The study evaluated the effect of JARDIANCE® 10 mg and 25 mg as an add-on to standard of care therapies, including:

CV

81%	ACE inhibitors or ARBs
65%	Beta-blockers
43%	Diuretics
81%	Lipid-lowering agents
89%	Anti-thrombotic therapy

T2D

74%	Metformin
48%	Insulin
43%	Sulfonylurea

Investigators were encouraged to adjust glucose-lowering therapies as appropriate to achieve glycemic control, and to manage other cardiovascular risks (including dyslipidemia and hypertension) according to guidelines.[‖]

ACE = angiotensin-converting enzyme; ARB = angiotensin-receptor blocker; CV = cardiovascular; T2D = type 2 diabetes.

‖ Background glucose-lowering therapy (including metformin, insulin, sulfonylurea, DPP-4 inhibitors, thiazolidinediones, and GLP-1 agonists) remained unchanged for the first 12 weeks, after which investigators were encouraged to adjust therapy to achieve glycemic control according to local guidelines. Throughout the trial, investigators were encouraged to treat CV risk factors to achieve the best available standard of care according to local guidelines.

Indications and Clinical Use:
Monotherapy: JARDIANCE® (empagliflozin) is indicated for use as an adjunct to diet and exercise to improve glycemic control in adult patients with type 2 diabetes mellitus for whom metformin is inappropriate due to contraindications or intolerance.

Add-on combination: JARDIANCE® is indicated in adult patients with type 2 diabetes mellitus to improve glycemic control, when metformin used alone does not provide adequate glycemic control, in combination with:
- metformin,
- metformin and a sulfonylurea,
- pioglitazone (alone or with metformin),
- linagliptin and metformin,
- basal or prandial insulin (alone or with metformin), when the existing therapy, along with diet and exercise, does not provide adequate glycemic control.

Add-on combination in patients with established cardiovascular disease: JARDIANCE® is indicated as an adjunct to diet, exercise and standard care therapy to reduce the incidence of cardiovascular death in patients with type 2 diabetes mellitus and established cardiovascular disease.

Important Limitation of Use: Use of JARDIANCE® with insulin mix (regular or analogue mix) has not been studied. Therefore, JARDIANCE® should not be used with insulin mix.

Contraindications:
- Patients with severe renal impairment (eGFR <30 mL/min), end-stage renal disease and patients on dialysis

Most Serious Warning and Precaution:
Diabetic Ketoacidosis (DKA): Cases of DKA, a serious, life-threatening condition requiring urgent hospitalization, have been reported for JARDIANCE® and other SGLT2i, including fatal cases and atypical cases with blood glucose <13.9 mmol/L (250 mg/dL). Assess for DKA immediately if non-specific symptoms occur, regardless of blood glucose level, and **discontinue JARDIANCE® immediately**. JARDIANCE® should not be used for the treatment of DKA or in patients with a history of DKA. JARDIANCE® is not indicated, and should not be used, in patients with type 1 diabetes.

Other Relevant Warnings and Precautions:
- Not recommended in volume-depleted patients; drops in blood pressure; monitor volume status and electrolytes
- Caution in patients at high risk for cerebrovascular accidents
- Temporarily discontinue in situations predisposing to ketoacidosis
- Caution when reducing concomitant insulin dose
- Hypoglycemia when used in combination with insulin secretagogues or insulin
- Risk and monitoring of LDL-C increases
- Genital mycotic infections
- Urinary tract infections
- Necrotizing fasciitis of the perineum (Fournier's gangrene)
- Caution in patients with elevated hematocrit
- Not recommended in patients with severe hepatic impairment
- Serious hypersensitivity reactions
- Intravascular volume contraction, increases in serum creatinine, decreases eGFR; assess renal function prior to initiation and regularly during treatment; monitor renal function with concomitant drug use; more intensive monitoring if eGFR <60 mL/min (especially if eGFR <45 mL/min); discontinue if eGFR <30 mL/min
- Acute kidney injury
- Use in settings of reduced oral intake or fluid loss
- Do not use during pregnancy or breastfeeding
- Do not use in patients <18 years; caution in patients ≥65 years and ≥75 years; not recommended in patients ≥85 years
- Patients will test positive for glucose in urine

For more information:
Refer to the Product Monograph at www.JardiancePM.ca for important information relating to adverse events, drug interactions, dosing, and conditions of clinical use. The Product Monograph is also available by calling 1-800-263-5103 ext. 84633.

References: 1. JARDIANCE Product Monograph. Boehringer Ingelheim, April 11, 2019. 2. Zinman B, *et al.* Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. *N Engl J Med.* 2015;373(22):2117-28.

PAAB MEMBER OF INNOVATIVE MEDICINES CANADA

EMP-CA-100830
EMP-LI-100830

Jardiance® (empagliflozin)

Boehringer Ingelheim

Lilly

JARDIANCE® was studied in EMPA-REG OUTCOME

A randomized, double-blind, placebo-controlled CV outcomes trial[1,2*]

JARDIANCE® is indicated as an adjunct to diet, exercise and standard care therapy to **reduce the incidence of cardiovascular death in patients with T2D and established CV disease.**

Jardiance® (empagliflozin)

CV = cardiovascular; T2D = type 2 diabetes.

