

Breakthrough results for empagliflozin confirm EMPEROR-Preserved as first and only successful trial for heart failure with preserved ejection fraction

The EMPEROR-Preserved Phase III trial met its primary endpoint and demonstrated significant risk reduction with empagliflozin for the composite of cardiovascular death or hospitalization for heart failure in patients with heart failure with preserved ejection fraction (HFpEF)

HFpEF has been classified as “the single largest unmet need in cardiovascular medicine”¹ based on prevalence, poor outcomes and the absence of clinically proven therapies to date²

With approval, empagliflozin would become the first and only clinically proven therapy to improve outcomes for the full spectrum of heart failure patients regardless of ejection fraction

Ingelheim, Germany and Indianapolis, US, 6 July 2021 – The EMPEROR-Preserved Phase III trial met its primary endpoint, establishing empagliflozin as the first and only therapy to significantly reduce the risk of the composite of cardiovascular death or hospitalization for heart failure in adults, with or without diabetes, who live with heart failure with preserved ejection fraction (HFpEF). Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced the topline results today. When added to the EMPEROR-Reduced trial results, these findings demonstrate empagliflozin’s efficacy in all forms of heart failure regardless of ejection fraction. The safety profile was generally consistent with the known safety profile of empagliflozin.

“We look forward to presenting the EMPEROR-Preserved results at ESC 2021, which should offer a breakthrough in cardiovascular medicine and a new hope for people with HFpEF, which is an increasingly prevalent public health issue. HFpEF has long been the most challenging form of heart failure to treat,” said Professor Stefan Anker, Heart Failure Cardiologist at Charité Berlin, Germany, and EMPEROR-Preserved Principal Investigator. “Building on previous results from the EMPA-REG-OUTCOME trial, and the EMPEROR-Reduced trial in heart failure with reduced ejection fraction, the EMPEROR-Preserved findings demonstrate that empagliflozin reduces cardiovascular death or hospitalization for heart failure and has the potential to transform the care of people living with heart failure.”

Heart failure poses a significant global disease burden: more than 60 million patients worldwide have heart failure and half of them have HFpEF.^{3,4} Heart failure is a leading cause of hospitalization and is becoming increasingly prevalent in Western countries due to aging populations.³ The risk of death in people with heart failure rises with each hospital admission.⁵ Heart failure with left ventricular preserved ejection

fraction occurs when the left ventricle of the heart is unable to fill properly, resulting in less blood being pumped to the body.⁶

“The totality of evidence from the trial points to the potential of empagliflozin to redefine treatment of heart failure with preserved ejection fraction, which affects approximately 30 million people worldwide,” said Waheed Jamal, M.D., Corporate Vice President and Head of CardioMetabolic Medicine, Boehringer Ingelheim. “Until now, there have been no clinical studies demonstrating reduced risk of heart failure hospitalizations or cardiovascular mortality for all adults with this prevalent and life-limiting condition. With the earlier EMPEROR-Reduced trial results, we are confident in the potential of empagliflozin to positively impact the lives of adults across the full spectrum of heart failure.”

“Empagliflozin was the first SGLT2 inhibitor to reduce cardiovascular death for people with type 2 diabetes and cardiovascular disease, and we have now reached another important milestone, this time in heart failure,” added Jeff Emmick, M.D., Ph.D., Vice President, Product Development, Lilly. “The EMPEROR-Preserved topline results offer promise in a type of heart failure that until now has traditionally been very challenging to treat effectively. The EMPEROR heart failure studies are part of our EMPOWER clinical trial program exploring the effect of empagliflozin across a spectrum of cardio-renal-metabolic diseases, aiming to significantly improve outcomes in these highly prevalent conditions that impact many people’s lives.”

