

Farxiga gets positive result in DECLARE-TIMI 58

This announcement contains inside information

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Farxiga achieved a positive result in the Phase III DECLARE-TIMI 58 trial, a large cardiovascular outcomes trial in 17,000 patients with type-2 diabetes

Farxiga met the primary composite endpoint of a statistically-significant reduction in hospitalisation for heart failure or CV death in a broad patient population

Results confirmed the well-established safety profile of Farxiga

AstraZeneca today announced positive results from the Phase III DECLARE-TIMI 58 cardiovascular (CV) outcomes trial (CVOT) for *Farxiga* (dapagliflozin), the broadest SGLT2 inhibitor CVOT conducted to date. The trial evaluated the CV outcomes of *Farxiga* vs. placebo over a period of up to five years, across 33 countries and in more than 17,000 adults with type-2 diabetes (T2D) who have multiple CV risk factors or established CV disease.

In the DECLARE (Dapagliflozin Effect on Cardiovascular Events)-TIMI 58 trial, *Farxiga* met its primary safety endpoint of non-inferiority for major adverse cardiovascular events (MACE). *Farxiga* achieved a statistically-significant reduction in the composite endpoint of hospitalisation for heart failure (hHF) or CV death, one of the two primary efficacy endpoints. Additionally, fewer MACE events were observed with *Farxiga* for the other primary efficacy endpoint, however, this did not reach statistical significance.

Data from DECLARE-TIMI 58 confirmed the well-established safety profile of *Farxiga*.

Elisabeth Björk, Vice President, Head of Cardiovascular, Renal and Metabolism, Global Medicines Development said: "*Farxiga* has achieved a statistically-significant and clinically-important reduction in hospitalisation for heart failure or CV death in a broad range of patients with type-2 diabetes and cardiovascular risk. The results from this landmark trial are especially important since heart failure is an early and frequent complication of diabetes and associated with hospitalisations that result in a considerable societal and economic burden." 1-7

Dr Stephen Wiviott of Brigham and Women's Hospital and Harvard Medical School, a senior investigator with the Thrombolysis in Myocardial Infarction (TIMI) study group and co-principal investigator of the trial, commented: "The DECLARE-TIMI 58 results offer compelling evidence that dapagliflozin helps to address an important medical need among a diverse group of patients with type-2 diabetes by reducing the composite of hospitalisation for heart failure or CV death, with a safety profile supportive of broad use."

Detailed trial results will be presented on 10 November at the American Heart Association Scientific Sessions 2018 in Chicago, USA.

About DECLARE-TIMI 58

DECLARE (Dapagliflozin Effect on Cardiovascular Events)-TIMI 58 is an AstraZeneca-sponsored, randomised, double-blinded, placebo-controlled, multicentre trial designed to evaluate the effect of *Farxiga* 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. DECLARE 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, USA) and the Hadassah Hebrew University Medical Center (Jerusalem, Israel).⁸

DECLARE is part of the extensive DapaCare clinical programme for *Farxiga*, which will enrol patients in randomised clinical trials, including a wide range of mechanistic studies, and is supported by a multinational real-world evidence study (CVD-REAL). The DapaCare clinical programme will generate data across a spectrum of people with CV risk factors, established CV disease and varying stages of renal disease, both with and without T2D. DECLARE is paving the way for three Phase III trials: Dapa-HF, DELIVER and Dapa-CKD.

About *Farxiga* (dapagliflozin)

Farxiga is a first-in-class, oral, once-daily selective inhibitor of human sodium-glucose co-transporter 2 (SGLT2) indicated as both monotherapy and as part of combination therapy to improve glycaemic control, with the additional benefits of weight loss and blood pressure reduction, as an adjunct to diet and exercise in adults with T2D. *Farxiga* is not indicated to reduce the risk of CV events, CV death or hHF. *Farxiga* has a robust clinical trial programme of more than 35 completed and ongoing Phase IIb/III trials in over 35,000 patients, as well as more than 1.8 million patient-years' experience.

About AstraZeneca in Cardiovascular, Renal & Metabolism (CVRM)

Cardiovascular, renal and metabolism together form one of AstraZeneca's main therapy areas and 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 co-morbidities. Our 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.

About AstraZeneca

AstraZeneca 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. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.

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References

1. International Diabetes Federation, IDF Diabetes Atlas, Eighth Edition Update, 2017.
2. Shah AD, Langenberg C, Rapsomaniki E, et al. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1.9 million people. *Lancet Diabetes Endocrinol.* 2015;3:105-113.
3. Faden, et al. The increasing detection of asymptomatic left ventricular dysfunction in patients with type 2 diabetes mellitus without overt cardiac disease: Data from the SHORTWAVE study. *Diabetes Res Clin Pract.* 2013;101(3):309-16.
4. Low Wang, Cecilia C. et al. "Atherosclerotic Cardiovascular Disease and Heart Failure in Type 2 Diabetes - Mechanisms, Management, and Clinical Considerations." *Circulation* 133.24 (2016): 2459-2502. PMC. Web. 19 Sept. 2018.
5. Heidenreich, Paul A. et al. "Forecasting the Impact of Heart Failure in the United States: A Policy Statement From the American Heart Association." *Circulation. Heart failure* 6.3 (2013): 606-619. PMC. Web. 19 Sept. 2018.
6. Nichols GA, Brown JB: The impact of cardiovascular disease on medical care costs in subjects with and without type 2 diabetes. *Diabetes Care* 25:482-486, 2002.
7. Nichols, et al. The incidence of congestive heart failure in type 2 diabetes. *Diabetes Care*, Volume 27, Number 8, Aug. 2004: <http://care.diabetesjournals.org/content/27/8/1879>.
8. Multicenter Trial to Evaluate the Effect of Dapagliflozin on the Incidence of Cardiovascular Events (DECLARE-TIMI 58). Sept. 2018. <https://clinicaltrials.gov/ct2/show/NCT01730534>.