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Update on ADJUVANT BR.31 Phase III trial of *Imfinzi* in non-small cell lung cancer

High-level results from the ADJUVANT BR.31 Phase III trial, sponsored by the Canadian Cancer Trials Group (CCTG), showed *Imfinzi* (durvalumab) did not achieve statistical significance for the primary endpoint of disease-free survival (DFS) versus placebo in early-stage (IB-IIIa) non-small cell lung cancer (NSCLC) after complete tumour resection in patients whose tumours express PD-L1 on 25% or more tumour cells.

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "We are disappointed in the ADJUVANT BR.31 results. *Imfinzi* has helped change the treatment landscape and achieved multiple positive Phase III trials for patients with earlier stages of lung cancer. We are committed to addressing the remaining unmet need in lung cancer through our broad development programme."

The safety profile for *Imfinzi* was consistent with its known safety profile, and no new safety concerns were reported. The data will be shared at a forthcoming medical meeting.

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.

Imfinzi is also being investigated as monotherapy and in combinations in several other early-stage lung cancer settings, including in medically inoperable or unresected Stage II NSCLC (PACIFIC-4) and unresectable, Stage III NSCLC (PACIFIC-5, 8 and 9).

Notes

Lung cancer

Each year, there are an estimated 2.4 million people diagnosed with lung cancer globally. 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 around 58% of patients with Stage IB disease will survive for five years. This decreases to 36-46% for patients with Stage II and 24% for patients with Stage IIIa disease, reflecting a high unmet medical need.¹⁰

ADJUVANT BR.31

ADJUVANT BR.31 is a randomised, multi-centre, double-blind Phase III trial sponsored by CCTG evaluating *Imfinzi* in the adjuvant treatment of 1,415 patients with Stage IB (≥ 4 cm), II or IIIa (Seventh Edition AJCC Cancer Staging Manual) NSCLC following complete tumour resection with or without adjuvant chemotherapy. AstraZeneca provided *Imfinzi* and support for the trial. Patients were randomised 2:1 to receive a 20mg/kg IV infusion of *Imfinzi* or placebo every four weeks for up to 48 weeks.

The trial is being conducted at 269 centres across 19 countries and regions including in Canada, the US, Australia, Europe and Asia. The primary endpoint is DFS in patients whose tumours express PD-L1 on 25% or more tumour cells and do not have known common EGFR mutations or ALK rearrangements. Key secondary endpoints include DFS in patients whose tumours express PD-L1 on 1% or more of cells and in patients regardless of PD-L1 tumour cell expression status, overall survival and safety. DFS is defined as time from randomisation to date of first recurrence, new cancer or death from any cause and is recognised as an important clinical measure by both physicians and patients.

Canadian Cancer Trials Group (CCTG)

CCTG is an academic cancer clinical trials research cooperative that runs Phase III trials to test anti-cancer and supportive therapies at over 85 hospitals and cancer centres across Canada. From the operations centre at Queen's University, CCTG has supported more than 600 trials enrolling 100,000 patients from 40 countries on 6 continents through a global network of 20,000 investigators and clinical trial staff. CCTG is a national program of the Canadian Cancer Society, and their aim is to improve survival and quality of life for all people with cancer.

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 chemoradiation therapy. *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.

Imfinzi also demonstrated statistically significant and clinically meaningful event-free survival results in patients with resectable early-stage NSCLC based on the AEGEAN Phase III trial. *Imfinzi* in combination with neoadjuvant

chemotherapy before surgery and as adjuvant monotherapy after surgery is approved for patients in Switzerland based on this trial.

In limited-stage SCLC, *Imfinzi* demonstrated statistically significant and clinically meaningful improvements in the dual primary endpoints of OS and progression-free survival (PFS) 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, 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

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](https://www.astrazeneca.com) and follow the Company on social media [@AstraZeneca](https://twitter.com/AstraZeneca).

Contacts

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