RNS Number : 7951C
AstraZeneca PLC
31 March 2025

31 March 2025

Imfinzi approved in the US as first and only perioperative immunotherapy for patients with muscle-invasive bladder cancer

Based on NIAGARA Phase III trial results which showed a 32% reduction in the risk of recurrence and a 25% reduction in the risk of death vs. neoadjuvant chemotherapy alone

AstraZeneca's *Imfinzi* (durvalumab) in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by *Imfinzi* as adjuvant monotherapy 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).

The approval was granted by the Food and Drug Administration (FDA) after securing Priority Review and was based on results from the NIAGARA Phase III trial which were presented during a Presidential Symposium at the 2024 European Society for Medical Oncology (ESMO) Congress and simultaneously published in *The New England Journal of Medicine*.

In 2024, over 20,000 people in the US were treated for MIBC.[1] Bladder cancer is considered muscle-invasive when there is evidence of the tumour invading the muscle wall of the bladder but no distant metastases.[2] This represents a curative-intent setting, where the current standard of care is neoadjuvant chemotherapy and radical cystectomy.[3] However, even after surgery, patients experience high rates of disease recurrence and have a poor prognosis.[3]

Matthew ND. Galsky, Lillian and Howard Stratton Professor of Medicine, Director of Genitourinary Medical Oncology, The Tisch Cancer Institute at the Icahn School of Medicine at Mount Sinai, New York, and NIAGARA investigator and steering committee member, said: "This approval for the durvalumab-based perioperative regimen is a major breakthrough for people with muscle-invasive bladder cancer, nearly half of whom see their cancer return despite chemotherapy and surgery with curative-intent. This durvalumab regimen significantly extended patients' lives in the NIAGARA trial and has the potential to transform care."

Dave Fredrickson, Executive Vice President, Oncology Haematology Business Unit, AstraZeneca, said: "Today's approval for *Imfinzi* represents a paradigm shift, bringing the first perioperative immunotherapy to patients in the US with muscle-invasive bladder cancer and addressing a significant need for better treatment options. The NIAGARA trial showed more than 80 per cent of patients were still alive at two years, underscoring the potential of this innovative perioperative regimen to become a new standard of care in this setting."

Meri-Margaret Deoudes, CEO of the Bladder Cancer Advocacy Network, said: "More than 20,000 people in the US were treated for muscle-invasive bladder cancer last year and there is a significant need for new treatment options that improve patient outcomes. The approval of the durvalumab perioperative regimen is welcome news, transforming how clinicians will tackle this disease in future and offering new hope to patients and their loved ones."

In the trial, patients were treated with four cycles of *Imfinzi* in combination with neoadjuvant chemotherapy before radical cystectomy followed by eight cycles of *Imfinzi* monotherapy, or neoadjuvant chemotherapy before radical cystectomy. In a planned interim analysis, the *Imfinzi*-based perioperative regimen demonstrated a 32% reduction in the risk of disease progression, recurrence, not undergoing surgery, or death versus the comparator arm (based on event-free survival [EFS] hazard ratio [HR] of 0.68; 95% confidence interval [CI] 0.56-0.82; p<0.0001). Estimated median EFS was not yet reached for the *Imfinzi* arm versus 46.1 months for the comparator arm. An estimated 67.8% of patients treated with the regimen were event free at two years compared to 59.8% in the comparator arm.

Results from the key secondary endpoint of overall survival (OS) showed that the *Imfinzi*-based perioperative regimen reduced the risk of death by 25% versus neoadjuvant chemotherapy with radical cystectomy (based on OS HR of 0.75; 95% CI 0.59-0.93; p=0.0106). Median survival was not yet reached for either arm. An estimated 82.2% of patients treated with the regimen were alive at two years compared to 75.2% in the comparator arm.

Imfinzi was generally well tolerated, and no new safety signals were observed in the neoadjuvant and adjuvant settings. Further, adding *Imfinzi* to neoadjuvant chemotherapy was consistent with the known profile for this combination and did not compromise patients' ability to complete surgery compared to neoadjuvant chemotherapy alone. Immune-mediated adverse events (imAEs) were consistent with the known profile of *Imfinzi*, manageable and mostly low-grade.

In February 2025, perioperative treatment with durvalumab (*Imfinzi*), neoadjuvant cisplatin-based chemotherapy and cystectomy was added to the NCCN Clinical Practical Guidelines in Oncology (NCCN Guidelines®) as a NCCN Category 1 Recommended regimen for patients with MIBC based on the data from NIAGARA.[4]

Imfinzi is also approved in Brazil in this setting based on the NIAGARA results. Regulatory applications are currently under review in the EU, Japan and several other countries.

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] In MIBC, approximately 50% of patients who undergo bladder removal surgery experience disease recurrence.[3] Treatment options that prevent disease recurrence after surgery are critically needed in this curative-intent setting.

NIAGARA

NIAGARA is a randomised, open-label, multi-centre, global Phase III trial evaluating perioperative *Imfinzi* as treatment for patients with MIBC before and after radical cystectomy. In the trial, 1,063 patients were randomised to receive *Imfinzi* plus neoadjuvant chemotherapy prior to cystectomy followed by *Imfinzi,* or neoadjuvant chemotherapy alone prior to cystectomy with no further treatment after surgery. NIAGARA is the largest global Phase III trial in this setting.

The trial is being conducted at 192 centres across 22 countries including in North America, South America, Europe, Australia and Asia. Its dual primary endpoints are EFS and pathologic complete response (pCR) at the time of cystectomy. Key secondary endpoints are OS and safety.

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 the indication in bladder cancer, *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* (tremelimumab) 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.

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.

In March 2025, perioperative *Imfinzi* added to standard-of-care chemotherapy met the primary endpoint of event-free survival in the MATTERHORN Phase III trial in resectable gastric and gastroesophageal junction cancers.

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 gastrointestinal and gynaecologic cancers, and other solid tumours.

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.

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. AstraZeneca PLC. Investor Relations Epidemiology Spreadsheet. Available at: https://www.astrazeneca.com/investor-relations.html. Accessed March 2025.

2. National Collaborating Centre for Cancer. Bladder Cancer: Diagnosis and Management. London: National Institute for Health and Care Excellence (NICE). Available at: https://www.ncbi.nlm.nih.gov/books/NBK356289. Accessed March 2025.

3. Witjes JA, et al. EAU Guidelines on muscle-invasive and metastatic bladder cancer. *Eur Urol*. 2021;1-94.

4. NCCN, National Comprehensive Cancer Network® (NCCN®). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer Version 7.2024.© National Comprehensive Cancer Network, Inc. [2025]. All rights reserved. Accessed [February 28, 2025]. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

5. World Health Organization. International Agency for Research on Cancer. Bladder Fact Sheet. Available at: https://gco.iarc.who.int/media/globocan/factsheets/cancers/30-bladder-fact-sheet.pdf. Accessed March 2025.

6. American Cancer Society. What Is Bladder Cancer? Available at: https://www.cancer.org/cancer/bladder-cancer/about/what-is-bladder-cancer.html. Accessed March 2025.

Adrian Kemp
Company Secretary
AstraZeneca PLC