

Press Release

Boehringer Ingelheim and Lilly announce Trajenta®'s CARMELINA® cardiovascular outcome trial met its primary endpoint

- Trajenta® demonstrates long-term cardiovascular safety in adults with type 2 diabetes

Ingelheim, Germany and Indianapolis, US, 19 July, 2018 – CARMELINA®¹ (CARDiovascular safety and Renal Microvascular outcomE with LINAgliptin in patients with type 2 diabetes at high vascular risk) met its primary endpoint, defined as time to first occurrence of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke (3-point MACE), with Trajenta® (linagliptin) demonstrating similar cardiovascular safety compared to placebo. Boehringer Ingelheim and Eli Lilly and Company (NYSE: LLY) announced today positive top-line results, which evaluated the impact of treatment with linagliptin vs. placebo on cardiovascular safety on top of standard of care.

The study included 6,979 adults with type 2 diabetes and high cardiovascular risk.¹ The majority of patients also had kidney disease, an important risk factor for cardiovascular disease. The overall safety profile of linagliptin in CARMELINA®, including adults with kidney disease, was consistent with previous data and no new safety signal was observed.

People who have diabetes are at an increased risk of cardiovascular disease and chronic kidney disease.^{2,3} Despite recent advancements in treatment options, cardiovascular disease remains the leading cause of death for people living with diabetes,⁴ and about two thirds of chronic kidney disease cases are attributable to metabolic conditions, such as diabetes, obesity and hypertension.^{5,6,7}

“CARMELINA® reinforces the long-term clinical safety profile of linagliptin in adults with type 2 diabetes, even in those most vulnerable for vascular complications,” said Waheed Jamal, MD, Corporate Vice President and Head of Cardiometabolic Medicine, Boehringer Ingelheim. “The trial adds important new evidence for patients at high risk for heart and kidney disease, a population that has previously been underrepresented in other cardiovascular outcome trials in diabetes.”

“Linagliptin demonstrated cardiovascular safety in adults with type 2 diabetes and high vascular risk, with no need for dose adjustments regardless of kidney function,” added Jeff Emmick, MD, PhD, Vice President, Product Development, Lilly Diabetes. “CARMELINA® provides confidence in linagliptin as an effective and well-tolerated treatment, with a simple dosing regimen, for adults with type 2 diabetes.”

The full results of CARMELINA® will be presented on 4 October at the 54th European Association for the Study of Diabetes Annual Meeting in Berlin, Germany.

About the Study

CARMELINA® (CARDiovascular safety and Renal Microvascular outcomE with LINAgliptin in patients with type 2 diabetes at high vascular risk) is a multi-national, randomised, double-blind, placebo-controlled clinical trial that involved 6,979 adults with type 2 diabetes from 27 countries at more than 600 sites observed for a median duration of 2.2 years.¹ The study was designed to assess the effect of Trajenta® (linagliptin) (5mg once daily) compared to placebo (both added to standard of care) on cardiovascular outcome in adults with type 2 diabetes and high cardiovascular risk, the majority of whom also had kidney disease. This population reflects patients that doctors see in their daily practice. CARMELINA® was led by an academic trial steering committee and the Boehringer Ingelheim and Eli Lilly and Company Diabetes Alliance. Compared to other recently reported outcome trials of dipeptidyl

peptidase-4 (DPP-4) inhibitors in type 2 diabetes, CARMELINA[®] included the highest number of patients with impaired kidney function.*

Standard of care included both glucose lowering agents and cardiovascular drugs (including antihypertensive and lipid lowering agents).

About Trajenta[®] (linagliptin)

Trajenta[®] is a one dose, once daily DPP-4-inhibitor that provides significant efficacy in the reduction of blood sugar levels for adults with type 2 diabetes. It can be prescribed for people with type 2 diabetes regardless of age, disease duration, ethnicity, body mass index (BMI), liver and kidney function.⁸ Trajenta[®] has the lowest kidney excretion rate of all DPP-4 inhibitors.^{8,9,10,11,12} It is prescribed at the same dose and has demonstrated proven efficacy regardless of kidney function,^{8,13,14} making it simple to administer and use.

