

CONTROL TODAY*

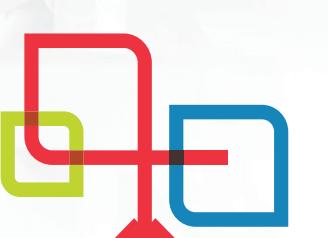
KEEP PACE WITH TOMORROW¹



*FORXIGA is indicated in adults for treatment of:

- Symptomatic chronic heart failure
- Chronic kidney disease
- Insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise

PI, prescribing information; Ref, references


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(dapagliflozin) 5mg, 10mg
film coated tablet

For Medical inquiries 



Reference

1. Forxiga Egyptian Drug Authority Approved Leaflet. Approval date 16/4/2023

CKD is under-recognized public health crisis.¹



90%
of US adults with CKD do
not know they have CKD²



~69%
of US adults eligible for
statin treatment are aware
they have high cholesterol³

(from 2011 to 2012 through 2015 to 2016)

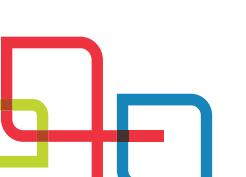


~77%*
of US adults have been
diagnosed with diabetes⁴

(2013–2016)



CKD, chronic kidney disease
*(95% CI)


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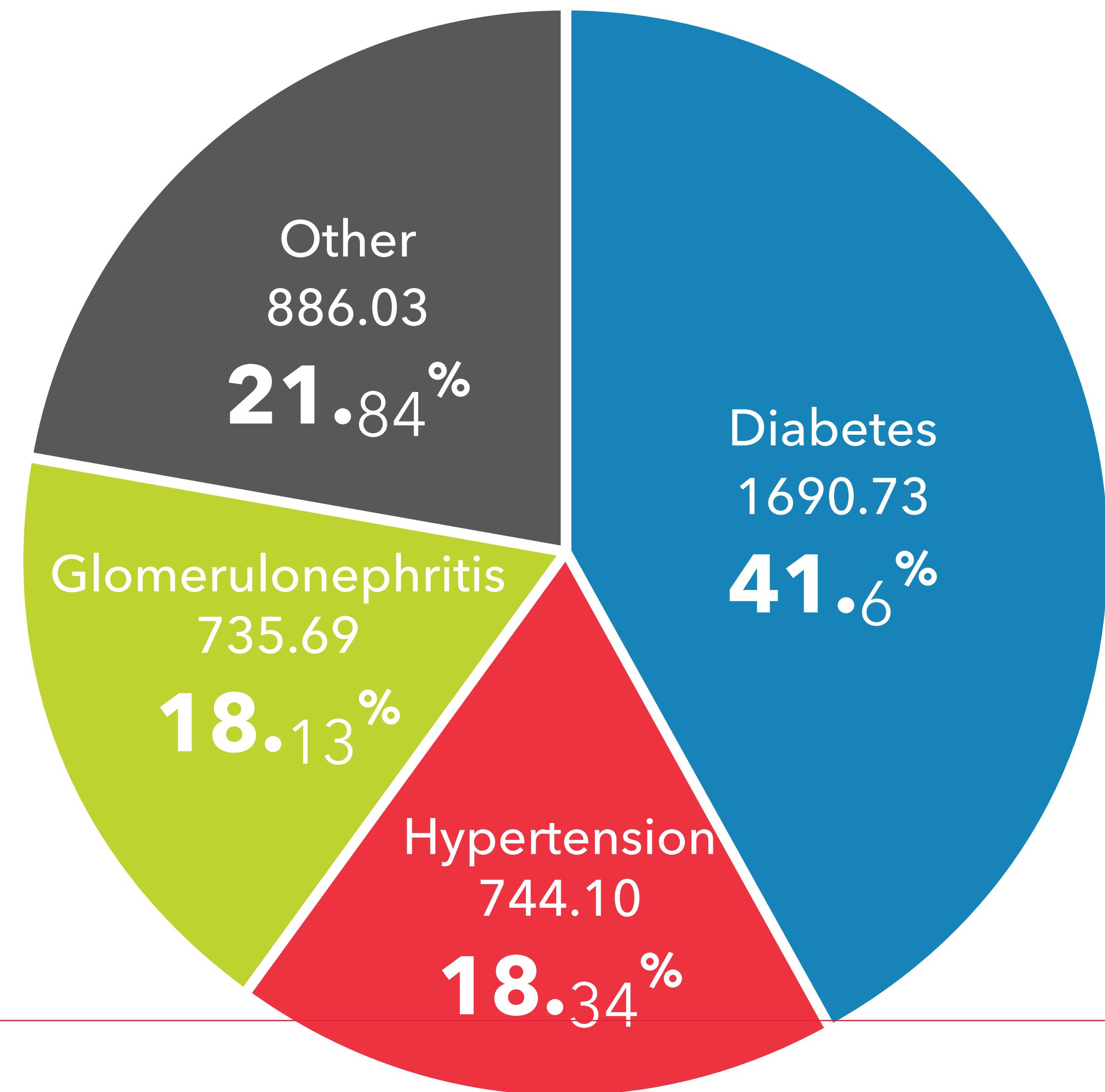


Reference

1. National Kidney Foundation. Kidney Disease: The Basics. Available at: <https://www.kidney.org/news/newsroom/factsheets/KidneyDiseaseBasics>. Last accessed: Dec. 2023
2. CDC - Chronic Kidney Disease in the United States, 2023. Available at: <https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html>. Last accessed: Dec. 2023
3. Patel N, Bhargava A, Kalra R, et al. Trends in Lipid, Lipoproteins, and Statin Use Among U.S. Adults. *J Am Coll Cardiol* 2019;74:2525–2528.
4. Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States. Available at: <https://www.cdc.gov/diabetes/data/statistics-report/index.html#print>. Last accessed: Dec. 2023

Causes of CKD are diverse, with diabetes and hypertension responsible for more than half of all cases¹

Age-standardized global prevalence rate per
100,000 persons in 2016



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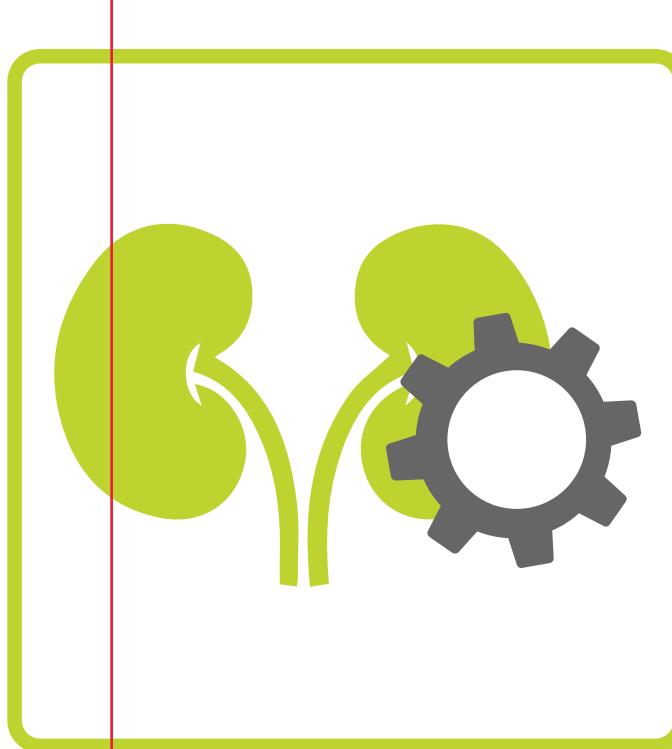


Reference

1. Xie Y, Bowe B, Mokdad A, et al. Analysis of the Global Burden of Disease study highlights the global, regional, and national trends of chronic kidney disease epidemiology from 1990 to 2016. *Kidney International* (2018) 94, 567–581 trends, and treatment patterns— NHANES 2007–2012. *BMJ Open Diabetes Research and Care* 2016;4:e000154.

Measurements for early CKD

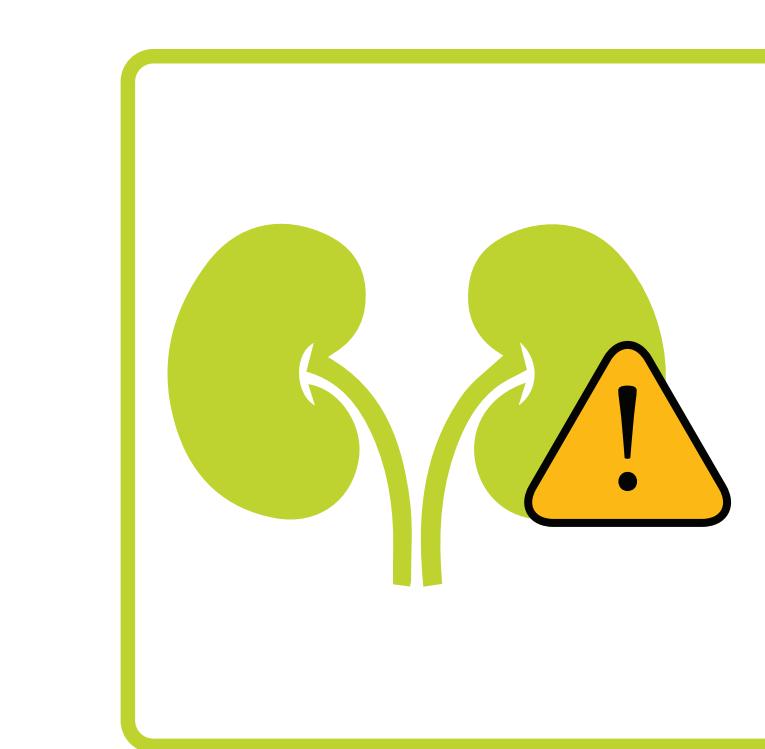
CKD screening should consist of a dual assessment of eGFR and UACR¹



Kidney function impairment²

Decreased GFR

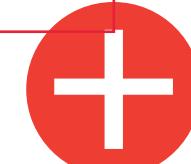
GFR <60 mL/min/1.73 m²
(stages G (grade) 3a–5)



Kidney damage²

Albuminuria

UACR ≥30 mg/g



**The criteria for definition of CKD is:
Duration >3 months, based on documentation or inference²**



eGFR, estimated glomerular filtration rate; UACR, urine albumin:creatinine ratio

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When eGFR is dipping, the clock is ticking



CV MORTALITY RISK ^{3*}	eGFR CATEGORIES (ml/min/ 1.73m ²)	ALBUMINURIA CATEGORIES (mg/g)
up to 4.3x greater	3a eGFR 45–60	A3 (ACR≥300)
up to 5.2x greater	3b eGFR 30–45	A3 (ACR≥300)
up to 14x greater	4 eGFR 15–30	A1 (ACR<10)

Patients with CKD have a much faster decline in kidney function:⁴

**18.1% of adults with Stage 3 CKD had
accelerated progression within 2 years^{4†}**

SD

SD

The relative risks from categorical meta-analysis.

