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Perioperative *Imfinzi* approved in the US in novel regimen with neoadjuvant enfortumab vedotin for patients with muscle-invasive bladder cancer

Based on VOLGA Phase III trial data which showed a 49% reduction in risk of recurrence and a 42% reduction in risk of death, with a manageable safety profile

Approval reinforces potential of Imfinzi as an immunotherapy backbone across muscle-invasive and non-muscle-invasive bladder cancer

AstraZeneca's *Imfinzi* (durvalumab) in combination with enfortumab vedotin (EV) as neoadjuvant treatment, followed by *Imfinzi* monotherapy as adjuvant treatment after radical cystectomy (surgery to remove the bladder), has been approved in the US for the treatment of adult patients with muscle-invasive bladder cancer (MIBC) who are ineligible for or have refused cisplatin-based chemotherapy.

The approval was granted by the Food and Drug Administration after securing Priority Review and was based on results from the VOLGA Phase III trial which were presented during a Presidential Symposium at the 2026 European Society for Medical Oncology (ESMO) Congress and simultaneously published in *The New England Journal of Medicine*.

In 2026, around 16,000 patients will be treated for MIBC in the United States.[1] Approximately one in four patients with bladder cancer has muscle-invasive disease, where the tumour invades the muscle wall of the bladder, without distant metastases.[2,3] As many as 50% of patients are ineligible for cisplatin-based chemotherapy due to impaired renal function or comorbidities.[4,5] The standard treatment for these patients has historically been radical cystectomy alone, but despite undergoing this major surgery, patients experience high rates of recurrence and have a poor prognosis.[4-6]

Jonathan E. Rosenberg, MD, Chief of the Genitourinary Oncology Service at the Memorial Sloan Kettering Cancer Center and member of the VOLGA Steering Committee, said: "This approval brings the first perioperative immunotherapy regimen where enfortumab vedotin is administered only in the neoadjuvant setting to patients with muscle-invasive bladder cancer who are not candidates for cisplatin-based chemotherapy. The results of VOLGA show a statistically significant and clinically meaningful improvement in both event-free and overall survival along with a manageable safety profile. Based on this, the VOLGA regimen has the potential to become a new standard of care in this curative-intent setting."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Today's approval offers a novel *Imfinzi*-based regimen that almost halved the risk of disease recurrence and reduced the risk of death by 42 per cent in the VOLGA trial, allowing physicians to optimise treatment for patients in this curative-intent setting. As our third bladder cancer indication in two years, this approval reinforces *Imfinzi* as an immunotherapy backbone across muscle-invasive and non-muscle-invasive disease."

In the trial, patients were treated with three cycles of *Imfinzi* and EV before radical cystectomy, followed by nine cycles of *Imfinzi* adjuvant monotherapy. In a planned interim analysis, perioperative *Imfinzi* plus neoadjuvant EV demonstrated a 49% reduction in the risk of disease progression, recurrence, not undergoing surgery or death versus radical cystectomy with or without approved adjuvant treatment (based on an event-free survival [EFS] hazard ratio [HR] of 0.51; 95% confidence interval [CI] 0.38-0.67; p<0.0001). Estimated median EFS was not yet reached for the *Imfinzi* combination versus 12.1 months for the comparator arm. An

estimated 64% of patients treated with the *Imfinzi* combination remained alive and event-free at two years compared to 45% in the comparator arm.

Results from the key secondary endpoint of overall survival (OS) showed that the *Imfinzi* combination reduced the risk of death by 42% compared to the comparator arm (based on an OS HR of 0.58; 95% CI 0.40-0.83; p=0.0027). Estimated median OS was not yet reached for the *Imfinzi* combination or comparator arm. An estimated 78% of patients treated with the *Imfinzi* combination were alive at two years compared to 69% in the comparator arm.

The safety and tolerability of *Imfinzi* plus EV was consistent with the known safety profiles of the individual medicines, with no new safety signals identified. Grade 3 and 4 adverse events due to any cause occurred in 64% of patients treated with the *Imfinzi* combination and 44% of patients in the comparator arm. Patient-reported quality of life was maintained after surgery in patients treated with the *Imfinzi* combination.