The EMPEROR-Preserved trial investigated empagliflozin 10 mg compared to placebo.⁷ Full results from the EMPEROR-Preserved trial are scheduled for presentation at the European Society of Cardiology (ESC) Congress 2021 on 27 August. Boehringer Ingelheim and Lilly plan for regulatory submissions in 2021. These results add to previous findings from the EMPEROR-Reduced Phase III trial, which showed that empagliflozin significantly reduced the combined relative risk of cardiovascular death or hospitalization for heart failure by 25 percent, compared to placebo in adults with heart failure with reduced ejection fraction (HFrEF).⁸

About the EMPEROR heart failure studies^{7,9}

The EMPEROR (EMPagliflozin outcome tRial in patients with chrOnic heaRt failure) chronic heart failure studies were two Phase III, randomized, double-blind trials that investigated once-daily empagliflozin compared to placebo in adults with chronic HFrEF or HFpEF, with or without diabetes:

- **EMPEROR-Reduced** [[NCT03057977](#)] investigated the safety and efficacy of empagliflozin in patients with chronic HFrEF.
 - Primary endpoint: time to first event of adjudicated cardiovascular death or adjudicated hospitalization for heart failure

- Number of patients: 3,730
- Completion: 2020
- **EMPEROR-Preserved** [NCT03057951] investigated the safety and efficacy of empagliflozin in patients with chronic HFpEF.
 - Primary endpoint: time to first event of adjudicated cardiovascular death or adjudicated hospitalization for heart failure
 - Number of patients: 5,988
 - Completion: 2021

Ejection fraction is a measurement of the percentage of blood the left ventricle pumps out with each contraction.¹⁰ When the heart relaxes, the ventricle refills with blood.

About the EMPOWER program

The Boehringer Ingelheim and Lilly Alliance has developed the EMPOWER program to explore the impact of empagliflozin on major clinical cardiovascular and renal outcomes in a spectrum of cardio-renal-metabolic conditions. Cardio-renal-metabolic conditions are the leading cause of mortality worldwide and account for up to 20 million deaths annually.¹¹ Through the EMPOWER program, the Alliance is working to advance knowledge of these interconnected systems and create care which offers integrated, multi-organ benefits. Comprised of nine clinical trials and a real-world evidence study, EMPOWER reinforces the long-term commitment of the Alliance to improve outcomes for people living with cardio-renal-metabolic conditions. With more than 400,000 adults enrolled worldwide in clinical trials, it is one of the broadest and most comprehensive clinical programs for an SGLT2 inhibitor to date.

About heart failure

Heart failure is a progressive, debilitating and potentially fatal condition that occurs when the heart cannot supply adequate circulation to meet the body's demands for oxygenated blood or to do so requires increased blood volume leading to fluid accumulation (congestion) in the lungs and peripheral tissues.¹² It is a common condition affecting over 60 million people worldwide and expected to increase as the population ages.^{3,4} Heart failure is highly prevalent in people with diabetes;¹³ however, approximately half of all people with heart failure do not have diabetes.¹⁴

About cardio-renal-metabolic conditions

Boehringer Ingelheim and Lilly are driven to transform care for people with cardio-renal-metabolic conditions, a group of interconnected disorders that affect more than one billion people worldwide and are a leading cause of death.⁴

The cardiovascular, renal and metabolic systems are interconnected, and share many of the same risk factors and pathological pathways along the disease continuum. Dysfunction in one system may accelerate the onset of others, resulting in progression of interconnected diseases such as type 2 diabetes, cardiovascular disease, heart failure, and kidney disease, which in turn leads to an increased risk of cardiovascular death. Conversely, improvements in one system can lead to positive effects throughout the others.^{15,16,17}

Through our research and treatments, our goal is to support people's health, restoring the balance between the interconnected cardio-renal-metabolic systems and reducing their risk of serious complications. As part of our commitment to those whose health is jeopardized by cardio-renal-metabolic conditions, we will continue embracing a multidisciplinary approach towards care and focusing our resources on filling treatment gaps.

About empagliflozin

Empagliflozin (marketed as Jardiance®) is an oral, once-daily, highly selective sodium-glucose cotransporter 2 (SGLT2) inhibitor and the first type 2 diabetes medicine to include cardiovascular death risk reduction data in its label in several countries.^{18,19,20}