*CV mortality risk compared to an eGFR baseline of 90–105 mL/min/1.73m² and an ACR <10. CV mortality ranges: Stage 3a (1.5 to 4.3), Stage 3b (2.2 to 5.2),

Stage 4 (4.8 to 14.0); †Accelerated progression defined as eGFR loss >4 mL/min/1.73m² per year; 36% of patients had T2D at baseline.⁴

ACR, albumin-to-creatinine ratio; CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; T2D, Type 2 diabetes.



Study Design³

Meta-analysis study design³:

KDIGO initiated a collaborative meta-analysis and sponsored a Controversies Conference in October 2009 to examine the relationship of estimated glomerular filtration rate (GFR) and albuminuria to mortality and kidney outcomes. On the basis of analyses in 45 cohorts that included 1,555,332 participants from general, high-risk, and kidney disease populations.

Application of only two criteria leads to a simple two-dimensional grid, in which all people with urine ACR $30 \geq \text{mg/g}$ or eGFR $< 60 \text{ ml/min per } 1.73 \text{ m}^2$ are defined as having chronic kidney disease, and staged according to the level of GFR.

KDIGO, Kidney Disease Improving Global Outcomes; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration;
KPNC, Kaiser Permanente Northern California



Study Design⁴

[†]Study design:

The study was based in KPNC, a large integrated health care delivery system currently providing comprehensive care to > 4.4 million members in the San Francisco and greater Bay Area. all adult18 years old and above. 36,195 eligible adults with eGFR 30–59 ml/min/1.73m². this study to examine annual rate of eGFR decline and to identify the subgroup of patients who experienced fast CKD progression.

Identified adults with estimated glomerular filtration rate (eGFR) 30–59 ml/min/1.73m² by CKD-EPI equation between 2008 and 2010 who had no previous dialysis or renal transplant, who had outpatient serum creatinine values spaced 10–14 months apart and who did not initiate renal replacement therapy, die or disenroll during the first 2 years of follow-up.

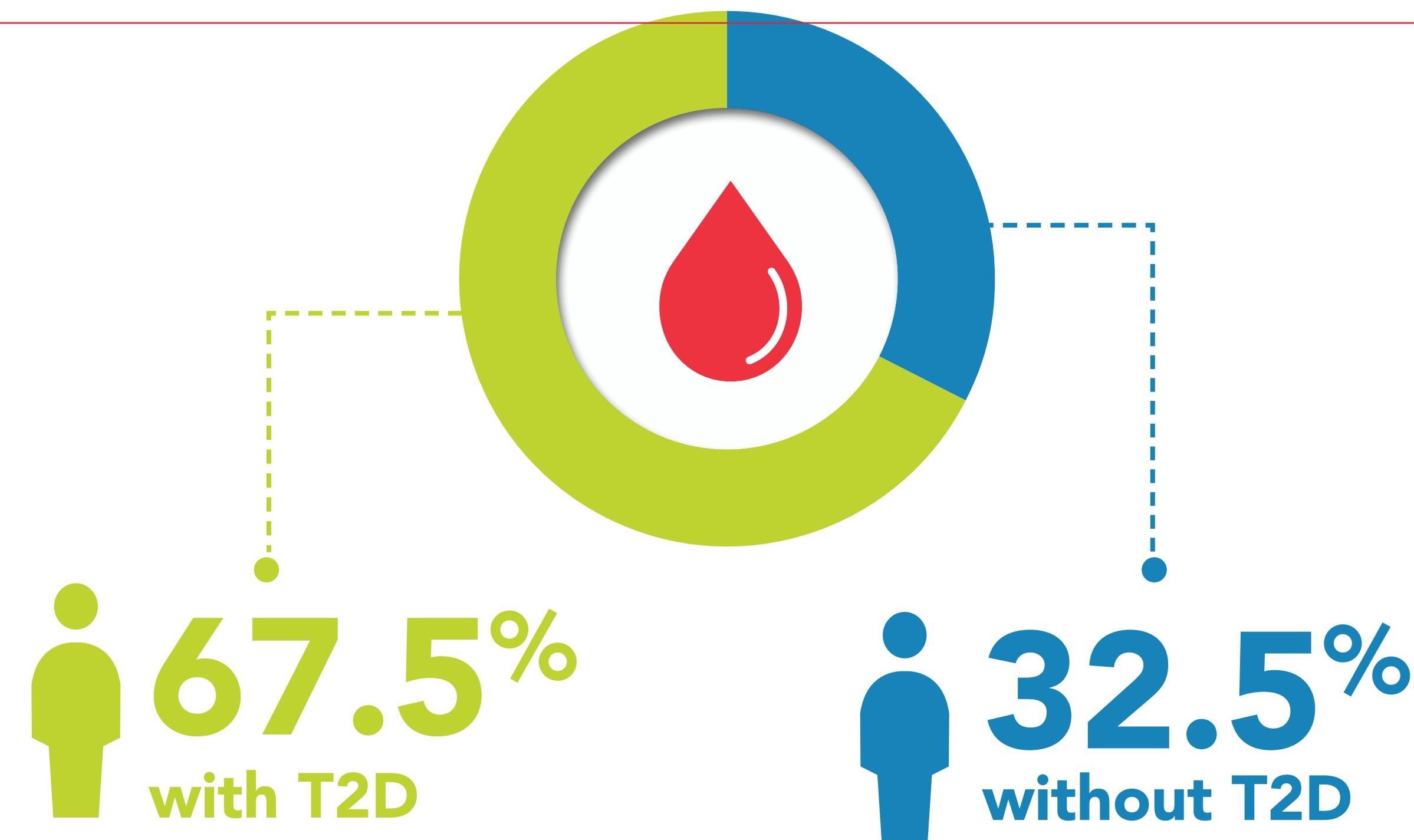
Patients whose index eGFR was not between the range of 30 and 59 ml/min/1.72 m² were excluded.



Reference

1. Shlipak MG, Tummalapalli SL, Boulware LE, et al. The case for early identification and intervention of chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney International* (2021) 99, 34–47
2. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int.* 2013;3(1):1–150
3. Levey, A.S. et al. (2011) 'The definition, classification, and prognosis of chronic kidney disease: A KDIGO controversies conference report', *Kidney International*, 80(1), pp. 17–28. doi:10.1038/ki.2010.483
4. Go AS et al. *BMC Nephrol.* 2018;19(1):146.

DAPA-CKD study participants¹



eGFR range: 25 to 75 mL/min/1.73m²

Mean BP: 137/78 mmHg²

UACR range: 200 to 5000 mg/g

97% of patients received ACEi/ARB therapy at maximum tolerated dose²



DAPA-CKD, Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease; T2D, type-2 diabetes; ESKD, end-stage kidney disease; CV, cardiovascular; UACR, urine albumin-to-creatinine ratio; BP, blood pressure; ACEi/ARB, angiotensin-converting enzyme inhibitor/angiotensin receptor blocker.

