Forxiga cardiovascular outcomes benefit approved in China

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Update to approval includes DECLARE-TIMI 58 Phase III trial that reduced the risk of composite of hospitalisation for heart failure or cardiovascular death in type-2 diabetes

China's National Medical Products Administration (NMPA) has updated the label for AstraZeneca's *Forxiga* (dapagliflozin) to include data from the DECLARE-TIMI 58 Phase III trial.

DECLARE-TIMI 58 demonstrated that *Forxiga* achieved a statistically significant reduction in the composite endpoint of hospitalisation for heart failure (hHF) or cardiovascular (CV) death, versus placebo, in adults with type-2 diabetes (T2D) and established CV disease or multiple CV risk factors. The trial confirmed the well-established safety profile of *Forxiga*.[1]

DECLARE-TIMI 58 is the largest sodium-glucose cotransporter 2 (SGLT2) inhibitor CV outcomes trial conducted to date, and data from the trial were published in *The New England Journal of Medicine* in January 2019.

There are an estimated 463 million people living with diabetes worldwide, with nearly 120 million in China.[2] Patients with T2D are two to five times more likely to develop chronic heart failure (HF) than those without T2D.[3]

Ruud Dobber, Executive Vice President, BioPharmaceuticals Business Unit, said: "Heart failure is one of the first cardiovascular complications for patients with type-2 diabetes. The DECLARE-TIMI 58 Phase III data show that *Forxiga* reduces the risk of hospitalisation for heart failure and, with this label update, we look forward to bringing this significant benefit to patients in China."

Forxiga is indicated as a monotherapy and as part of combination therapies to improve glycaemic control in adults with T2D. The NMPA label update, based on the DECLARE-TIMI 58 Phase III data, follows the update to the EU marketing authorisation in August 2019 and the approval by the US Food and Drug Administration (FDA) in October 2019 of an indication for *Forxiga* (known as *Farxiga* in the US) to reduce the risk of hHF in adults with T2D and established CV disease or multiple CV risk factors.

In May 2020, *Farxiga* was approved in the US to reduce the risk of CV death and hHF in adults with HF (NYHA class II-IV) with reduced ejection fraction (HFrEF) with and without T2D, and in October 2020 *Forxiga* was recommended for approval for HF in the EU by the Committee for Medicinal Products for Human Use. Additionally, the FDA granted *Farxiga* Breakthrough Therapy Designation in October 2020to accelerate the development and regulatory review for patients with chronic kidney disease (CKD), with and without T2D.

Type-2 diabetes

T2D is a chronic disease characterised by pathophysiologic defects leading to elevated glucose levels, or hyperglycaemia.[2] Over time, this sustained hyperglycaemia contributes to further progression of the disease.[2] The prevalence of diabetes is projected to reach 578 million people worldwide by 2030, and 700 million by 2045.[2] T2D accounts for approximately 90-95 percent of all cases of diagnosed diabetes.[4]

DECLARE-TIMI 58

DECLARE-TIMI 58 is an AstraZeneca-sponsored, Phase III, randomised, double-blinded, placebo-controlled, multicentre trial designed to evaluate the effect of *Forxiga* compared with placebo on CV outcomes in adults with T2D at risk of CV events, including patients with multiple CV risk factors or established CV disease, and also assessed key renal secondary endpoints. The trial included more than 17,000 patients across 882 sites in 33 countries and was independently run in collaboration with academic investigators from the TIMI study group (Boston, US) and the Hadassah Hebrew University Medical Center (Jerusalem, Israel).[1]

Forxiga

Forxiga (dapagliflozin) is a first-in-class, oral, once-daily SGLT2 inhibitor indicated in adults for the treatment of insufficiently controlled T2D as both monotherapy and as part of combination therapy as an adjunct to diet and exercise to improve glycaemic control, with the additional benefits of weight loss and blood-pressure reduction.

Forxiga has been evaluated in patients with CKD in the Phase III DAPA-CKD trial, with the full results announced in August 2020 demonstrating that *Forxiga* met all primary and secondary endpoints, providing overwhelming efficacy. *Forxiga* is currently being tested for patients with HF in the DELIVER (HF with preserved ejection fraction, HFpEF) and DETERMINE (HFrEF and HFpEF) Phase III trials. *Forxiga* will also be tested in patients without T2D following an acute myocardial infarction (MI) or heart attack in the DAPA-MI trial - a first of its kind, indication-seeking registry-based randomised controlled trial. *Forxiga* has a robust programme of clinical trials that includes more than 35 completed and ongoing Phase IIb/III trials in more than 35,000 patients, as well as more than 2.5 million patient-years' experience.

AstraZeneca in CVRM

Cardiovascular, Renal and Metabolism (CVRM) together forms one of AstraZeneca's three therapy areas and is a key growth driver for the Company. By following the science to understand more clearly the underlying links between the heart, kidneys and pancreas, AstraZeneca is investing in a portfolio of medicines to protect organs and improve outcomes by slowing disease progression, reducing risks and tackling comorbidities. The Company's ambition is to modify or halt the natural course of CVRM diseases and potentially regenerate organs and restore function, by continuing to deliver transformative science that improves treatment practices and

cardiovascular health for millions of patients worldwide.

AstraZeneca

AstraZeneca (LSE/STO/Nasdaq: AZN) is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas - Oncology, 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

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

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