Regulatory applications are currently under review in the European Union (EU), Japan and several other countries based on the results of the VOLGA trial.

Imfinzi is approved in over 50 countries for patients with cisplatin-eligible MIBC based on the NIAGARA Phase III trial. *Imfinzi* in combination with Bacillus Calmette-Guérin (BCG) induction and maintenance therapy is approved in the US, Japan and other countries for patients with BCG-naïve, high-risk non-muscle-invasive bladder cancer, based on the POTOMAC Phase III trial. In July 2026, positive high-level results from the NILE Phase III trial showed *Imfinzi* plus chemotherapy demonstrated a statistically significant and clinically meaningful improvement in OS versus chemotherapy as 1st-line treatment for patients with PD-L1 high unresectable, locally advanced or metastatic urothelial cancer.

Notes

Bladder cancer

Bladder cancer is the 8th most common cancer in the world, with more than 635,000 cases diagnosed each year.[7] The most common type is urothelial carcinoma, which begins in the urothelial cells of the urinary tract.[8]

In 2025, the NIAGARA Phase III trial established a new standard of care in MIBC by adding perioperative *Imfinzi* to neoadjuvant cisplatin-based chemotherapy and radical cystectomy.[9] However, up to half of patients are not eligible to receive cisplatin, and approximately 50% of MIBC patients who undergo bladder removal surgery experience disease recurrence. New treatment options that prevent both progression before surgery and recurrence after surgery are critically needed in this curative-intent setting.[4,6]

VOLGA

VOLGA is a Phase III, randomised, open-label, multi-centre global trial evaluating perioperative *Imfinzi* with or without *Imjudo* (tremelimumab) in combination with neoadjuvant EV as treatment for patients with MIBC undergoing radical cystectomy who are ineligible for or have refused cisplatin compared to radical cystectomy with or without approved adjuvant therapy. In the trial, 695 patients were randomised 1:1:1 to Arm 1 (three cycles of *Imfinzi* and EV, plus two cycles of *Imjudo* prior to surgery, followed by nine cycles of *Imfinzi* plus one cycle of *Imjudo* as adjuvant therapy), Arm 2 (three cycles of *Imfinzi* and EV prior to surgery, followed by nine cycles of *Imfinzi* adjuvant monotherapy) and Arm 3, the comparator arm.

The trial was conducted in 182 centres across 25 countries in Europe, North America, South America and Asia. Its dual primary endpoints are EFS, defined as the time from randomisation to first recurrence post-radical cystectomy, first progression in patients who did not undergo radical cystectomy, failure to undergo radical cystectomy in patients with residual disease or

death due to any cause, for both experimental arms versus the comparator arm. Secondary endpoints include OS (Arm 1 vs. Arm 3 and Arm 2 vs. Arm 3), pathologic complete response, disease-free survival and pathologic downstaging across both experimental arms.

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 addition to its bladder cancer indications, *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) and in combination with chemotherapy (etoposide and either carboplatin or cisplatin) for the treatment of extensive-stage SCLC.

Imfinzi is also approved in combination with chemotherapy in locally advanced or metastatic biliary tract cancer and in combination with *Imjudo* in unresectable hepatocellular carcinoma (HCC). It is also approved as a monotherapy in unresectable HCC in Japan, China and the EU, and in resectable, early-stage and locally advanced gastric and gastroesophageal junction cancers in the US, EU and Japan. Additionally, in April 2026, *Imfinzi* in combination with *Imjudo*, lenvatinib and transarterial chemoembolisation (TACE) demonstrated a statistically significant and clinically meaningful improvement in the primary endpoint of progression-free survival versus TACE alone for patients with unresectable HCC eligible for embolisation in the EMERALD-3 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, EU and China). *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, an estimated 600,000 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 gastrointestinal cancers.

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/NYSE: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development, and commercialisation of prescription medicines in Oncology, Rare Disease, 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.

Dr. Rosenberg has financial interests related to AstraZeneca.

Contacts
For details on how to contact the Investor Relations Team, please click here. For Media contacts, click here.

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