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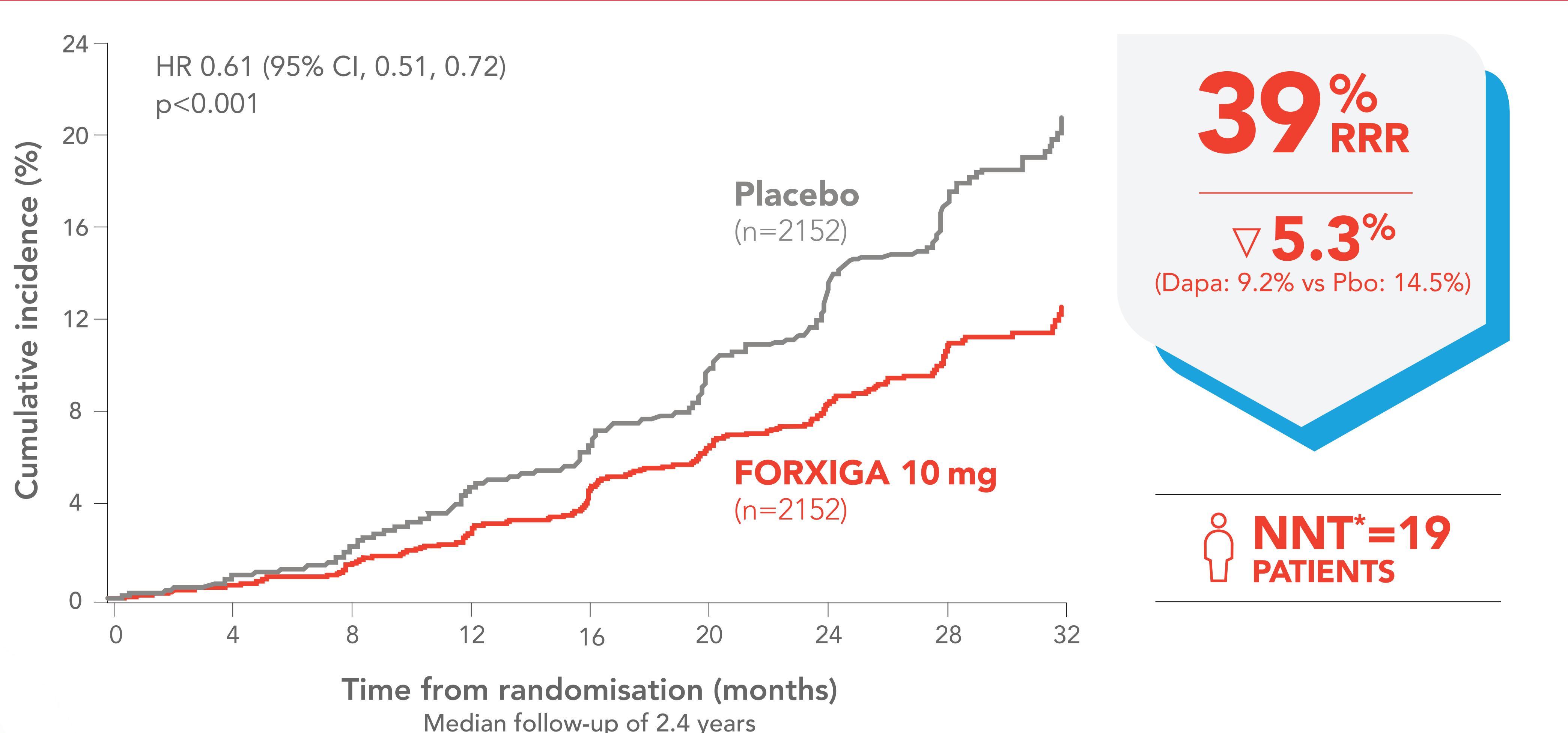


Reference

1. Heerspink H, Stefansson BV, Correa-Rotter R, Chertow GM, Greene T et. al. Dapagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med* 2020; 383:1436-46
2. Wheeler DC, Stefansson BV, Batiushin M, Bilchenko O, Cherney DZI et. al. The dapagliflozin and prevention of adverse outcomes in chronic kidney disease (DAPA-CKD) trial: baseline characteristics. *Nephrol Dial Transplant* (2020); 35: 1700-11

FORXIGA reduced the risk of the composite of declining kidney function, ESKD, and renal or CV death in patients with CKD Vs Placebo¹

DAPA-CKD PRIMARY COMPOSITE OUTCOME: DECLINE OF AT LEAST 50% IN THE eGFR, ESKD, AND RENAL OR CV DEATH



*The number of participants who needed to be treated during the trial period to prevent one primary outcome event was 19 (95% CI, 15 to 27).¹

CKD, chronic kidney disease; T2D, type 2 diabetes; ESKD, end-stage kidney disease; CV, cardiovascular; HR, hazard ratio; CI, confidence interval; RRR, relative risk reduction; ▽, risk reduction; Dapa, dapagliflozin; Pbo, placebo; NNT, number needed to treat; SD, study design; IgA, immunoglobulin A.

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Study Design¹

Objective:

Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial to assess the longterm efficacy and safety of the SGLT2 inhibitor dapagliflozin in patients with chronic kidney disease, with or without type 2 diabetes.

Study design:

DAPA-CKD was a double-blind, placebo-controlled, multicenter clinical trial; where 4304 patients were randomly assigned to receive either dapagliflozin (at a dose of 10 mg once daily) or matching placebo. The median duration of follow up was 2.4 year.

Primary end point:

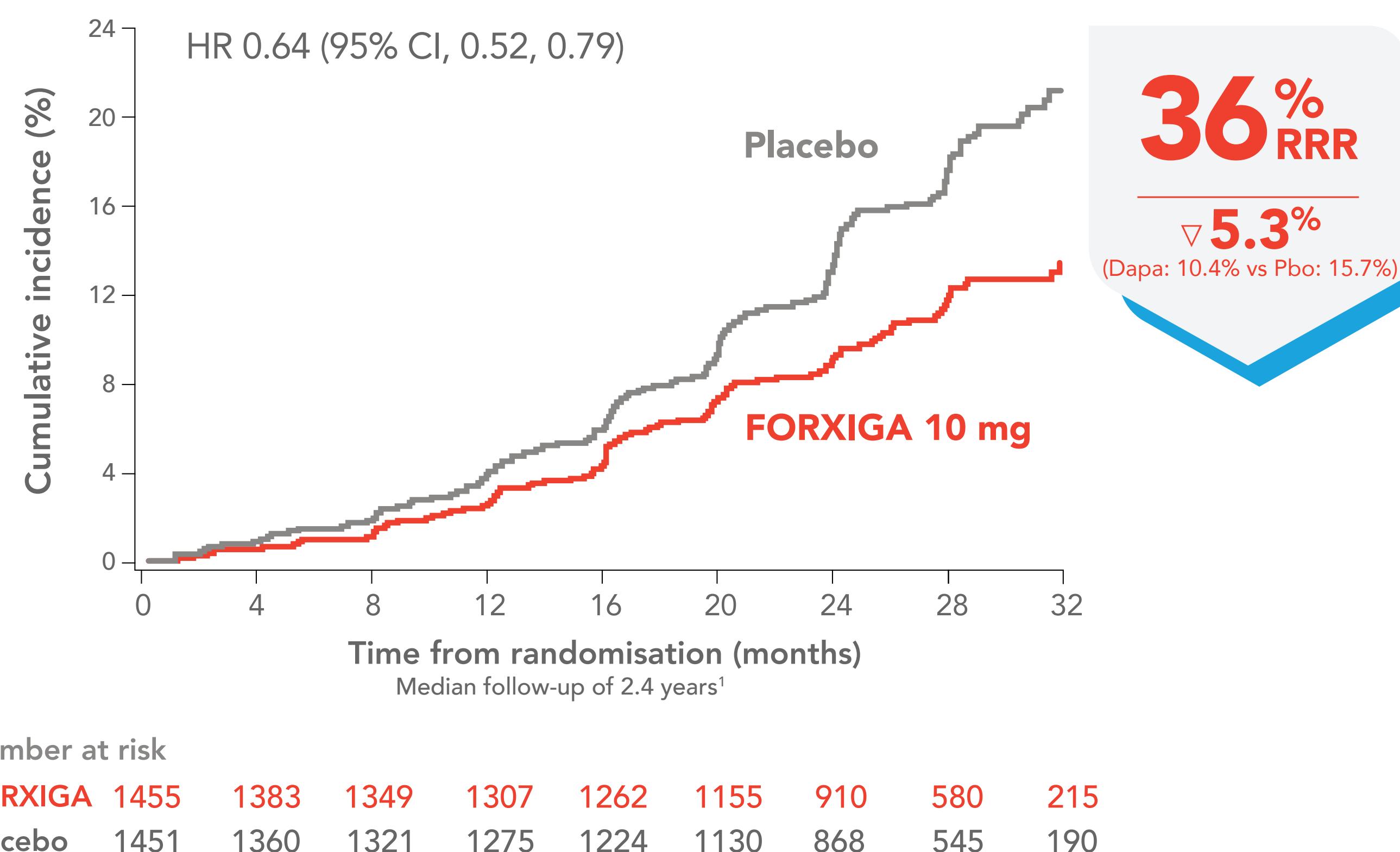
Composite of declining kidney function, end-stage kidney disease & renal or cardiovascular death.



