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Imfinzi approved in the US as first and only immunotherapy regimen for patients with limited-stage small cell lung cancer

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 US for the treatment of adult patients with limited-stage small cell lung cancer (LS-SCLC) whose disease has not progressed following concurrent platinum-based chemotherapy and radiation therapy.

The approval was granted by the Food and Drug Administration (FDA) after securing Priority Review and Breakthrough Therapy Designation. It was based on results from the ADRIATIC Phase III trial which were presented during the Plenary Session of the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting and subsequently published in the *New England Journal of Medicine*.

SCLC is a highly aggressive form of lung cancer.[1] LS-SCLC typically recurs and progresses rapidly, despite initial response to standard-of-care chemotherapy and radiotherapy.[2-3] The prognosis for LS-SCLC is particularly poor, as only 15-30% of patients will be alive five years after diagnosis.[4]

Suresh Senan, PhD, Professor of Clinical Experimental Radiotherapy at the Amsterdam University Medical Centers, The Netherlands, and international coordinating investigator in the trial, said: "Durvalumab is the first and only systemic treatment following curative-intent, platinum-based chemoradiotherapy to show improved survival for patients with this aggressive form of lung cancer. This finding represents the first advance for this disease in four decades. The ADRIATIC trial showed 57 percent of patients were still alive at three years after being treated with durvalumab, which underscores the practice-changing potential of this medicine in this setting."

Dave Fredrickson, Executive Vice President, Oncology Business Unit, AstraZeneca, said: "This approval for *Imfinzi* marks a breakthrough for patients with limited-stage small cell lung cancer, allowing them to receive immunotherapy for the first time. The ADRIATIC trial showed an improvement in median overall survival of 22.5 months, setting a new benchmark. *Imfinzi* is now the only immunotherapy approved for both limited- and extensive-stage small cell lung cancer, underscoring our commitment to improving survival rates."

Dusty Donaldson, Founder and Executive Director of LiveLung, said: "This new treatment option is a game changer for patients with limited-stage small cell lung cancer, a disease known for its high rate of recurrence. Historically, more often than not, clinical trials to identify new treatment options for this type of cancer have failed to show benefit. We are therefore so excited that many more people will now have the opportunity to access this immunotherapy treatment that holds the potential to significantly improve outcomes."

In the trial, *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 also approved in Switzerland in this setting based on the ADRIATIC results. Regulatory applications are currently under review in the EU, Japan and several other countries in this indication.

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.[5-6] Lung cancer is broadly split into non-small cell lung cancer (NSCLC) and SCLC, with about 15% of cases classified as SCLC.[7]

LS-SCLC (Stage I-III) is classified as SCLC that is generally only in one lung or one side of the chest.[8] LS-SCLC accounts for approximately 30% of SCLC diagnoses and the prognosis remains poor despite curative-intent treatment with standard-of-care cCRT.[9]

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 indication in LS-SCLC, *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 CRT. Additionally, *Imfinzi* is approved as a perioperative treatment in combination with neoadjuvant chemotherapy in resectable NSCLC, in combination with chemotherapy (etoposide and either carboplatin or cisplatin) for the treatment of extensive-stage SCLC, 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.

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.

Imfinzi is also under review by global regulatory authorities as perioperative treatment in combination with neoadjuvant chemotherapy based on the results of the NIAGARA Phase III trial, which demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of event-free survival and the key secondary endpoint of OS versus neoadjuvant chemotherapy.

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, 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.

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
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Contacts
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