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Imfinzi approved in the EU as first and only immunotherapy for limited-stage small cell lung cancer

Approval based on ADRIATIC Phase III trial results which showed a 27% reduction in the risk of death versus placebo

AstraZeneca's *Imfinzi* (durvalumab) has been approved in the European Union (EU) as monotherapy for the treatment of adults with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following platinum-based chemoradiation therapy (CRT).

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 ADRIATIC Phase III trial, which were published in *The New England Journal of Medicine*.

SCLC is a highly aggressive form of lung cancer, with an estimated 8,000 people treated for LS-SCLC across the five major European countries each year.[1-2] LS-SCLC typically recurs and progresses rapidly, despite initial response to standard-of-care chemotherapy and radiotherapy.[3-4] The prognosis for LS-SCLC is particularly poor, as only 15-30% of patients survive for five years after diagnosis.[5]

Suresh Senan, PhD, radiation oncologist at the Amsterdam University Medical Centers, The Netherlands, and principal investigator in the trial, said: "This approval marks a turning point for patients with limited-stage small cell lung cancer in Europe, bringing them an immunotherapy option for the first time. An unprecedented 57% of patients treated with durvalumab were still alive at three years in the ADRIATIC trial. This significant advance establishes a new benchmark in a setting where the standard of care has remained unchanged for decades."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: *"Imfinzi* has the potential to transform how limited-stage small cell lung cancer is treated as the first immunotherapy approved in Europe in this setting. As the only immunotherapy approved for both early and late-stage disease, *Imfinzi* is poised to become the foundation for transforming outcomes for people with small cell lung cancer."

In the trial, results showed *Imfinzi* reduced the risk of death by 27% versus placebo (based on an overall survival [OS] hazard ratio [HR] of 0.73; 95% confidence interval [CI] 0.57-0.93; p=0.0104). Estimated median OS was 55.9 months for *Imfinzi* versus 33.4 months for placebo. An estimated 57% of patients treated with *Imfinzi* were alive at three years compared to 48% for placebo.

Imfinzi also reduced the risk of disease progression or death by 24% (based on a progression-free survival [PFS] HR of 0.76; 95% CI 0.61-0.95; p=0.0161) versus placebo. Median PFS was 16.6 months for *Imfinzi* versus 9.2 months for placebo. An estimated 46% of patients treated with *Imfinzi* had not experienced disease progression at two years compared to 34% for placebo.

The safety profile for *Imfinzi* was generally manageable and consistent with the known profile of this medicine. No new safety signals were observed.

Imfinzi is approved in the US and several other countries in this setting based on the ADRIATIC results. Regulatory applications are currently under review in Japan and several other countries for this indication. *Imfinzi* is also approved in combination with chemotherapy for the treatment of extensive-stage SCLC based on the CASPIAN Phase III trial.

Notes

Small cell 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 non-small cell lung cancer (NSCLC) and SCLC, with about 15% of cases classified as SCLC.[8]

LS-SCLC (Stage I-III) accounts for approximately 30% of SCLC diagnoses and is classified when the disease is generally only in one lung or one side of the chest.[9] The prognosis for patients with LS-SCLC remains poor despite curative-intent treatment with standard-of-care concurrent CRT (cCRT).[10]

ADRIATIC

The ADRIATIC trial is a randomised, double-blind, placebo-controlled, multi-centre global Phase III trial evaluating *Imfinzi* monotherapy and *Imfinzi* plus *Imjudo* (tremelimumab) versus placebo in the treatment of 730 patients with LS-SCLC who had not progressed following cCRT. In the experimental arms, patients were randomised to receive a 1500mg fixed dose of *Imfinzi* with or without *Imjudo* 75mg every four weeks for up to four doses/cycles each, followed by *Imfinzi* every four weeks for up to 24 months.

The dual primary endpoints were PFS and OS for *Imfinzi* monotherapy versus placebo. Key secondary endpoints included OS and PFS for *Imfinzi* plus *Imjudo* versus placebo, safety and quality of life measures. The trial included 164 centres in 19 countries across North and South America, Europe 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 SCLC, *Imfinzi* is also 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 CRT. Additionally, *Imfinzi* is approved as a perioperative treatment in combination with neoadjuvant chemotherapy in resectable NSCLC; and in combination with a short course of *Imjudo* and chemotherapy for the treatment of metastatic NSCLC.

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 event-free survival in the MATTERHORN Phase III trial in resectable gastric and gastroesophageal junction cancers.

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

References

1. National Cancer Institute. NCI Dictionary - Small Cell Lung Cancer. Available at:

1. National Cancer Institute. NCI Dictionary - Small Cell Lung Cancer. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/small-cell-lung-cancer. Accessed March 2025.
2. AstraZeneca PLC. Investor Relations Epidemiology Spreadsheet. Available at: https://www.astrazeneca.com/investor-relations.html. Accessed March 2025.
3. Qin A, Kalemkerian GP. Treatment Options for Relapsed Small-Cell Lung Cancer: What Progress Have We Made? *J Oncol Pract*. 2018;14(6):369-370.
4. Cheng Y, et al. Durvalumab after Chemoradiotherapy in Limited-Stage Small-Cell Lung Cancer. *N Engl J Med*. 2024;391(14):1313-1327.
5. Bebb DG, et al. Symptoms and Experiences with Small Cell Lung Cancer: A Mixed Methods Study of Patients and Caregivers. *Pulm Ther*. 2023;9:435-450.
6. World Health Organization. International Agency for Research on Cancer. Lung Fact Sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/cancers/15-trachea-bronchus-and-lung-fact-sheet.pdf. Accessed March 2025.
7. World Health Organization. International Agency for Research on Cancer. World Fact Sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/populations/900-world-fact-sheet.pdf. Accessed March 2025.
8. LUNGevity Foundation. Types of Lung Cancer. Available at: https://www.lungevity.org/for-patients-caregivers/lung-cancer-101/types-of-lung-cancer. Accessed March 2025.
9. American Cancer Society. Small Cell Lung Cancer Stages. Available at: https://www.cancer.org/cancer/types/lung-cancer/detection-diagnosis-staging/staging-sclc.html. Accessed March 2025.
10. Senan S, et al. ADRIATIC: A phase III trial of durvalumab ± tremelimumab after concurrent chemoradiation for patients with limited stage small cell lung cancer. *Ann Oncol*. 2019;30(suppl. 2):ii25.

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