Results of the primary endpoint in patients with T2D²

DAPA-CKD PRE-SPECIFIED SUBGROUP ANALYSIS²

Patients with T2D



DAPA-CKD PRE-SPECIFIED
SUBGROUP Analysis

CKD patients with T2D

CKD patients without T2D

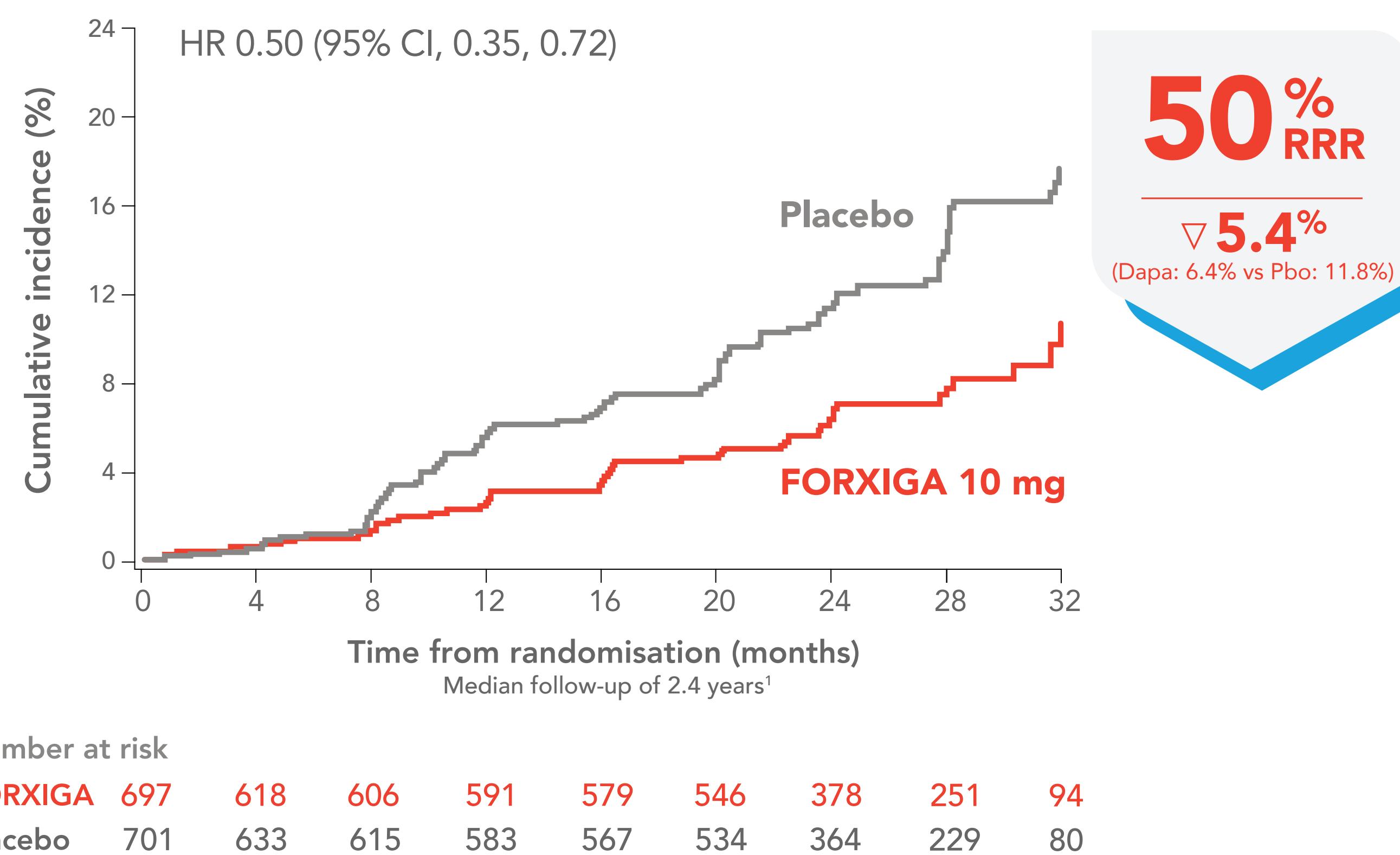
SD



Results of the primary endpoint in patients without T2D²

DAPA-CKD PRE-SPECIFIED SUBGROUP ANALYSIS²

Patients without T2D



DAPA-CKD PRE-SPECIFIED
SUBGROUP Analysis

CKD patients with T2D

CKD patients without T2D



Study Design²

Objective:

In DAPA-CKD, dapagliflozin reduced the risk of kidney failure, death from cardiovascular causes or hospital admission for heart failure, and death from any cause.¹² In this prespecified analysis of DAPA-CKD, here it was aimed to investigate whether the presence or absence of type 2 diabetes at baseline and the underlying aetiology of kidney disease modified the effects of dapagliflozin on these clinical outcomes.

Study design:

DAPA-CKD was a multicentre, double-blind, placebo-controlled, randomised trial done at 386 study sites in 21 countries, where 4304 patients were randomly assigned to receive either dapagliflozin (at a dose of 10 mg once daily) or matching placebo. The median duration of follow up was 2.4 year. A prespecified analysis was performed of the effects of dapagliflozin on the primary and secondary efficacy outcomes in participants with and without type 2 diabetes.

Primary end point:

The primary outcome of the trial was a composite of declining kidney function, end-stage kidney disease & renal or cardiovascular death.



Reference

1. Heerspink H, Stefansson BV, Correa-Rotter R, Chertow GM, Greene T et. al. Dapagliflozin in Patients with Chronic Kidney Disease. *N Engl J Med* 2020; **383**:1436-46
2. Wheeler DC, Stefansson BV, Jongs N, Chertow GM, Greene T et. al. Effects of dapagliflozin on major adverse kidney and cardiovascular events in patients with diabetic and non-diabetic chronic kidney disease: a prespecified analysis from the DAPA-CKD trial. *Lancet Diabetes Endocrinol* 2021; **9**:22-31

2022 KDIGO Guidelines for Diabetes management in Chronic Kidney Disease:¹



Ref

PI

Sodium-glucose Co-transporter 2 inhibitors

Recommendations and statements	GoR	QoE
We recommend treating patients with type 2 diabetes, CKD, and an eGFR ≥ 20 ml/min per 1.73 m^2 with an SGLT2i	I	A

adapted from ref. 1



KDIGO, Kidney Disease Improving Global Outcomes; GOR, grade of recommendation;
QoE, quality of evidence



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CKD
Burden

CKD
Causes

CKD
Assessment

Keep Pace

Guidelines

All Cause
Mortality

Control Today

Dose

2023 ESH Guidelines for the Management of Arterial Hypertension:²



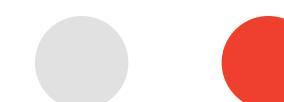
Ref

PI

Treatment Strategies in Patients With CKD

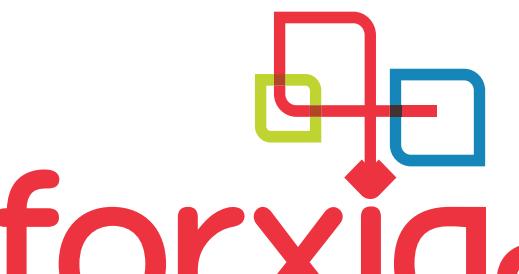
Recommendations and statements	CoR	LoE
SGLT2is inhibitors are recommended for patients with diabetic and non-diabetic nephropathies CKD if eGFR is at least 20 ml/min/1.73 ^a .	I	A

adapted from ref. 2



^aAdditional eGFR and albuminuria criteria apply for initiation of treatment with different SGLT2is according to their respective approval.

ESH, European Society of Hypertension; CoR, class of recommendation; LoE, level of evidence


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Reference

1. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. Kidney International (2022) 102 (Suppl 5S), S1–S127. Accessed at: <https://www.kidney-international.org/action/showPdf?pii=S0085-2538%2822%2900507-5> . Last access date: 4.12.2023
2. 2023 ESH Guidelines for the management of arterial hypertension. Journal of Hypertension 2023, 41:1874–2071. Accessed at: https://journals.lww.com/jhypertension/fulltext/2023/12000/2023_esh_guidelines_for_the_management_of_arterial.2.aspx . Last access date: 4.12.2023



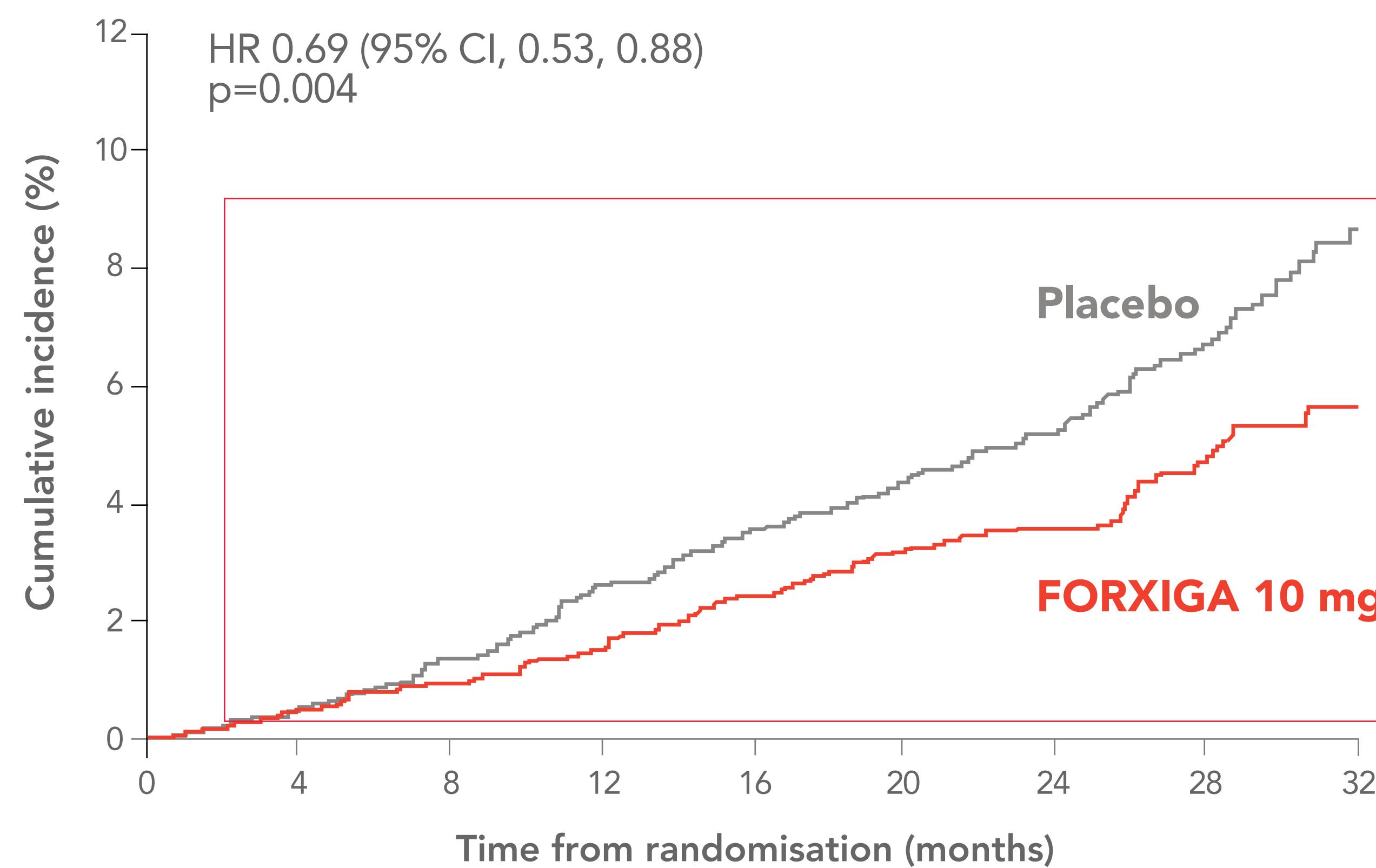
Ref

PI

In patients with CKD, with or without T2D

Fewer patients receiving FORXIGA died from any cause vs placebo in DAPA-CKD¹

DAPA-CKD SECONDARY ENDPOINT



31% RRR
in death from any cause
▼ 2.1%
(Dapa: 4.7% vs Pbo: 6.8%)

