AstraZeneca

Imfinzi improved pCR in gastric and GEJ cancers

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Imfinzi plus chemotherapy significantly improved pathologic complete response in gastric and gastroesophageal junction cancers in MATTERHORN Phase III trial

First global Phase III trial of immunotherapy and chemotherapy combination to demonstrate clinical benefit in this setting

Trial will continue to assess event-free survival

Positive high-level results from a planned interim analysis of the MATTERHORN Phase III trial showed treatment with AstraZeneca's *Imfinzi* (durvalumab) added to standard-of-care FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel) neoadjuvant (before surgery) chemotherapy demonstrated a statistically significant and clinically meaningful improvement in the key secondary endpoint of pathologic complete response (pCR) versus neoadjuvant chemotherapy alone for patients with resectable, early-stage and locally advanced (Stages II, III, IVA) gastric and gastroesophageal junction (GEJ) cancers.

The trial will continue as planned to assess EFS and overall survival to which the trial team, investigators and participants remain blinded.

The safety and tolerability of adding *Imfinzi* to neoadjuvant FLOT chemotherapy was consistent with the known profile of this combination and did not decrease the number of patients able to undergo surgery versus chemotherapy alone.

Josep Tabernero, MD, PhD, head of the Medical Oncology Department, Vall d'Hebron University Hospital, Barcelona, Spain, and principal investigator of the MATTERHORN trial, said: "Patients with resectable gastric and gastroesophageal junction cancers urgently need better treatment options, because today, one in four patients still progress within one year even after surgery with curative intent. These results demonstrate an increase in pathologic complete response after adding durvalumab treatment to FLOT chemotherapy and surgery. This is an encouraging early sign that this regimen may deliver long-term clinical benefit for these patients, as pathologic complete response has been correlated with both event-free and overall survival in multiple settings."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "These early results from MATTERHORN support harnessing the immune system together with chemotherapy and surgery as a new treatment approach to improve outcomes for patients with earlier stages of gastric and gastroesophageal junction cancers. These findings reinforce our focus on delivering novel *Imfinzi*-based treatments that have the potential to redefine care for patients with gastrointestinal cancers."

Gastric cancer is the fourth leading cause of cancer death globally, with more than one million people diagnosed each year. By 2030, approximately 70,000 patients in the US, EU and Japan will be newly diagnosed with Stage II-III gastric or GEJ cancers.[1] Approximately one in four patients with gastric cancer who undergo surgery with curative intent develop recurrent disease within one year, reflecting a high unmet medical need.[2]

These data will be shared with health authorities and presented at a forthcoming medical meeting.

Notes

Gastric and gastroesophageal junction cancers

Gastric (stomach) cancer is the fifth most common cancer worldwide and the fourth highest leading cause of cancer mortality.[3] Approximately one million new patients were diagnosed with gastric cancer in 2020, with 768,000 deaths reported globally.[3]

GEJ cancer is a type of gastric cancer that arises from and spans the area where the esophagus connects to the stomach.[4]

Disease recurrence is common in patients with resectable gastric cancer despite undergoing curative-intent surgery and treatment with neoadjuvant/adjuvant chemotherapy.[2] Additionally, the five-year survival rate for gastric cancer remains poor, with only up to a third of patients alive at five years.[5,6]

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 gastroesophageal cancers. Perioperative therapy includes treatment before and after surgery, also known as neoadjuvant/adjuvant therapy. In the trial, 958 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, 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 disease progression or death. 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 overall survival (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) in the US, EU, Japan and several other countries based on the TOPAZ-1 and HIMALAYA Phase III trials, respectively.

In addition to its indications in gastrointestinal (GI) cancers, *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 based on the PACIFIC Phase III trial.

Imfinzi is also approved in the US, EU, Japan, China and many other countries around the world for the treatment of extensive-stage small-cell lung cancer (SCLC) based on the CASPIAN Phase III trial. Additionally, *Imfinzi* is approved in combination with a short course of *Imjudo* and chemotherapy for the treatment of metastatic NSCLC in the US, EU and Japan based on the POSEIDON Phase III trial. *Imfinzi* is approved in previously treated patients with advanced bladder cancer in a small number of countries.

Since the first approval in May 2017, more than 200,000 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, several GI cancers, ovarian cancer, endometrial cancer and other solid tumours.

In GI cancers specifically, AstraZeneca has several ongoing registrational trials investigating *Imfinzi* across multiple liver cancer settings (EMERALD-1, EMERALD-2 and EMERALD-3) and in locally advanced esophageal cancer (KUNLUN).

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 2020, GI cancers collectively represented approximately 5.1 million new cancer cases leading to approximately 3.6 million deaths.[7]

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.

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

Lynparza (olaparib), 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 also recently entered into a global exclusive license agreement with KYM Biosciences Inc. for CMG901. CMG901 is a potential first-in-class antibody drug conjugate targeting Claudin 18.2, a promising therapeutic target in gastric cancer, currently in Phase I development.

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 aims to reimagine cancer care and help transform outcomes for patients with *Imfinzi* as a single treatment and in combination with *Imjudo* as well as other novel immunotherapies and modalities. The Company is also exploring next-generation immunotherapies like bispecific antibodies and therapeutics that harness different aspects of immunity to target cancer.

AstraZeneca is boldly 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. 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 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.

Contacts
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References

1. Kantar Health, validated with SEER stage at diagnosis and Cabasag et al. and Kuzuu et al. 2021
2. Li Y, *et al*. Postoperative recurrence of gastric cancer depends on whether the chemotherapy cycle was more than 9 cycles. *Medicine*. 2022;101(5):e28620.
3. World Health Organisation. International Agency for Research on Cancer. Stomach Fact Sheet. Available at: http://gco.iarc.fr/today/data/factsheets/cancers/7-Stomach-fact-sheet.pdf. Accessed May 2023.
4. National Cancer Institute. Gastroesophageal junction. Available at: http://www.cancer.gov/publications/dictionaries/cancer-terms/def/gastroesophageal-junction.
5. American Cancer Society. Stomach Cancer Survival Rates. Available at: http://www.cancer.org/cancer/types/stomach-cancer/detection-diagnosis-staging/survival-rates.html. Accessed May 2023.
6. Cancer Research UK. Survival for stomach cancer. Available at: http://www.cancerresearchuk.org/about-cancer/stomach-cancer/survival. Accessed May 2023.
7. World Health Organisation. World Cancer Fact Sheet. Available at: http://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed May 2023.

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