

Imfinzi plus Imjudo demonstrated sustained overall survival benefit in advanced liver cancer with an unprecedented one in four patients alive at four years in HIMALAYA Phase III trial

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DETAILED NEWS

Longest survival follow-up reported to date for a Phase III trial in this setting Updated results from the HIMALAYA Phase III trial showed AstraZeneca's Imfinzi (durvalumab) plus Imjudo (tremelimumab) demonstrated a sustained, clinically meaningful overall survival (OS) benefit at four years for patients with unresectable hepatocellular carcinoma (HCC) who had not received prior systemic therapy and were not eligible for localised treatment. These results from HIMALAYA will be presented today at the 2023 European Society for Medical Oncology (ESMO) World Congress on Gastrointestinal Cancer in Barcelona, Spain (abstract #SO-15). At four years of follow-up, these latest data show that a single priming dose of Imjudo added to Imfinzi, called the STRIDE regimen (Single Tremelimumab Regular Interval Durvalumab), reduced the risk of death by 22% compared to sorafenib (based on a hazard ratio [HR] of 0.78; 95% confidence interval [CI] 0.67-0.92; 78% data maturity).

An estimated 25.2% of patients treated with the STRIDE regimen were alive at four years versus 15.1% for those treated with sorafenib.

An ad-hoc exploratory analysis showed that the treatment effects of the STRIDE regimen versus sorafenib were consistent across all clinically relevant subgroups of patients, as well as those surviving at least three years, regardless of the underlying disease cause (hepatitis B virus [HBV], hepatitis C virus [HCV] or nonviral) or other baseline demographics. Bruno Sangro, MD, PhD, Director of the Liver Unit and Professor of Internal Medicine at Clínica Universidad de Navarra, Pamplona, Spain and a lead investigator in the trial, said: "Historically, only seven per cent of patients with advanced liver cancer have survived five years, making the HIMALAYA long-term survival data especially meaningful."

One in four patients treated with the STRIDE regimen were still alive at four years, reinforcing this novel regimen as a standard of care in this setting." Susan Galbraith, Executive Vice President, Oncology R&D, AstraZeneca, said: "The remarkable four-year survival benefit shown with Imfinzi and Imjudo in this advanced liver cancer setting supports the use of the STRIDE regimen to treat a broad, eligible patient population globally."

These latest results from HIMALAYA are part of a series of clinical trials aiming to deliver innovative treatments for patients at different stages of liver cancer.”Summary of updated results: HIMALAYA STRIDE regimen SorafenibOSi, ii (n=393) (n=389)Number of patients with events (%) 291 (74.0) 316 (81.2)Median OS, in months (95% CI) 16.4 (14.2-19.6) 13.8 (12.3-16.1)Median duration of follow-up in censored patients, in months (95% CI) 49.12 (46.95-50.17) 47.31 (45.08-49.15)Hazard ratio (95% CI) 0.78 (0.67-0.92)p-value (2-sided) 0.0037OS rate at 36 months 30.7% 19.8%OS rate at 48 months 25.2% 15.1%.

Updated analysis data cut-off: 23 January 2023, with 78% overall OS data maturity ii.

OS HRs and 95% CIs were calculated using a Cox proportional hazards model adjusting for treatment, aetiology, ECOG performance status, and macrovascular invasion.

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The OS rate at 36-months had a nominal 2-sided p-value of 0.0006.The safety profile of the STRIDE regimen was consistent with the known profiles of each medicine, and no new safety signals were observed with longer follow-up.

Serious treatment-related adverse events (TRAEs), defined as Grade 3 or 4 and including death, were experienced by 17.5% of patients treated with the STRIDE regimen versus 9.6% of patients treated with sorafenib, with no new events occurring after the primary analysis for STRIDE (17.5%).Imfinzi in combination with Imjudo is approved for the treatment of adults with advanced or unresectable HCC in the US, EU (in the 1st-line setting), Japan and several other countries.

Imfinzi monotherapy is also approved in Japan in this setting.NotesLiver cancer Liver cancer is the third-leading cause of cancer death and the sixth most commonly diagnosed cancer worldwide.^{1,2} About 75% of all primary liver cancers in adults are HCC.³ Advanced-stage HCC prognosis is poor, with a 5-year survival rate of only 7%.⁴ Between 80-90% of all patients with HCC also have cirrhosis.³ Chronic liver diseases such as cirrhosis are associated with inflammation that over time can lead to the development of HCC.⁵ More than half of patients are diagnosed at advanced stages of the disease, often when symptoms first appear.⁶ A critical unmet need exists for patients with HCC who face limited treatment options.

The unique immune environment of liver cancer provides clear rationale for investigating medications that harness the power of the immune system to treat HCC.⁶HIMALAYA HIMALAYA is a randomised, open-label, multicentre, global Phase III trial of Imfinzi monotherapy and a regimen comprising a single priming dose of Imjudo 300mg added to Imfinzi 1500mg followed by Imfinzi every four weeks (STRIDE regimen) versus sorafenib, a standard-of-care multi-kinase inhibitor.The trial included a total of 1,324 randomised patients with unresectable, advanced HCC who had not been treated with prior systemic therapy and were not eligible for locoregional therapy (treatment localised to the liver and surrounding tissue).The trial was conducted in 181 centres across 16 countries, including in the US, Canada, Europe, South America and Asia.

The primary endpoint was OS for the combination versus sorafenib and key secondary endpoints included OS for Imfinzi versus sorafenib, objective response rate and progression-free survival (PFS) for the combination and for Imfinzi alone. 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 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 2023, AstraZeneca announced positive results for Phase III trials including combinations with Imfinzi in ovarian (DUO-O) and endometrial (DUO-E) cancers, as well as in resectable NSCLC (AEGEAN). In GI cancers specifically, AstraZeneca has several ongoing registrational trials investigating Imfinzi across multiple liver cancer settings (EMERALD-1, EMERALD-2 and EMERALD-3), in resectable gastric and gastroesophageal junction cancers (MATTERHORN) and in locally advanced oesophageal cancer (KUNLUN).

In June 2023, Imfinzi added to standard-of-care neoadjuvant chemotherapy met a key secondary endpoint of pathologic complete response in the MATTERHORN Phase III trial. Imjudo (tremelimumab) is a human monoclonal antibody that targets the activity of cytotoxic T-lymphocyte-associated protein 4 (CTLA-4).

Imjudo blocks the activity of CTLA-4, contributing to T-cell activation, priming the immune response to cancer and fostering cancer cell death. In addition to its approved indications in liver and lung cancers, Imjudo is being tested in combination with Imfinzi across multiple tumour types including locoregional HCC (EMERALD-3), SCLC (ADRIATIC) and bladder cancer (VOLGA and NILE). 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 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). 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.

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