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Imfinzi approved in the US as first and only perioperative immunotherapy for patients with early gastric and gastroesophageal cancers

Based on MATTERHORN Phase III trial results which showed a 29% reduction in the risk of progression, recurrence or death and a 22% reduction in the risk of death for the Imfinzi regimen vs. chemotherapy alone

AstraZeneca's *Imfinzi* (durvalumab) in combination with standard-of-care FLOT chemotherapy (fluorouracil, leucovorin, oxaliplatin, and docetaxel) has been approved in the US for the treatment of adult patients with resectable, early-stage and locally advanced (Stages II, III, IVA) gastric and gastroesophageal junction (GEJ) cancers. The approved regimen includes neoadjuvant/*Imfinzi* in combination with chemotherapy before surgery, followed by adjuvant *Imfinzi* in combination with chemotherapy, then *Imfinzi* monotherapy.

The approval follows Priority Review by the Food and Drug Administration (FDA) and is based on event-free survival (EFS) and overall survival (OS) data from the MATTERHORN Phase III trial. The EFS results were presented during the Plenary Session at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting and simultaneously published in *The New England Journal of Medicine*. OS results from MATTERHORN were presented in a Proffered Paper session at the European Society for Medical Oncology (ESMO) Congress 2025.

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 6,500 drug-treated patients in the US in early-stage and locally advanced gastric or GEJ cancer.[2]

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "This approval ushers in a new clinical paradigm for patients with early gastric and gastroesophageal junction cancers, with *Imfinzi* plus FLOT delivering a durable survival benefit that increases over time. As the third US approval for a perioperative *Imfinzi*-based regimen, this milestone further validates the perioperative approach and underscores our focus on bringing novel treatments to early-stage cancers where cure is the goal."

Yelena Y. Janjigian, MD, Chief Attending Physician of the Gastrointestinal Medical Oncology Service, Memorial Sloan Kettering Cancer Center (MSK), New York and principal investigator in the MATTERHORN trial, said: "Today's approval marks the first immunotherapy regimen approved in the neoadjuvant setting for gastric and gastroesophageal junction cancers-with durvalumab demonstrating a clear overall survival benefit and opening an entirely new chapter in the treatment of early-stage disease. Nearly seven in 10 patients were alive at three years following treatment with the durvalumab-based perioperative regimen. This survival benefit, observed regardless of PD-L1 status, establishes a new standard of care in this curative-intent setting."

Aki Smith, Founder and Executive Director, Hope for Stomach Cancer, said: "From personal experience as a caregiver to my father, I know that for too long patients diagnosed with early gastric or gastroesophageal junction cancer have faced a high risk of their cancer returning, even after undergoing surgery and therapy intended to cure it. Today's approval represents a major step forward in improving outcomes and offering renewed hope to those affected by this devastating disease."

In a planned interim analysis, patients treated with the *Imfinzi*-based perioperative regimen showed a 29% reduction in the risk of disease progression, recurrence or death versus chemotherapy alone (based on an EFS hazard ratio [HR] of 0.71; 95% confidence interval [CI] 0.58-0.86; p<0.001). Estimated median EFS was not yet reached for the *Imfinzi* arm versus 32.8 months for the comparator arm. An estimated 78.2% of patients treated with the *Imfinzi*-based perioperative regimen were event-free at one year, compared to 74.0% in the comparator arm; the estimated 24-month EFS rate was 67.4% versus 58.5%, respectively.

In the final OS analysis, results showed the *Imfinzi* and FLOT perioperative regimen reduced the risk of death by 22% compared with chemotherapy alone (based on a HR of 0.78; 95% CI 0.63-0.96; p=0.021). An estimated 69% of patients treated with the *Imfinzi*-based regimen were alive at three years compared with 62% in the FLOT-only arm. With longer follow-up, the OS curves showed continued separation, signaling a greater magnitude of benefit over time for the *Imfinzi*-based regimen. An OS benefit was observed regardless of PD-L1 status.

The safety profile for *Imfinzi* and FLOT chemotherapy was consistent with the known profiles of each medicine, and the percentage of patients that completed surgery was similar compared to chemotherapy alone. Grade 3 or higher adverse events due to any cause were similar between the two arms (71.6% for *Imfinzi* and FLOT arm; 71.2% for FLOT-only arm).

The US regulatory submission was reviewed under Project Orbis, which provides a framework for concurrent submission and review of oncology medicines among participating international partners. As part of Project Orbis, the *Imfinzi* and FLOT perioperative regimen is also under review by regulatory authorities in Australia, Canada, and Switzerland for the same indication. Regulatory applications are also under review in the European Union (EU), Japan

Switzerland for the same indication. Regulatory applications are also under review in the European Union (EU), Japan and several other countries.

