, which were published in *The New England Journal of Medicine*.

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.

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: "Adding perioperative durvalumab to neoadjuvant chemotherapy significantly improved outcomes for patients with resectable non-small cell lung cancer, who experience high rates of recurrence and poor outcomes. Today's recommendation marks an important step towards patients and their clinicians in Europe gaining access to an innovative treatment that should become a backbone combination approach in this curative-intent setting."

Susan Galbraith, Executive Vice President, Oncology Haematology R&D, AstraZeneca, said: "This recommendation highlights the potential of *Imfinzi* to address an unmet need for patients with resectable lung cancer who need new treatment options that increase the time they live without recurrence or progression. AEGEAN underscores our commitment to transforming care in the early stages of lung cancer where there is the greatest potential for cure."

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 early enough 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]

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 and several other countries in this setting based on the AEGEAN results. Regulatory applications are also currently under review in China, Japan and additional countries.

Imfinzi is the global standard of care based on OS in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease has 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.[5]

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 small cell lung cancer (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.

Imfinzi is also approved in combination with chemotherapy (carboplatin and paclitaxel) followed by *Imfinzi* monotherapy in primary advanced or recurrent endometrial cancer that is mismatch repair deficient (dMMR) in the US. In the EU, *Imfinzi* plus chemotherapy followed by *Lynparza* (olaparib) and *Imfinzi* is approved for patients with mismatch repair proficient (pMMR) advanced or recurrent endometrial cancer, and *Imfinzi* plus chemotherapy followed by *Imfinzi* alone is approved for patients with dMMR disease. In Japan, *Imfinzi* plus chemotherapy followed by *Imfinzi* monotherapy has also been approved as 1st-line treatment in primary advanced or recurrent endometrial cancer, and *Imfinzi* plus chemotherapy followed by *Imfinzi* and *Lynparza* has been approved for patients with pMMR disease.

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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