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High-level results from the final analysis of the Phase III CASPIAN trial showed AstraZeneca's *Imfinzi* (durvalumab) in combination with a choice of standard-of-care (SoC) chemotherapies confirmed a sustained, clinically meaningful overall survival (OS) benefit for patients with extensive-stage small cell lung cancer (ES-SCLC) treated in the 1st-line setting.

In June 2019, the CASPIAN trial met one primary endpoint for *Imfinzi* plus SoC (etoposide and either carboplatin or cisplatin chemotherapy) by demonstrating a statistically significant and clinically meaningful improvement in OS versus SoC alone at a planned interim analysis.

The second experimental arm testing tremelimumab, an anti-CTLA4 monoclonal antibody, added to *Imfinzi* and SoC did not meet its primary endpoint of demonstrating a statistically significant improvement in OS in this analysis.

José Baselga, Executive Vice President, Oncology R&D, said: "We are pleased to see the sustained and meaningful survival benefit of *Imfinzi* for patients with small cell lung cancer after more than two years median follow up. We have already received the first global regulatory approval for *Imfinzi* with etoposide plus either carboplatin or cisplatin and remain on track for more approvals soon as we provide patients an important new 1st-line treatment option."

The safety and tolerability for *Imfinzi* and tremelimumab were consistent with the known safety profiles of these medicines. The data will be presented at a forthcoming medical meeting.

Imfinzi in combination with etoposide and either carboplatin or cisplatin is currently under regulatory review for the treatment of ES-SCLC in the 1st-line setting based on the Phase III CASPIAN trial in the US, EU and Japan. The US Food and Drug Administration has granted a Priority Review with a Prescription Drug User Fee Act date set for the first quarter of 2020.

As part of a broad development programme, *Imfinzi* is also being tested following concurrent chemoradiation therapy in patients with limited-stage SCLC in the Phase III ADRIATIC trial with data anticipated in 2021.

Small cell lung cancer

Lung cancer is the leading cause of cancer death among both men and women and accounts for about one-fifth of all cancer deaths.[1] Lung cancer is broadly split into non-small cell lung cancer (NSCLC) and SCLC, with about 15% classified as SCLC.[2] SCLC is a highly aggressive, fast-growing form of lung cancer that typically recurs and progresses rapidly despite initial response to chemotherapy.[3,4] About two thirds of SCLC patients are diagnosed with extensive-stage disease, in which the cancer has spread widely through the lung or to other parts of the body.[5] Prognosis is particularly poor, as only 6% of all SCLC patients will be alive five years after diagnosis.[5]

CASPIAN

CASPIAN is a randomised, open-label, multi-centre, global, Phase III trial in the 1st-line treatment of 805 patients with ES-SCLC. The trial compared *Imfinzi* in combination with etoposide and either carboplatin or cisplatin chemotherapy, or *Imfinzi* and chemotherapy with the addition of a second immunotherapy, tremelimumab, versus chemotherapy alone. In the experimental arms, patients were treated with four

cycles of chemotherapy. In comparison, the control arm allowed up to six cycles of chemotherapy and optional prophylactic cranial irradiation. The trial was conducted in more than 200 centres across 23 countries, including the US, in Europe, South America, Asia and the Middle East. The primary endpoint was OS in each of the two experimental arms.

Imfinzi

Imfinzi (durvalumab) is a human monoclonal antibody that binds to PD-L1 and blocks the interaction of PD-L1 with PD-1 and CD80, countering the tumour's immune-evading tactics and releasing the inhibition of immune responses.

Imfinzi is approved in the curative-intent setting of unresectable, Stage III NSCLC after chemoradiation therapy in the US, Japan, China, across the EU and in many other countries, based on the Phase III PACIFIC trial. *Imfinzi* recently received its first global approval for the 1st-line treatment of ES-SCLC in combination with SoC chemotherapy in Singapore. *Imfinzi* is also approved for previously treated patients with advanced bladder cancer in the US and a small number of other countries.

As part of a broad development programme, *Imfinzi* is also being tested as a monotherapy and in combination with tremelimumab, an anti-CTLA4 monoclonal antibody and potential new medicine, as a treatment for patients with NSCLC, SCLC, bladder cancer, head and neck cancer, liver cancer, biliary tract cancer, cervical cancer and other solid tumours.

