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Imfinzi demonstrated statistically significant and clinically meaningful improvement in event-free survival and overall survival for muscle-invasive bladder cancer in NIAGARA Phase III trial

First immunotherapy regimen before and after surgery to extend survival in bladder cancer

Positive high-level results from the NIAGARA Phase III trial showed AstraZeneca's *Imfinzi* (durvalumab) in combination with chemotherapy demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of event-free survival (EFS) and the key secondary endpoint of overall survival (OS) versus neoadjuvant chemotherapy for patients with muscle-invasive bladder cancer (MIBC). Patients were treated with *Imfinzi* in combination with neoadjuvant chemotherapy before cystectomy (surgery to remove the bladder) followed by *Imfinzi* as adjuvant monotherapy.

Approximately one in four patients with bladder cancer has evidence of the tumour invading the muscle wall of the bladder (without distant metastases), known as MIBC.[1,2] In the MIBC setting, approximately 117,000 patients are treated with current standard of care.[3] Standard treatment includes neoadjuvant chemotherapy and radical cystectomy.[4] However, even after cystectomy, patients experience high rates of recurrence and a poor prognosis.[4]

Professor Thomas Powles, MD, Professor, Director of Barts Cancer Centre (QMUL), London, UK, and investigator in the trial, said: "Nearly half of patients with muscle-invasive bladder cancer who receive standard of care still experience disease recurrence or progression. These NIAGARA data show for the first time that adding durvalumab to chemotherapy before surgery followed by durvalumab extends patients' lives."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "The NIAGARA results support our strategy to move immunotherapy to the early stages of cancer treatment. This perioperative regimen with *Imfinzi* improved survival and reduced the rate at which patients experience disease recurrence or progression. We are eager to bring this regimen with the potential to transform the standard of care to patients as soon as possible."

Imfinzi was generally well-tolerated and no new safety concerns were observed in either the neoadjuvant or adjuvant setting. The safety profile of *Imfinzi* and neoadjuvant chemotherapy was consistent with the known profile of the individual medicines. The addition of *Imfinzi* did not increase the discontinuation rate due to adverse events and did not compromise patients' ability to complete surgery compared to neoadjuvant chemotherapy alone. These data will be presented at a forthcoming medical meeting and shared with global regulatory authorities.

Notes

Muscle-invasive bladder cancer

Bladder cancer is the 9th most common cancer in the world, with more than 614,000 patients diagnosed each year.[5] The most common type of bladder cancer is urothelial carcinoma, which begins in the urothelial cells of the urinary tract.[6]

Muscle-invasive bladder cancer, named for its growth into the muscle wall of the bladder, accounts for about a quarter of all bladder cancer cases.[1,2] Approximately 50% of patients who undergo bladder removal surgery experience disease recurrence.[4] Treatment options that prevent disease recurrence after surgery are critically needed.

NIAGARA

NIAGARA is a randomised, open-label, multi-centre, global Phase III trial evaluating *Imfinzi* as treatment for patients with MIBC before and after radical cystectomy. In the trial, 1063 patients were randomised to receive *Imfinzi* plus chemotherapy or chemotherapy alone prior to cystectomy, followed by *Imfinzi* or no further treatment after surgery.

The trial is being conducted at 192 centres across 22 countries and regions including in North America, South America, Europe, Australia and Asia. Its dual primary endpoints are EFS, defined as the time from treatment randomisation to an event like tumour recurrence or progression and pathologic complete response. Key secondary endpoints are OS and safety.

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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 non-small cell lung cancer (NSCLC) in patients whose disease has not progressed after chemoradiation therapy. *Imfinzi* is also approved for the treatment of extensive-stage small cell lung cancer (SCLC) and in combination with a short course of *Imjudo* (tremelimumab) and chemotherapy for the treatment of metastatic NSCLC.

Imfinzi in combination with neoadjuvant platinum-containing chemotherapy before surgery and as adjuvant monotherapy after surgery has been approved in Switzerland for the treatment of adult patients with resectable NSCLC and no known epidermal growth factor receptor (EGFR) mutations or anaplastic lymphoma kinase (ALK) rearrangements.

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.

Imfinzi is being tested across early- and late-stage bladder cancer in various treatment combinations, including in non-muscle invasive disease (POTOMAC), patients with MIBC who are cisplatin-ineligible or refusing cisplatin (VOLGA) and locally advanced or metastatic disease (NILE).

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 as well as 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.

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