Number at risk								
FORXIGA	2152	2039	2029	2017	1998	1925	1531	1028
Placebo	2152	2035	2018	1993	1972	1902	1502	1009

SGLT2i, sodium-glucose co-transporter 2 inhibitor; CKD, chronic kidney disease; T2D, type 2 diabetes; DAPA-CKD, Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease; HR, hazard ratio; CI, confidence interval; RRR, relative risk reduction; ▽, risk difference; Dapa, dapagliflozin; Pbo, placebo; SD, study design; Ref, references; PI, prescribing information

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Study Design¹

Objective:

Dapagliflozin and Prevention of Adverse Outcomes in Chronic Kidney Disease (DAPA-CKD) trial to assess the longterm efficacy and safety of the SGLT2 inhibitor dapagliflozin in patients with chronic kidney disease, with or without type 2 diabetes.

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Primary end point:

Composite of declining kidney function, end-stage kidney disease & renal or cardiovascular death.



Reference

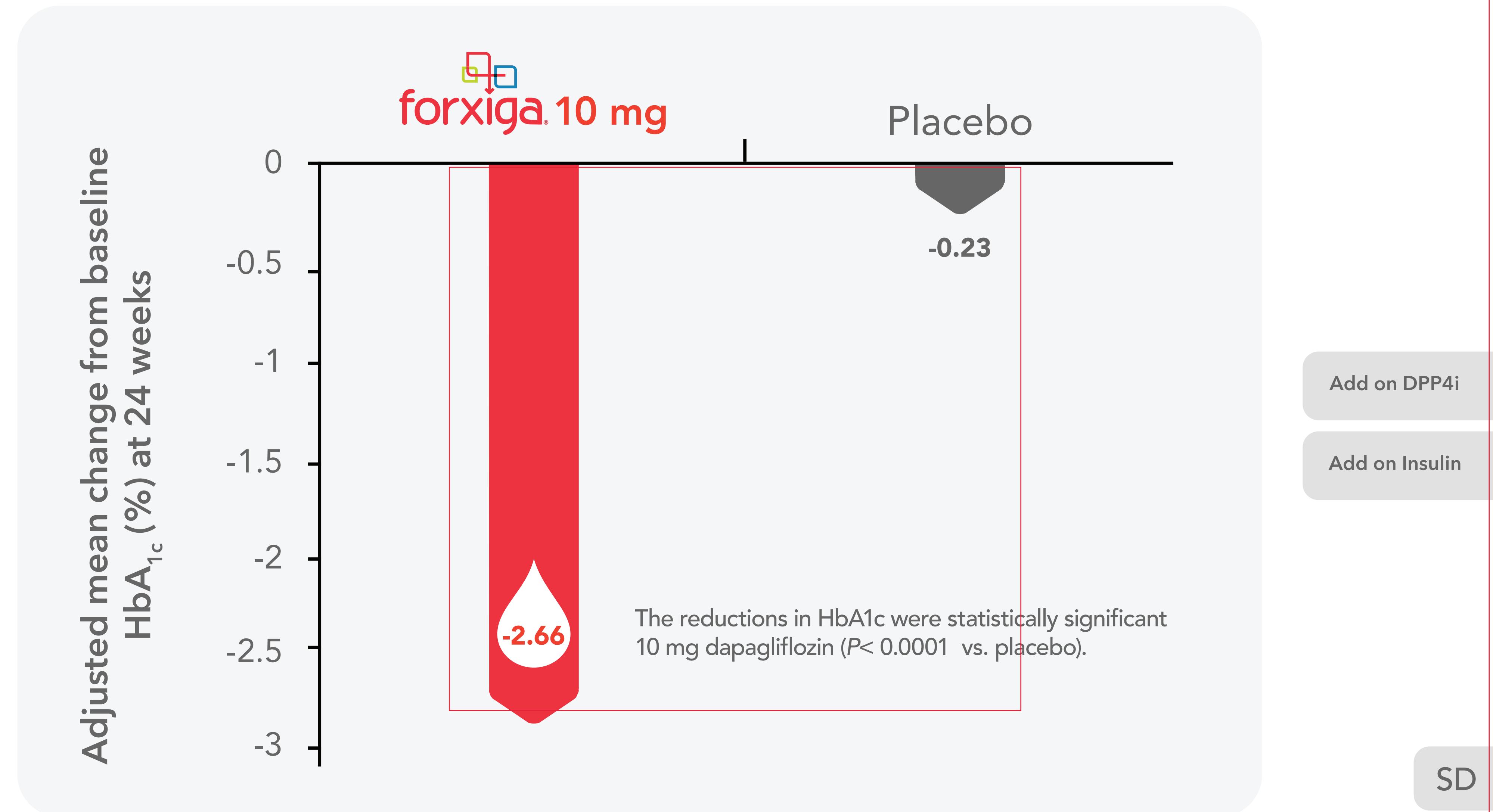
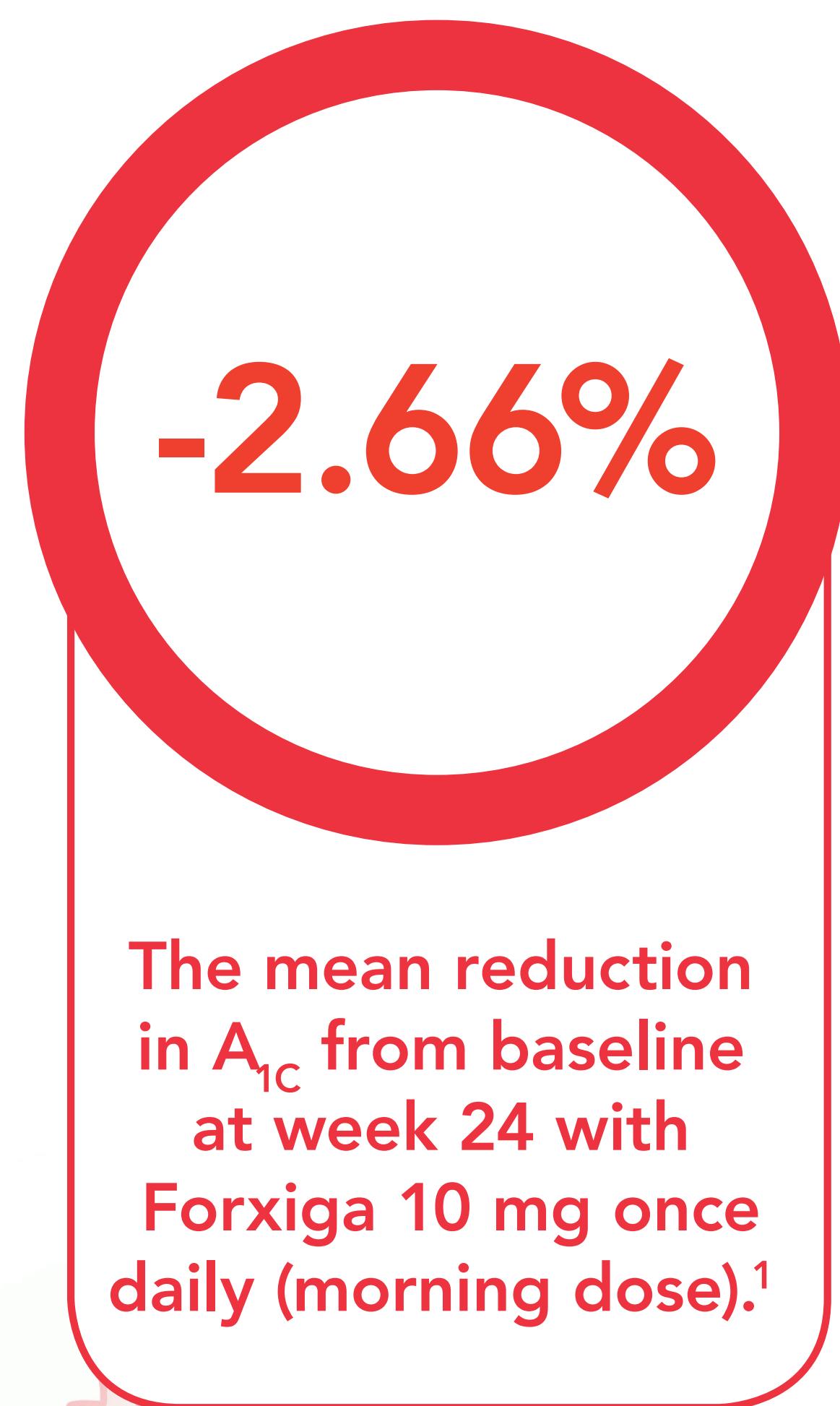
1. Heerspink H, Stefansson BV, Correa-Rotter R, Chertow GM, Greene T et. al. Dapagliflozin in Patients with Chronic Kidney Disease. N Engl J Med 2020; 383:1436-46



