Imfinzi recommended for approval in the EU for BTC

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Imfinzi plus chemotherapy recommended for approval in the EU by CHMP as first immunotherapy regimen for advanced biliary tract cancer

Positive opinion based on TOPAZ-1 Phase III trial updated survival results showing Imfinzi combination reduced risk of death by 24% vs. chemotherapy alone

AstraZeneca's *Imfinzi* (durvalumab) has been recommended for marketing authorisation in the European Union (EU) for the 1st-line treatment of adult patients with unresectable or metastatic biliary tract cancer (BTC) in combination with chemotherapy (gemcitabine plus cisplatin).

The Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency based its positive opinion on the primary results from the TOPAZ-1 Phase III trial published in the *New England Journal of Medicine Evidence*, and on the updated results presented at the European Society for Medical Oncology Congress 2022.

At the interim analysis, *Imfinzi* plus chemotherapy reduced the risk of death by 20% versus chemotherapy alone (hazard ratio [HR] 0.80; 95% confidence interval [CI] 0.66-0.97; p=0.021).

Updated results from TOPAZ-1 after an additional 6.5 months of follow-up showed a 24% reduction in the risk of death versus chemotherapy alone (HR 0.76; 95% CI, 0.64-0.91), with more than two times as many patients estimated to be alive at two years versus chemotherapy alone (23.6% versus 11.5%). Updated median overall survival (OS) was 12.9 months versus 11.3 with chemotherapy.

BTC is a group of rare and aggressive cancers that occur in the bile ducts and gallbladder.[1,2] There are approximately 210,000 new patients diagnosed with gallbladder and biliary tract cancer each year, and about 40,000 of these occur across Europe.[3] These patients have a poor prognosis, with approximately 5% to 15% of patients with BTC surviving five years.[4]

Juan W. Valle, MD, Professor of Medical Oncology at the University of Manchester, UK, and a lead investigator in the TOPAZ-1 Phase III trial, said: "This positive opinion is welcome news for patients with advanced biliary tract cancer in the European Union who face a poor prognosis and limited treatment options. The combination of durvalumab and chemotherapy is a significant advance for patients after more than a decade of limited progress, and this regimen should become a new standard of care option once approved."

Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "If approved, *Imfinzi* plus chemotherapy will provide patients with advanced biliary tract cancer the first opportunity for treatment with an immunotherapy-based combination. This innovative regimen has been shown to significantly prolong patients' lives, and we look forward to bringing this option to those in the European Union as soon as possible."

Imfinzi plus chemotherapy was generally well tolerated, with no new safety signals observed, and did not increase the discontinuation rate due to adverse events (AEs) compared to chemotherapy alone. Grade 3 or 4 treatment-related AEs were experienced by 60.9% of patients treated with *Imfinzi* and chemotherapy, and by 63.5% of patients treated with chemotherapy alone.

Imfinzi plus chemotherapy is approved in the US, Canada, South Korea and Brazil for the treatment of patients with locally advanced or metastatic BTC. Regulatory applications are also

currently under review in Japan and several other countries based on the TOPAZ-1 results.

Notes

Biliary tract cancer

BTC is a group of rare and aggressive gastrointestinal (GI) cancers that form in the cells of the bile ducts (cholangiocarcinoma), gallbladder or ampulla of Vater (where the bile duct and pancreatic duct connect to the small intestine).[1,2]

Early-stage BTC affecting the bile ducts and gallbladder often presents without clear symptoms and most new cases of BTC are therefore diagnosed at an advanced stage, when treatment options are limited and the prognosis is poor.[4-6] Cholangiocarcinoma is more common in China and Southeast Asia and is on the rise in Western countries.[1,4]

TOPAZ-1

TOPAZ-1 is a randomised, double-blind, placebo controlled, multicentre, global Phase III trial of *Imfinzi* in combination with chemotherapy (gemcitabine plus cisplatin) versus placebo in combination with chemotherapy as a 1st-line treatment in 685 patients with unresectable advanced or metastatic BTC including intrahepatic and extrahepatic cholangiocarcinoma, and gallbladder cancer. Patients with ampullary carcinoma were excluded.

The primary endpoint is overall survival and key secondary endpoints included progression-free survival, objective response rate and safety. The trial was conducted in 105 centres across 17 countries including in the US, Europe, South America and several countries in Asia including South Korea, Thailand, Japan and China.

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 also the only approved immunotherapy in unresectable or metastatic biliary tract cancer and hepatocellular carcinoma [in combination with *Imjudo* (tremelimumab)]. It is also approved in combination with *Imjudo* and chemotherapy in metastatic non-small cell lung cancer (NSCLC) and in the curative-intent setting of unresectable, Stage III NSCLC in patients whose disease has not progressed after chemoradiotherapy. It is the global standard of care in this setting based on the PACIFIC Phase III trial.

Imfinzi is also approved for previously treated patients with advanced bladder cancer in several countries.

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.

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.

Imfinzi is approved in the US and several other countries in combination with chemotherapy (gemcitabine plus cisplatin) for advanced biliary tract cancer and in the US in combination with *Imjudo* (tremelimumab) in unresectable hepatocellular carcinoma. *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 in immuno-oncology (IO)
AstraZeneca 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. Marcano-Bonilla L, *et al.* Biliary tract cancers: epidemiology, molecular pathogenesis and genetic risk associations. *CCO*. 2016;5(5).

2. ESMO. What is Biliary Tract Cancer. Available at:

   http://www.esmo.org/content/download/266801/5310983/1/EN-Biliary-Tract-Cancer-Guide-for-Patients.pdf. Accessed November 2022.

3. Ouyang G, *et al.* The global, regional, and national burden of gallbladder and biliary tract cancer and its attributable risk factors in 195 countries and territories, 1990 to 2017: A systematic analysis for the Global Burden of Disease Study 2017. *Cancer*. 2021;127:2238-2250.

4. Turkes F, *et al*. Contemporary Tailored Oncology Treatment of Biliary Tract Cancers. *Gastroenterol Res Pract.* 2019;2019:7698786.

5. Rawla P, *et al*. Epidemiology of gallbladder cancer. *Clin Exp Hepatol*. 2019;5(2):93-102.

6. Banales JM, *et al*. Cholangiocarcinoma 2020: the next horizon in mechanisms and management. *Nat Rev Gastroenterol Hepatol*. 2020;17:557-588.

7. WHO. World Cancer Fact Sheet. Available at: http://gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed November 2022.

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