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] Nearly one million new patients were diagnosed with gastric cancer in 2022, with approximately 660,000 deaths reported globally.[1] In many regions, its incidence has been increasing in patients younger than 50 years old, along with other gastrointestinal (GI) malignancies.[3] In 2024, there were roughly 43,000 drug-treated patients in the US, 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.[4]

GEJ cancer is a type of gastric cancer that arises from and spans the area where the oesophagus connects to the stomach.[5]

Disease recurrence is common in patients with resectable gastric cancer despite undergoing surgery with curative intent and treatment with neoadjuvant/adjuvant chemotherapy.[6] Approximately one in four patients with gastric cancer who undergo surgery develop recurrent disease within one year, and the five-year survival rate remains poor, with less than half of patients alive at five years.[6-7]

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 time from randomisation until the date of one of the following events (whichever occurred first): RECIST (version 1.1, per blinded independent central review assessment) progression that precludes surgery or requires non-protocol therapy during the neoadjuvant period; RECIST progression/recurrence during the adjuvant period; non-RECIST progression that precludes surgery or requires non-protocol therapy during the neoadjuvant period or discovered during surgery; progression/recurrence confirmed by biopsy post-surgery; or death due to any cause. Key secondary endpoints include pathologic complete response 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.

In GI cancer, *Imfinzi* is approved in combination with chemotherapy 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 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 for the treatment of extensive-stage SCLC.

Perioperative *Imfinzi* in combination with neoadjuvant chemotherapy is approved in the US, EU, Japan and other countries for patients with muscle-invasive bladder cancer based on results from the NIAGARA Phase III trial. Additionally, in May 2025, *Imfinzi* added to Bacillus Calmette-Guérin induction and maintenance therapy met the primary endpoint of disease-free survival for patients with high-risk non-muscle-invasive bladder cancer in the POTOMAC Phase III trial.

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 the 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 the EU and Japan.

Since the first approval in May 2017, more than 414,000 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 NSCLC, bladder cancer, breast cancer, ovarian cancer and several GI cancers.

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.[8]

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 (ADC), 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 in 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).

The Company is also assessing rilvegostomig (AZD2936), a PD-1/TIGIT bispecific antibody, in combination with chemotherapy as an adjuvant therapy in BTC, in combination with bevacizumab with or without *Imjudo* as a 1st-line treatment in patients with advanced HCC, and as a 1st-line treatment in patients with HER2-negative, locally advanced unresectable or metastatic gastric and GEJ cancers. Rilvegostomig is also being evaluated in combination with *Enhertu* in previously untreated, HER2-expressing, locally advanced or metastatic BTC.

AstraZeneca is advancing multiple modalities that provide complementary mechanisms for targeting Claudin 18.2, a promising therapeutic target in gastric cancer. These include sonesitatug vedotin, a potential first-in-class ADC 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 AZD4360, an antibody drug conjugate, currently being evaluated in a Phase I/II trial in patients with advanced solid tumours.

In early development, AstraZeneca is developing C-CAR031 / AZD7003, a Glypican 3 (GPC3) armoured CAR T, in HCC. C-CAR031 / AZD7003is being co-developed with AbelZeta in China where it is under evaluation in an IIT.

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.

References

1. World Health Organization. International Agency for Research on Cancer. Stomach Fact Sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/cancers/7-stomach-fact-sheet.pdf. Accessed November 2025.
2. AstraZeneca PLC. Investor Relations Epidemiology Spreadsheet. Available at: https://www.astrazeneca.com/investor-relations.html. Accessed November 2025.
3. Li Y, et al. Global burden of young-onset gastric cancer: a systematic trend analysis of the global burden of disease study 2019. *Gastric Cancer*. 2024;27(4):684-700.
4. Kantar Health, validated with SEER stage at diagnosis and Cabasag et al. And Kuzuu et al. 2021.
5. National Cancer Institute. Gastroesophageal junction. Available at: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/gastroesophageal-junction. Accessed November 2025.
6. 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.
7. Ilic M, Ilic I. Epidemiology of stomach cancer. *World J Gastroenterol*. 2022;28(12):1187-1203.
8. World Health Organization. World Cancer Fact Sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/populations/900-world-fact-sheet.pdf. Accessed November 2025.

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MSK Disclosure: Dr. Janjigian provides consulting and advisory services to AstraZeneca.

Matthew Bowden
Company Secretary
AstraZeneca PLC

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