Ref

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FORXIGA provides a considerable statistically significant reduction in HbA1C levels in treatment-naïve patients vs. placebo¹



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CKD
BurdenCKD
CausesCKD
Assessment

Keep Pace

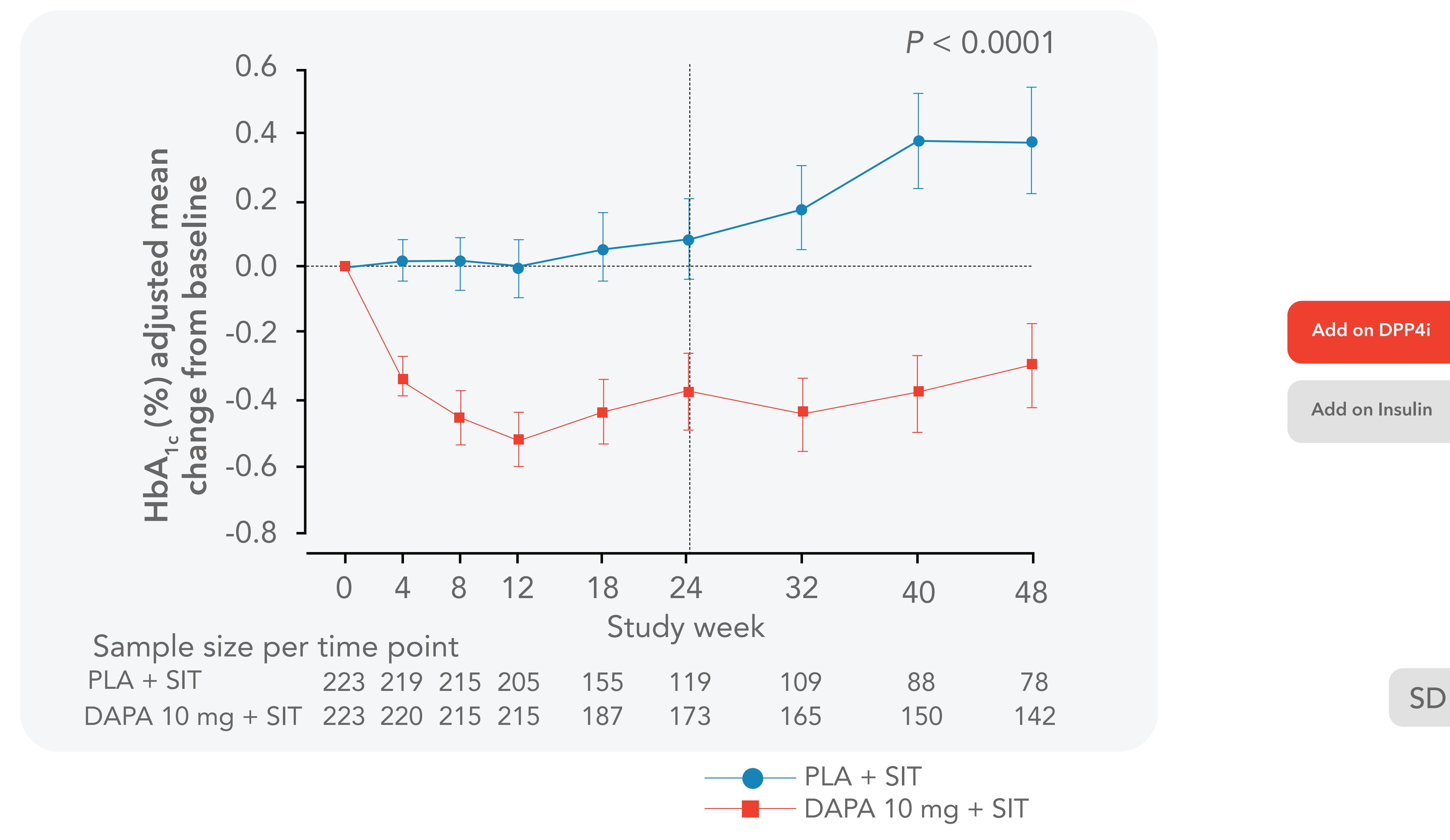
Guidelines

All Cause
Mortality

Control Today

Dose

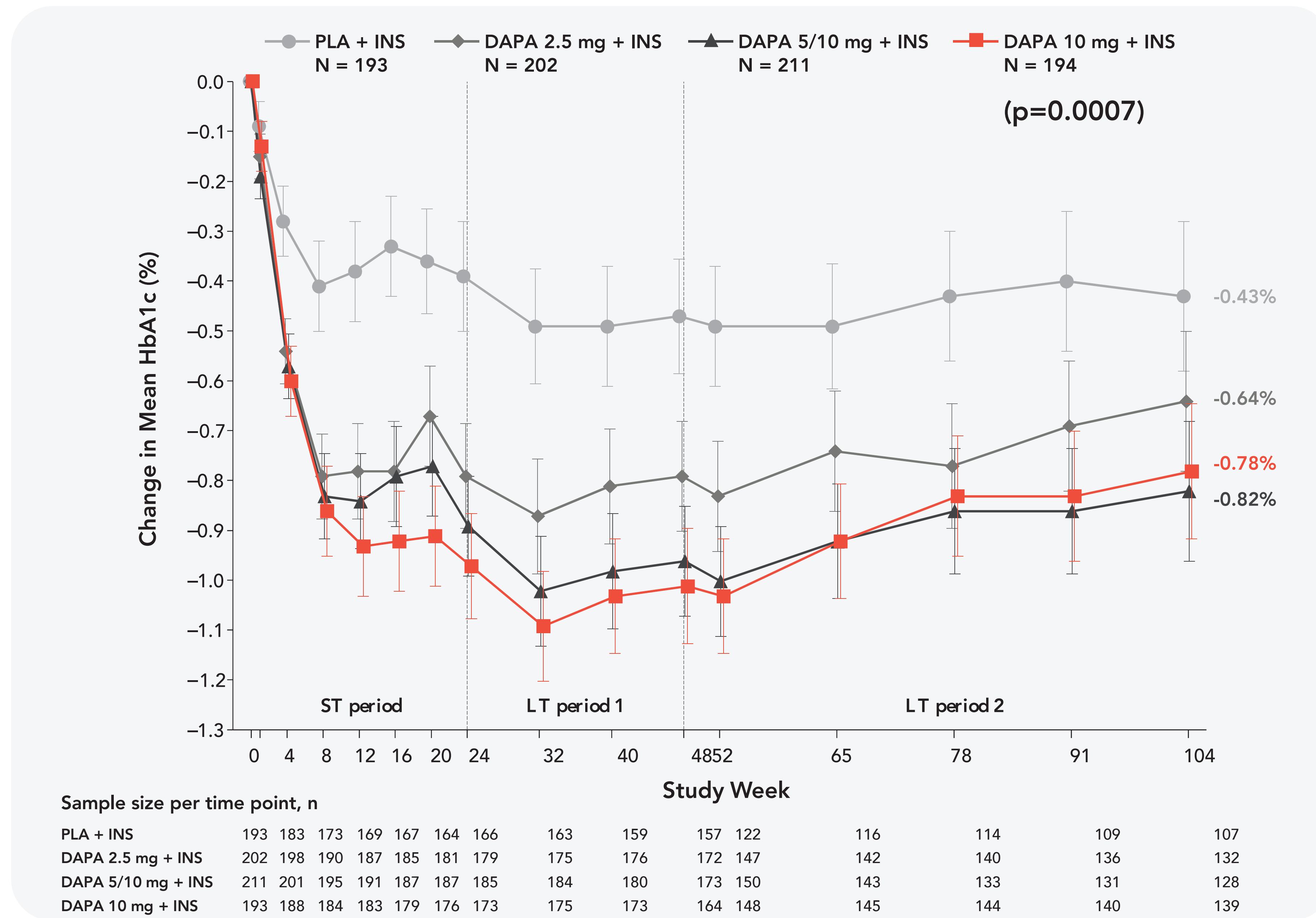
FORXIGA significantly reduced HbA1C from baseline when added to DPP4i compared to placebo in T2D patients ($p<0.0001$) at week 24 and the improvements were maintained through 48 weeks²





FORXIGA significantly reduced HbA1C from baseline when added to insulin compared to placebo in T2D patients that was covered over 104 weeks³

Long-term reductions in HbA1c over 104 weeks were evident in all dapagliflozin groups.*³

