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Imfinzi-based regimen demonstrated statistically significant and clinically meaningful improvement in event-free survival in resectable early-stage gastric and gastroesophageal junction cancers

MATTERHORN is first global, randomised Phase III trial to demonstrate superior event-free survival with an immunotherapy combination over standard of care in this setting

Imfinzi plus chemotherapy more than doubled pathologic complete response rate in previously reported analysis of this trial in 2023

Positive high-level results from the MATTERHORN Phase III trial showed perioperative treatment with AstraZeneca's *Imfinzi* (durvalumab) in combination with standard-of-care FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) chemotherapy demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of event-free survival (EFS). Patients were treated with neoadjuvant *Imfinzi* in combination with chemotherapy before surgery, followed by adjuvant *Imfinzi* in combination with chemotherapy, then *Imfinzi* monotherapy. The trial evaluated this regimen versus perioperative chemotherapy alone for patients with resectable, early-stage and locally advanced (Stages II, III, IVA) gastric and gastroesophageal junction (GEJ) cancers.

For the secondary endpoint of overall survival (OS), a strong trend was observed in favour of the *Imfinzi*-based regimen at this interim analysis. The trial will continue to follow OS, which will be formally assessed at the final analysis.

Gastric cancer is the fifth leading cause of cancer death globally, with nearly one million people diagnosed each year.[1] In 2024, there were roughly 43,000 drug-treated patients in the US, European Union (EU) and Japan in early-stage and locally advanced gastric or GEJ cancer.[2] Approximately 62,000 patients in these regions are expected to be newly diagnosed in this setting by 2030.[3]

Yelena Y Janjigian, MD, Chief Attending Physician of the Gastrointestinal Medical Oncology Service, Memorial Sloan Kettering Cancer Center, New York and principal investigator in the trial, said: "Despite receiving curative-intent chemotherapy and surgery, patients with gastric cancer commonly face disease recurrence and have a poor prognosis. These exciting data from MATTERHORN show that a durvalumab-based perioperative regimen resulted in a clinically meaningful improvement in patient outcomes, including decreasing the risk of the cancer coming back."

Cristian Massacesi, Chief Medical Officer and Oncology Chief Development Officer, AstraZeneca, said: "MATTERHORN is the first Phase III trial of an immunotherapy to show a statistically significant improvement in event-free survival in patients with resectable gastric and gastroesophageal junction cancers. This perioperative approach with *Imfinzi* underscores our commitment to moving into earlier stages of cancer where novel therapies can have the biggest impact on patients' lives."

The safety profile for *Imfinzi* and FLOT chemotherapy was consistent with the known profiles of each medicine, and there were no new safety findings.

In a previously reported interim analysis for the key secondary endpoint of pathologic complete response (pCR), the *Imfinzi* combination more than doubled the pCR rate compared to neoadjuvant chemotherapy alone (19% versus 7%, odds ratio 3.08; p<0.00001).[4]

Data will be presented at a forthcoming medical meeting and shared with global regulatory authorities.

Notes

Gastric and gastroesophageal junction cancers

Gastric (stomach) cancer is the fifth most common cancer worldwide and the fifth-highest leading cause of cancer mortality.[1] In many regions, its incidence has been increasing in patients younger than 50 years old, along with other gastrointestinal (GI) malignancies.[5] Nearly one million new patients were diagnosed with gastric cancer in 2022, with approximately 660,000 deaths reported globally.[1]

GEJ cancer is a type of gastric cancer that arises from and spans the area where the oesophagus connects to the stomach.[6]

Disease recurrence is common in patients with resectable gastric cancer despite undergoing surgery with curative intent and treatment with neoadjuvant/adjuvant chemotherapy. Approximately one in four patients with gastric cancer who undergo surgery develop recurrent disease within one year, and one in

patients with gastric cancer who undergo surgery develop recurrent disease within one year, and one in four patients do not survive beyond two years, reflecting high unmet medical need.[7-8] Additionally, the five-year survival rate remains poor, with less than half of patients alive at five years.[9]

MATTERHORN

MATTERHORN is a randomised, double-blind, placebo-controlled, multi-centre, global Phase III trial evaluating *Imfinzi* as perioperative treatment for patients with resectable Stage II-IVA gastric and GEJ cancers. Perioperative therapy includes treatment before and after surgery, also known as neoadjuvant/adjuvant therapy. In the trial, 948 patients were randomised to receive a 1500mg fixed dose of *Imfinzi* plus FLOT chemotherapy or placebo plus FLOT chemotherapy every four weeks for two cycles prior to surgery. This was followed by *Imfinzi* or placebo every four weeks for up to 12 cycles after surgery (including two cycles of *Imfinzi* or placebo plus FLOT chemotherapy and 10 additional cycles of *Imfinzi* or placebo monotherapy).