About our cardiovascular outcome trials

Cardiovascular outcome trials are highly relevant, as cardiovascular disease is a major complication and the leading cause of death in type 2 diabetes. Worldwide, most people with type 2 diabetes die of a cardiovascular event.¹⁵ In 2015, Boehringer Ingelheim and Eli Lilly and Company announced results from the landmark cardiovascular outcome trial EMPA-REG OUTCOME[®] with the SGLT2 inhibitor empagliflozin, which demonstrated a 38% relative risk reduction in cardiovascular death in adults with type 2 diabetes and established cardiovascular disease.^{†16,17}

CARMELINA[®] is one of two cardiovascular outcome trials with the DPP-4 inhibitor linagliptin. CAROLINA[®],¹⁸ will be the first DPP-4 inhibitor cardiovascular outcome trial to compare commonly used second line treatments - linagliptin and the sulphonylurea glimepiride. This trial includes adults with type 2 diabetes at increased cardiovascular risk, however, the majority did not yet have heart and kidney disease. The study is expected to complete in 2018. CARMELINA[®] and CAROLINA[®] will provide the most comprehensive clinical database on the long-term safety profile of a DPP-4-inhibitor in a broad range of adults with type 2 diabetes.

Boehringer Ingelheim and Eli Lilly and Company

In January 2011, Boehringer Ingelheim and Eli Lilly and Company announced an alliance in diabetes that centres on compounds representing several of the largest diabetes treatment classes. The alliance leverages the strengths of two of the world's leading pharmaceutical companies. By joining forces, the companies demonstrate commitment in the care of people with diabetes and stand together to focus on patient needs. Depending on geographies, the companies either co-promote or separately promote the respective molecules each contributed to the alliance.

Boehringer Ingelheim

Improving the health and quality of life of patients is the goal of the research-driven pharmaceutical company Boehringer Ingelheim. The focus in doing so is on diseases for which no satisfactory treatment option exists to date. The company therefore concentrates on developing innovative therapies that can extend patients' lives. In animal health, Boehringer Ingelheim stands for advanced prevention.

Family-owned since it was established in 1885, Boehringer Ingelheim is one of the pharmaceutical industry's top 20 companies. Some 50,000 employees create value through innovation daily for the three business areas human pharmaceuticals, animal health and biopharmaceuticals. In 2017, Boehringer Ingelheim achieved net sales of nearly 18.1 billion euros. R&D expenditure, exceeding three billion euros, corresponded to 17.0 per cent of net sales.

* glomerular filtration rate below 30 mL/min/m²

† Adult patients with type 2 diabetes and coronary artery disease, peripheral artery disease, or a history of myocardial infarction or stroke

As a family-owned company, Boehringer Ingelheim plans in generations and focuses on long-term success, rather than short-term profit. The company therefore aims at organic growth from its own resources with simultaneous openness to partnerships and strategic alliances in research. In everything it does, Boehringer Ingelheim naturally adopts responsibility towards mankind and the environment.

More information about Boehringer Ingelheim can be found on www.boehringer-ingenheim.com or in our annual report: <http://annualreport.boehringer-ingenheim.com>.

About Lilly Diabetes

Lilly has been a global leader in diabetes care since 1923, when we introduced the world's first commercial insulin. Today we are building upon this heritage by working to meet the diverse needs of people with diabetes and those who care for them. Through research and collaboration, a wide range of therapies and a continued determination to provide real solutions—from medicines to support programs and more—we strive to make life better for all those affected by diabetes around the world. For more information, visit www.lillydiabetes.com.

About Eli Lilly and Company

Lilly is a global healthcare leader that unites caring with discovery to make life better for people around the world. We were founded more than a century ago by a man committed to creating high-quality medicines that meet real needs, and today we remain true to that mission in all our work. Across the globe, Lilly employees work to discover and bring life-changing medicines to those who need them, improve the understanding and management of disease, and give back to communities through philanthropy and volunteerism. To learn more about Lilly, please visit us at www.lilly.com and newsroom.lilly.com/social-channels.

Intended audiences

This press release is issued from Boehringer Ingelheim Corporate Headquarters in Ingelheim, Germany and is intended to provide information about our global business. Please be aware that information relating to the approval status and labels of approved products may vary from country to country, and a country-specific press release on this topic may have been issued in the countries where Boehringer Ingelheim and Eli Lilly and Company do business.

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about Jardiance and its safety profile, and reflects Lilly's current belief. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. Among other things, there can be no guarantee that future study results will be consistent with the results to date or that Jardiance will receive additional regulatory approvals. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

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