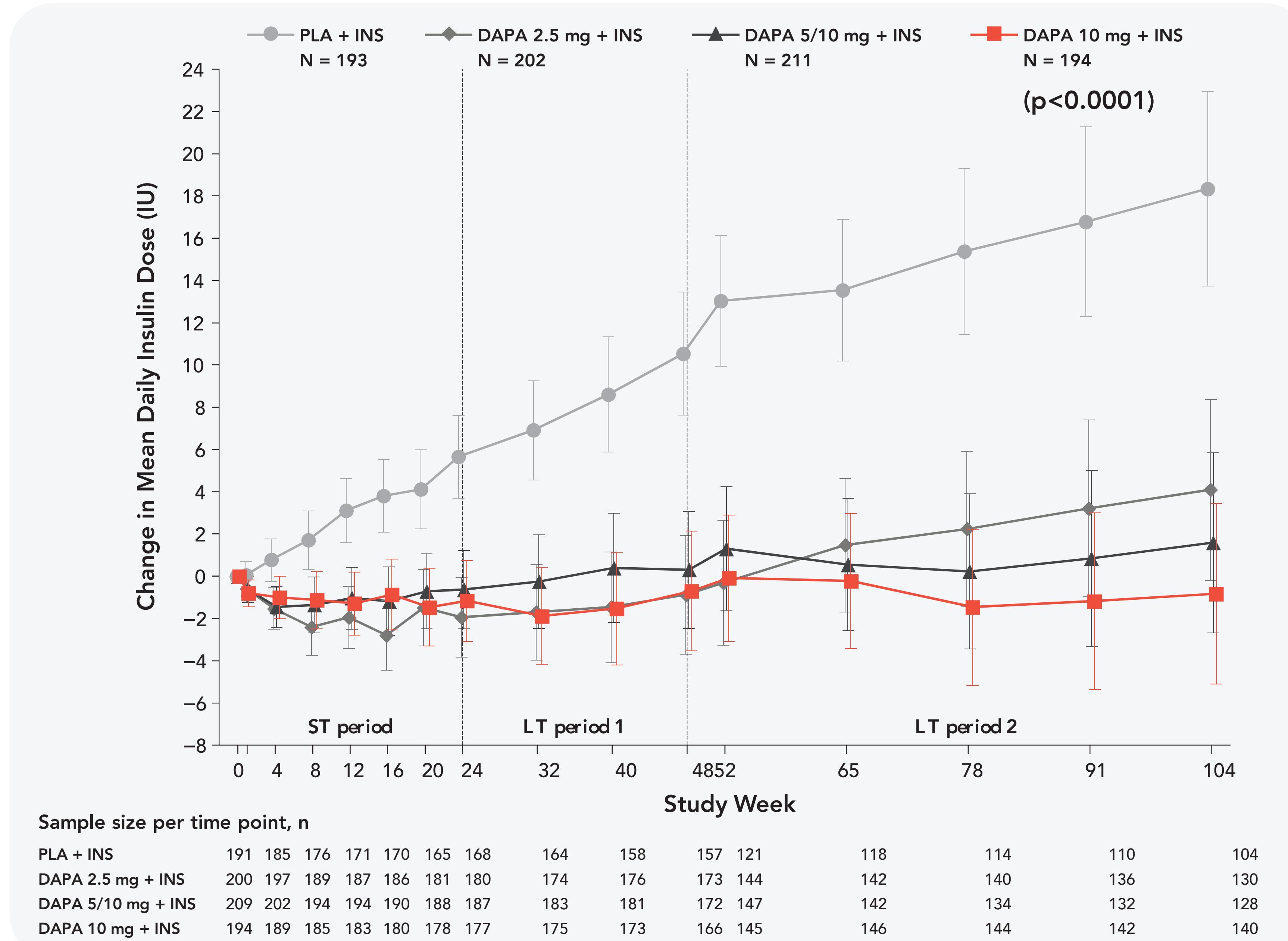


DAPA, dapagliflozin; HbA1c, glycated hemoglobin; INS, insulin; LT, long-term; PBO, placebo; ST, short-term,
OADs: oral antidiabetic drug,

FORXIGA resulted in a significant reduction in insulin dose reached up to 19.2 IU. at 104 weeks compared with placebo in T2D patients³



Change in Insulin Dose over Time *³



*Data are adjusted mean change from baseline \pm 95% CI derived from a mixed model and include data after insulin up-titration
DAPA, dapagliflozin; INS, insulin; PBO, placebo; ST, short-term; LT, long-term

Add on DPP4i

Add on Insulin

Insulin Units

Weight

SD

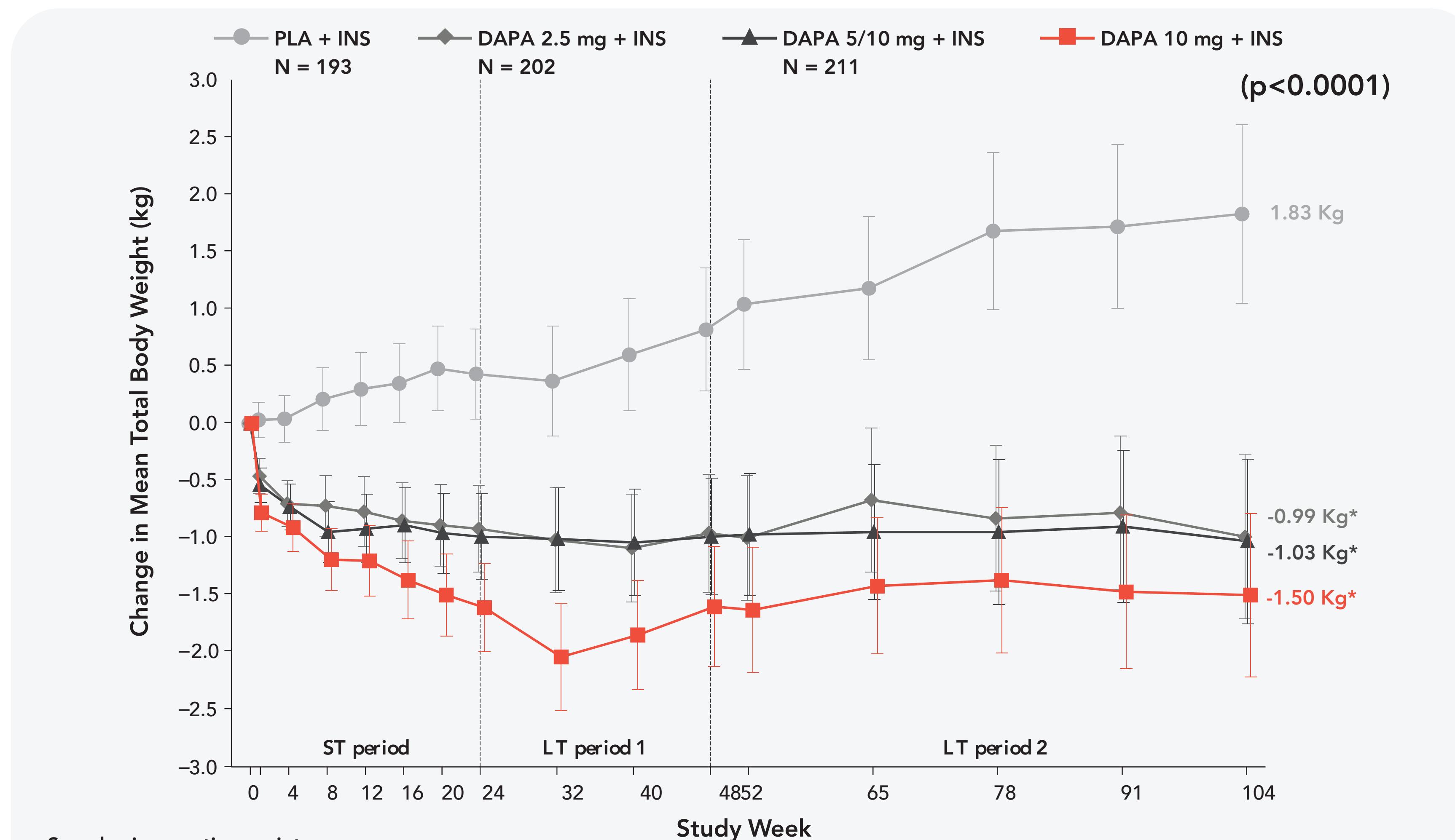
The differences from placebo in adjusted mean change in daily insulin dose from baseline at 104 weeks were:

- Dapagliflozin 10-mg groups -19.2 U (95% CI -25.5 , -12.9 ; $p<0.0001$)⁶

FORXIGA resulted in a significant reduction in body weight reached up to 3.33 KG at 104 weeks compared with placebo in T2D patients³



Change in Mean Total Body Weight Over Time*



*Adjusted mean change from baseline at week 104, based on the number of patients in the full analysis set with non-missing baseline and week (t) values. Analyses used the full analysis set and included data after insulin up-titration.

DAPA, dapagliflozin; INS, insulin; LT, long-term; PBO, placebo; ST, short-term

- Add on DPP4i
- Add on Insulin
- Insulin Units
- Weight

SD

The differences from placebo in adjusted mean change in total body weight from baseline at 104 weeks were:

- Dapagliflozin 10-mg groups
-3.33 kg (95% CI -4.38, -2.27;
p<0.0001)⁶



Study Design¹

Objective:

To evaluate the efficacy and safety of dapagliflozin in treatment naive patients with type 2 diabetes.

Methods:

This was a 24-week randomized, parallel- group, double-blind, placebocontrolled phase 3 trial with a 2-week diet/exercise placebo lead-in (1 week for patients with enrollment A1C 10.1– 12.0%). A total of 485 patients. They were randomly assigned to the main morning dose and exploratory evening dose cohorts. In addition, 74 patients were randomly assigned to the exploratory, high-A1C cohort, of which 73 patients took at least one dose of study medication.

End-points:

The primary efficacy end point was change from baseline in A1C at week 24 in the main patient cohort. Secondary efficacy measures included change from baseline at week 24 in FPG and body weight. Efficacy measures assessed in the exploratory evening dose and high-A1C cohorts included change from baseline at week 24 in A1C, FPG, and body weight. Safety assessments included vital signs, laboratory measurements, and adverse events

A1C: glycated hemoglobin; FPG: fasting plasma glucose



Study Design²

Objective:

The current study assesses the efficacy and safety of dapagliflozin in patients whose HbA1c levels were not adequately controlled with a dipeptidyl peptidase-4 (DPP-4) inhibitor, sitagliptin. Dapagliflozin was evaluated as a dual combination therapy with sitagliptin and as a triple combination therapy with sitagliptin plus metformin.