Tremelimumab

Tremelimumab is a human monoclonal antibody and potential new medicine that targets the activity of cytotoxic T-lymphocyte-associated protein 4 (CTLA-4). Tremelimumab blocks the activity of CTLA-4, contributing to T cell activation, priming the immune response to cancer and fostering cancer cell death. Tremelimumab is being tested in a clinical trial programme in combination with *Imfinzi* in NSCLC, SCLC, bladder cancer, head and neck cancer and liver cancer.

AstraZeneca in lung cancer

AstraZeneca has a comprehensive portfolio of approved and potential new medicines in late-stage development for the treatment of different forms of lung cancer spanning different histologies, several stages of disease, lines of therapy and modes of action. We aim to address the unmet needs of patients with EGFR-mutated tumours as a genetic driver of disease, which occur in 10-15% of NSCLC patients in the US and EU and 30-40% of NSCLC patients in Asia, with the approved medicines *Iressa* (gefitinib) and *Tagrisso* (osimertinib), and its ongoing Phase III trials ADAURA, LAURA, and FLAURA2.[6-8] We are also committed to addressing tumour mechanisms of resistance through the ongoing Phase II trials SAVANNAH and ORCHARD which test *Tagrisso* in combination with savolitinib, a selective inhibitor of c-MET receptor tyrosine kinase, along with other potential new medicines. *Enhertu* (trastuzumab deruxtecan), a HER2-directed antibody drug conjugate is in development for metastatic non-squamous HER2-overexpressing or HER2-mutated NSCLC including trials in combination with other anticancer treatments.

An extensive late-stage Immuno-Oncology programme focuses on lung cancer patients without a targetable genetic mutation which represents up to three-quarters of all patients with lung cancer.[9] *Imfinzi*, an anti-PDL1 antibody, is in development for patients with advanced disease (Phase III trials POSEIDON, and PEARL) and for patients in earlier stages of disease including potentially-curative settings (Phase III trials AEGEAN, ADJUVANT BR.31, PACIFIC-2, PACIFIC-4, PACIFIC-5, and ADRIATIC) both as monotherapy and in combination with tremelimumab and/or chemotherapy. *Imfinzi* is also in development in the Phase II combination trials NeoCOAST, COAST and HUDSON in combination with potential new medicines from the early-stage pipeline.

AstraZeneca's approach to Immuno-Oncology (IO)

Immuno-oncology (IO) is a therapeutic approach designed to stimulate the body's immune system to attack tumours. The Company's IO portfolio is anchored by immunotherapies that have been designed to overcome anti-tumour immune suppression. AstraZeneca believes that IO-based therapies offer the potential for life-changing cancer treatments for the clear majority of patients.

The Company is pursuing a comprehensive clinical-trial programme that includes *Imfinzi* as a monotherapy and in combination with tremelimumab in multiple tumour types, stages of disease, and lines of therapy, and where relevant using the PD-L1 biomarker as a decision-making tool to define the best potential treatment path for a patient. In addition, the ability to combine the IO portfolio with radiation, chemotherapy, small targeted molecules from across AstraZeneca's Oncology pipeline, and from research partners, may provide new treatment options across a broad range of tumours.

AstraZeneca in Oncology

AstraZeneca has a deep-rooted heritage in oncology and offers a quickly growing portfolio of new medicines that has the potential to transform patients' lives and the Company's future. With six new medicines launched between 2014 and 2020, and a broad pipeline of

small molecules and biologics in development, the Company is committed to advance oncology as a key growth driver for AstraZeneca focused on lung, ovarian, breast and blood cancers. In addition to AstraZeneca's main capabilities, the Company is actively pursuing innovative partnerships and investments that accelerate the delivery of our strategy, as illustrated by the investment in Acerta Pharma in haematology.

By harnessing the power of four scientific platforms - Immuno-Oncology, Tumour Drivers and Resistance, DNA Damage Response and Antibody Drug Conjugates - and by championing the development of personalised combinations, AstraZeneca has the vision to redefine cancer treatment and one day eliminate cancer as a cause of death.

AstraZeneca

AstraZeneca (LSE/STO/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, Cardiovascular, Renal and Metabolism, and Respiratory. Based in Cambridge, UK, AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. Please visit astrazeneca.com and follow the Company on Twitter @AstraZeneca.

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