* EMPA-REG OUTCOME study: double-blind, placebo-controlled, event-driven study evaluating empagliflozin 10 mg and 25 mg as add-on to standard of care therapy in reducing CV events in T2D patients with ≥1 of: coronary artery disease, peripheral artery disease, history of MI, history of stroke. Primary endpoint was time to first event in composite endpoint of CV death, non-fatal MI, or non-fatal stroke (Major Adverse Cardiovascular Events [MACE-3]).

Published in
The New England Journal of Medicine

Canadian-led trial

42 countries

3.1 years of median observation time

7,020 patients with T2D and ***established CV disease,*** **which may include...**

Vascular manifestations:

- Coronary artery disease (CAD)
  - Evidence of multi-vessel or single-vessel
- Peripheral artery disease (PAD)

OR

Prior atherothrombotic event:

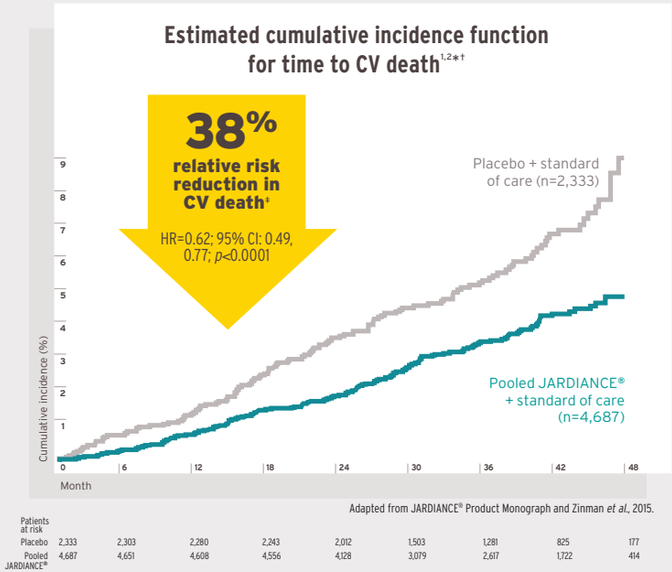
- History of myocardial infarction (MI)
- History of stroke

>75% **of patients had CAD**

20.8% of patients had PAD
46.6% of patients had history of MI
23.3% of patients had history of stroke

In patients with type 2 diabetes and established CV disease,
JARDIANCE®, as an adjunct to standard of care therapy, demonstrated...

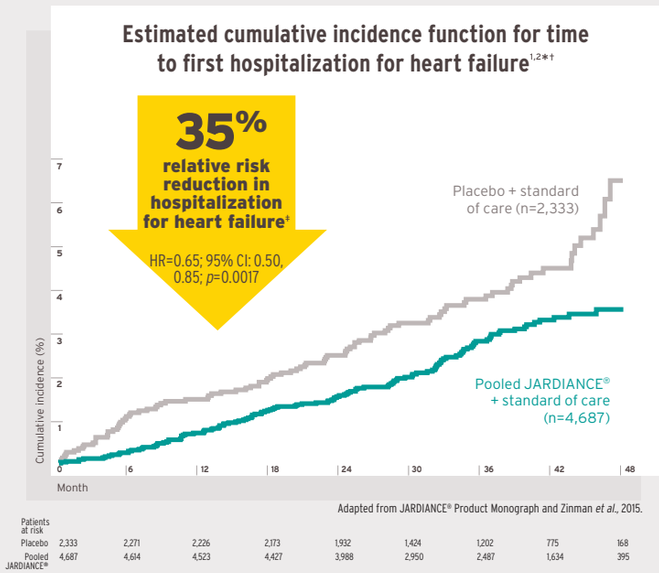
significant reductions in the risk of CV death vs. placebo. (other adjudicated endpoint)



Absolute risk for CV death:
5.9% placebo vs. 3.7% pooled JARDIANCE®

NNT=46

significant reductions in the risk of heart failure requiring hospitalization vs. placebo. (other adjudicated endpoint)



Absolute risk for heart failure hospitalization:
4.1% placebo vs. 2.7% pooled JARDIANCE®

NNT=72

JARDIANCE® demonstrated superiority vs. placebo in the MACE-3 primary analysis.[1,2*†]

Patients with event: 490 (10.5%) pooled JARDIANCE® vs. 282 (12.1%) placebo; HR=0.86; 95% CI: 0.74, 0.99; *p*=0.0382.

There was no significant change in non-fatal MI or non-fatal stroke.

CV = cardiovascular; NNT = number needed to treat; T2D = type 2 diabetes.
* EMPA-REG OUTCOME study: double-blind, placebo-controlled, event-driven study evaluating empagliflozin 10 mg and 25 mg as add-on to standard of care therapy in reducing CV events in T2D patients with ≥1 of: coronary artery disease, peripheral artery disease, history of MI, history of stroke. Primary endpoint was time to first event in composite endpoint of CV death, non-fatal MI, or non-fatal stroke (Major Adverse Cardiovascular Events [MACE-3]).
† Pre-specified analysis of pooled data for both 10 and 25 mg doses of JARDIANCE® against placebo.
‡ Treated set: patients who received ≥1 dose of study drug.