Methods:

This 24-week, multicenter, randomized, double-blind, placebo-controlled, parallel-group, international phase 3 study (NCT00984867) was conducted in Argentina, Germany, Mexico, Poland, the U.K., and the U.S. 451 patients were randomized to receive dapagliflozin ($n = 225$) or placebo ($n = 226$). Of the patients randomized to dapagliflozin, 208 (92%) completed the 24-week double-blind period, with 202 (90%) going on to complete the additional 24-week extension period.

End-points:

The primary end point was change in HbA1c from baseline at week 24. Key secondary end points were change in total body weight, HbA1c (in patients with baseline HbA1c $\geq 8\%$), FPG, seated SBP in patients, and glycemic response rate. Exploratory end points included proportion of subjects achieving a therapeutic glycemic response, seated SBP, percent change in fasting lipids, and change in b-cell function.

HbA1c: glycated hemoglobin; FPG: fasting plasma glucose; SBP: systolic blood pressure



Study Design³

Objective:

This study aimed to evaluate the durability of dapagliflozin effect in patients with T2DM over a background of insulin treatment after a total of 104 weeks of dapagliflozin treatment.

Methods:

This double-blinded, placebo-controlled, parallel-group trial (Clinical trial No.: NCT00673231) was conducted at 126 centres worldwide from 30 April 2008 to 12 January 2011. A total of 808 patients were initially randomized on a 1 : 1 : 1 : 1 basis to placebo or dapagliflozin 2.5, 5 or 10 mg once daily, in addition to open-label therapy with their usual daily insulin dose and existing OADs. Following completion of 48 weeks of treatment, patients receiving the dapagliflozin 5-mg dose were switched to the 10-mg dose for the remainder of the study.

End-points:

The primary efficacy variable was change in HbA1c from baseline to week 24. Four key secondary efficacy variables at 24 weeks included: (i) change in total body weight from baseline; (ii) change in calculated mean daily insulin dose; (iii) proportion of patients with calculated mean daily insulin dose reduction $\geq 10\%$ from baseline and (iv) change in fasting plasma glucose (FPG) from baseline. At 104 weeks, we assessed whether the effects on HbA1c, FPG, insulin dose, body weight and urinary glucose excretion were maintained. The long-term safety and tolerability of dapagliflozin treatment over 104 weeks was assessed by collecting data on adverse events (AEs), laboratory parameters and vital signs.



Reference

1. Ferrannini E, Ramos SJ, Salsali A, Tang W, List JF. Dapagliflozin monotherapy in type 2 diabetic patients with inadequate glycemic control by diet and exercise: a randomized, double-blind, placebo-controlled, phase 3 trial. *Diabetes Care* 2010; **33** (10): 2217-24.
2. Jabbour SA, Hardy E, Sugg J, Parikh S; Study 10 Group. Dapagliflozin is effective as add-on therapy to sitagliptin with or without metformin: a 24-week, multicenter, randomized, double-blind, placebo-controlled study. *Diabetes Care*. 2014; **37**(3):740-50.
3. Wilding JP, Woo V, Rohwedder K, Sugg J, Parikh S; Dapagliflozin 006 Study Group. Dapagliflozin in patients with type 2 diabetes receiving high doses of insulin: efficacy and safety over 2 years. *Diabetes Obes Metab*. 2014 Feb; **16**(2):124-36.



Ref

PI

In patients with CKD, with or without T2D



FORXIGA dosing and administration¹



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film coated tablet

Reference

1. Forxiga Egyptian Drug Authority Approved Leaflet. Approval date 16/4/2023

Abbreviated prescribing information



COMPOSITION:

Forxiga 5 mg film-coated tablets:

Each tablet contains dapagliflozin propanediol monohydrate equivalent to 5 mg dapagliflozin.

Forxiga 10 mg film-coated tablets:

Each tablet contains dapagliflozin propanediol monohydrate equivalent to 10 mg dapagliflozin.

INDICATIONS:

Type 2 Diabetes Mellitus:

Forxiga is indicated in adults for the treatment of insufficiently controlled type 2 diabetes mellitus as an adjunct to diet and exercise.

- As monotherapy when metformin is considered inappropriate due to intolerance.

- In addition to other medicinal products for the treatment of Type 2 Diabetes.

Heart Failure:

Forxiga is indicated in adults for the treatment of symptomatic chronic heart failure.

Chronic Kidney Disease:

Forxiga is indicated in adults for the treatment of chronic kidney disease.

SPECIAL POPULATIONS:

Renal impairment: it is not recommended to initiate treatment with Forxiga in patients with eGFR<15mL/min/1.7m².

No dose adjustment is required based on renal function.

Hepatic impairment: No dose adjustment is necessary for patients with mild or moderate hepatic impairment. In patients with severe hepatic impairment, a starting dose of 5 mg is recommended. If well tolerated the dose may be increased to 10 mg.

Elderly (> 65 years): No dose adjustment is recommended based on age.

Pediatric Population: The safety and efficacy of dapagliflozin in children < 18 years have not yet been established. No data are available.

CONTRAINDICATIONS:

Hypersensitivity to the active substance or to any of the excipients (Tablet Core "Microcrystalline cellulose, Lactose, Cross Povidone, Silicone dioxide, Magnesium stearate" & Film-Coating "Polyvinyl alcohol, Titanium dioxide, Macrogel, Talc, Iron oxide yellow").

Special warnings and precautions for use:

Renal impairment: There is limited experience, with initiating treatment with Forxiga in patients with eGFR<25mL/min/1.7m². The glucose lowering efficacy of dapagliflozin is dependent on renal function and is reduced in patients with eGFR<45mL/min/1.7m² and is likely absent in patients with severe renal impairment. In patients with moderate renal impairment eGFR<60mL/min/1.7m², a higher proportion of patients treated with dapagliflozin had adverse reactions of increase in parathyroid hormone (PTH) and hypotension, compared with placebo.

Hepatic impairment: There is limited experience in clinical studies in patients with hepatic impairment.

Dapagliflozin exposure is increased in patients with severe hepatic impairment.

Abbreviated prescribing information



Use in patients at risk of volume depletion and/or hypotension:

Caution should be exercised in patients for whom a dapagliflozin- induced drop in blood pressure could pose a risk, such as patients on antihypertensive therapy with a history of hypotension or elderly patients.

Diabetic ketoacidosis:

Sodium glucose co-transporter 2 (SGLT2) Inhibitors should be used with caution in patients with increased risk of DKA.

In patients where DKA is suspected or diagnosed, dapagliflozin treatment should be discontinued immediately. Type 1 diabetes mellitus: In type 1 diabetes mellitus studies with dapagliflozin, DKA was reported with common frequency. Dapagliflozin should not be used for treatment of patients with type 1 diabetes mellitus.

Necrotizing fasciitis of the perineum (Fournier's gangrene): If Fournier's gangrene is suspected, Forxiga should be discontinued and prompt treatment (including antibiotics and surgical debridement) should be instituted.

Urinary tract infections: Urinary glucose excretion may be associated with an increased risk of urinary tract infection; therefore, temporary interruption of dapagliflozin should be considered when treating pyelonephritis or urosepsis.

Elderly (≥65 years): Elderly patients may be at a greater risk for volume depletion and are more likely to be treated with diuretics. Elderly patients are more likely to have impaired renal function, and/or to be treated with anti-hypertensive medicinal products that may cause changes in renal function such as angiotensin-converting enzyme inhibitors (ACE-I) and angiotensin II type I receptor blockers (ARB). The same recommendations of renal function apply to elderly patients as to all patients.
Cardiac failure: Experience with dapagliflozin in NYHA class IV is limited.

Chronic kidney disease: There is no experience with dapagliflozin for the treatment of chronic kidney disease in patients without diabetes who do not have albuminuria.

Lower limb amputations: An increase of cases of lower limb amputation (primarily of the toe) has been observed in long term, clinical studies in type 2 diabetes mellitus with SGLT2 inhibitors. It is unknown whether this constitutes a class effect. It is important to counsel patients with diabetes on routine preventative foot care.

Urine laboratory assessment: Due to its mechanism of action, patients taking Forxiga will test positive for glucose in their urine.

Lactose: The tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucosegalactose malabsorption should not take this medicinal product.

Abbreviated prescribing information



THE MOST COMMON SIDE EFFECTS:

- **Very common ($\geq 1/10$):** Hypoglycaemia -when used with sulphonyl urea or insulin.
- **Common ($\geq 1/100$ to $< 1/10$):** Vulvovaginitis, balanitis, related genital infections and urinary tract infection, Dizziness, Rash, Back pain, Dysuria, Polyuria, Increased Haematocrit, Decreased creatinine renal clearance during initial treatment, Dyslipidaemia.

PREGNANCY AND BREAST-FEEDING:

When pregnancy is detected, treatment with Dapagliflozin should be discontinued. Dapagliflozin shouldn't be used while breast-feeding.

Fertility:

The effect of dapagliflozin on fertility in humans has not been studied. In male and female rats, dapagliflozin showed no effects on fertility at any dose tested.

DRIVING AND USING MACHINES:

Forxiga has no or negligible influence on the ability to drive and use machines. Patients should be alerted to the risk of hypoglycaemia when dapagliOozin is used in combination with a sulphonylurea or insulin.

- Always read the full prescribing information.
- Healthcare professionals are asked to report any suspected adverse reactions to the Egyptian pharmacovigilance center (EPVC)
e-mail: pv.followup@edaegypt.gov.eg
hotline: 15301
website: www.edaegypt.gov.eg
- Egyptian Drug Authority Forxiga leaflet approval date: 16/4/2023



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