In the MATTERHORN trial, the primary endpoint is EFS, defined as the time from randomisation until progression that precludes surgery or requires non-protocol therapy, local or distant recurrence or progression of disease, or death due to any cause as assessed by blinded independent central review (BICR) according to RECIST 1.1 and/or local pathology testing. Key secondary endpoints include pCR rate, defined as the proportion of patients who have no detectable cancer cells in resected tumour tissue following neoadjuvant therapy, and OS. The trial enrolled participants in 176 centres in 20 countries, including in the US, Canada, Europe, South America 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.

Imfinzi is approved in combination with chemotherapy (gemcitabine plus cisplatin) in locally advanced or metastatic biliary tract cancer (BTC) and in combination with *Imjudo* (tremelimumab) in unresectable hepatocellular carcinoma (HCC). *Imfinzi* is also approved as a monotherapy in unresectable HCC in Japan and the EU.

In addition to its indications in GI cancers, *Imfinzi* is the global standard of care based on OS in the curative-intent setting of unresectable, Stage III non-small cell lung cancer (NSCLC) in patients whose disease has not progressed after chemoradiotherapy (CRT). Additionally, *Imfinzi* is approved as a perioperative treatment in combination with neoadjuvant chemotherapy in resectable non-small cell lung cancer (NSCLC), and in combination with a short course of *Imjudo* and chemotherapy for the treatment of metastatic NSCLC. *Imfinzi* is also approved for limited-stage small cell lung cancer (SCLC) in patients whose disease has not progressed following concurrent platinum-based CRT; and in combination with chemotherapy (etoposide and either carboplatin or cisplatin) for the treatment of extensive-stage SCLC.

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 GI and gynaecologic cancers, and other solid tumours.

AstraZeneca in GI cancers

AstraZeneca has a broad development programme for the treatment of GI cancers across several medicines and a variety of tumour types and stages of disease. In 2022, GI cancers collectively represented approximately 5 million new cancer cases leading to approximately 3.3 million deaths.[10]

Within this programme, the Company is committed to improving outcomes in gastric, liver, biliary tract, oesophageal, pancreatic, and colorectal cancers.

In addition to its indications in BTC and HCC, *Imfinzi* is being assessed in combinations, including with *Imjudo*, in liver, oesophageal and gastric cancers in an extensive development programme spanning early to late-stage disease across settings.

The Company is also assessing rilvegostomig (AZD2936), a PD-1/TIGIT bispecific antibody, in combination with chemotherapy as an adjuvant therapy in BTC and as a 1st-line treatment in patients with HER2-negative, locally advanced unresectable or metastatic gastric and GEJ cancers.

Enhertu (trastuzumab deruxtecan), a HER2-directed antibody drug conjugate, is approved in the US and several other countries for HER2-positive advanced gastric cancer. *Enhertu* is jointly developed and commercialised by AstraZeneca and Daiichi Sankyo.

Lynparza, a first-in-class PARP inhibitor, is approved the US and several other countries for the treatment of BRCA-mutated metastatic pancreatic cancer. *Lynparza* is developed and commercialised in collaboration with MSD (Merck & Co., Inc. inside the US and Canada).

AstraZeneca is advancing multiple modalities that provide complementary mechanisms for targeting Claudin 18.2, a promising therapeutic target in gastric cancer. These include AZD0901, a potential first-in-class antibody drug conjugate licensed from KYM Biosciences Inc., currently in Phase III development; AZD5863, a novel Claudin 18.2/CD3 T-cell engager bispecific antibody licensed from Harbour Biomed in Phase I development; and AZD6422, an armoured autologous chimeric antigen receptor T-cell (CAR T) therapy, currently being evaluated in an Investigator Initiated Trial (IIT) in collaboration with AbelZeta in China.

In early development, AstraZeneca is developing two Glypican 3 (GPC3) armoured CAR Ts in HCC. AZD5851, currently in Phase I development, is being developed globally, and C-CAR031 / AZD7003 is being co-developed with

AbelZeta in China where it is under evaluation in an III.

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.

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Dr. Janjigian provides consulting and advisory services to AstraZeneca.

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