CONFIDENCE

Combination effect of finerenone and empagliflozin in participants with CKD and T2D using a UACR endpoint study (CONFIDENCE)

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CKD, chronic kidney disease; EMA, European medicines agency; FDA, US food and drug administration, T2D, type 2 diabetes.

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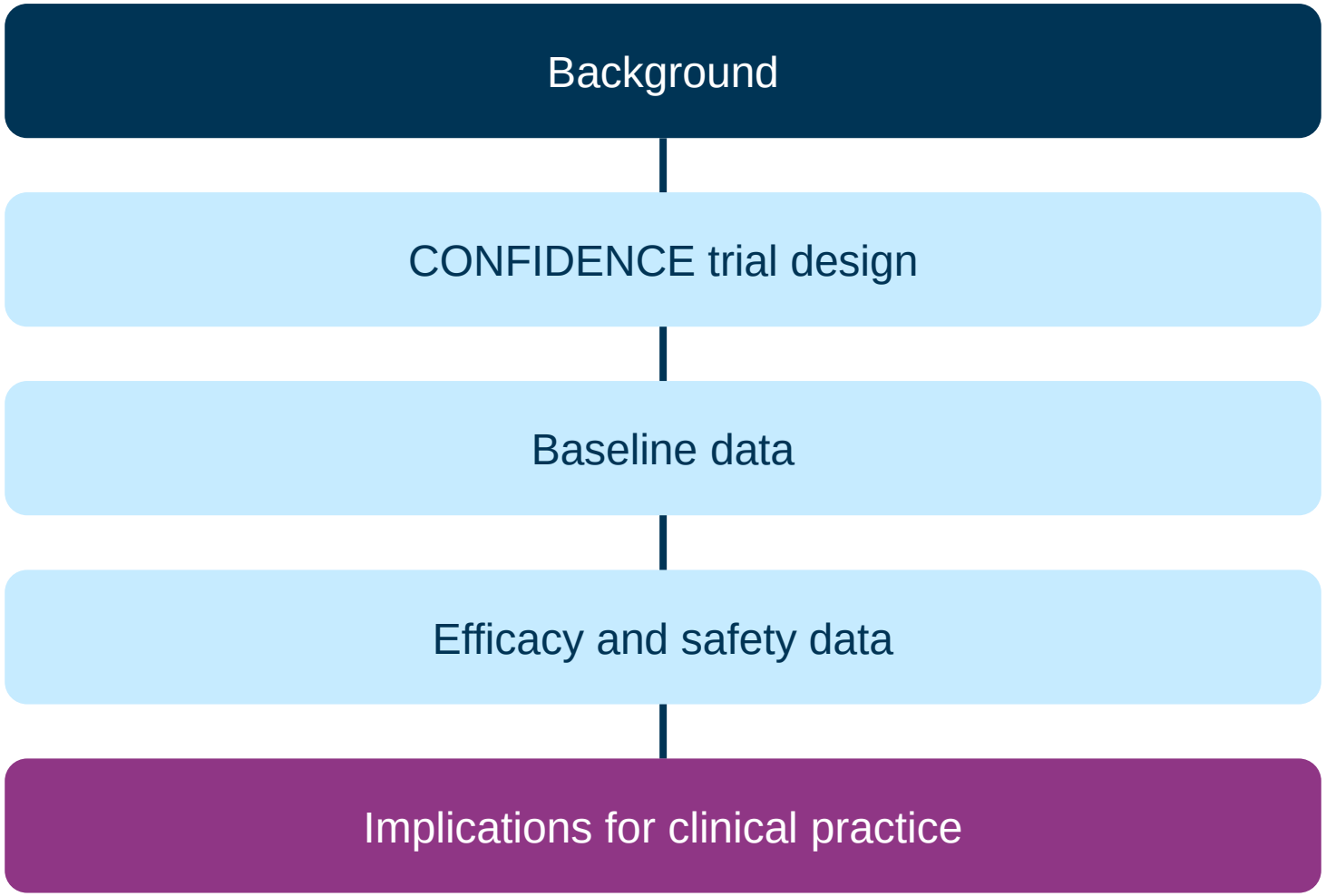
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Background to the CONFIDENCE trial

The complementary MoAs of finerenone and SGLT-2is may translate to additive clinical benefits

Finerenone: Inhibits MR overactivation, which may contribute to CKD progression (driven by metabolic factors, hemodynamic factors, inflammation and fibrosis)

SGLT-2i: Kidney hemodynamic effect that induces glucosuria and natriuresis, resulting in a reduction in intraglomerular hypertension

Complementary MoA → potential additive clinical benefits in CKD + T2D and CVD

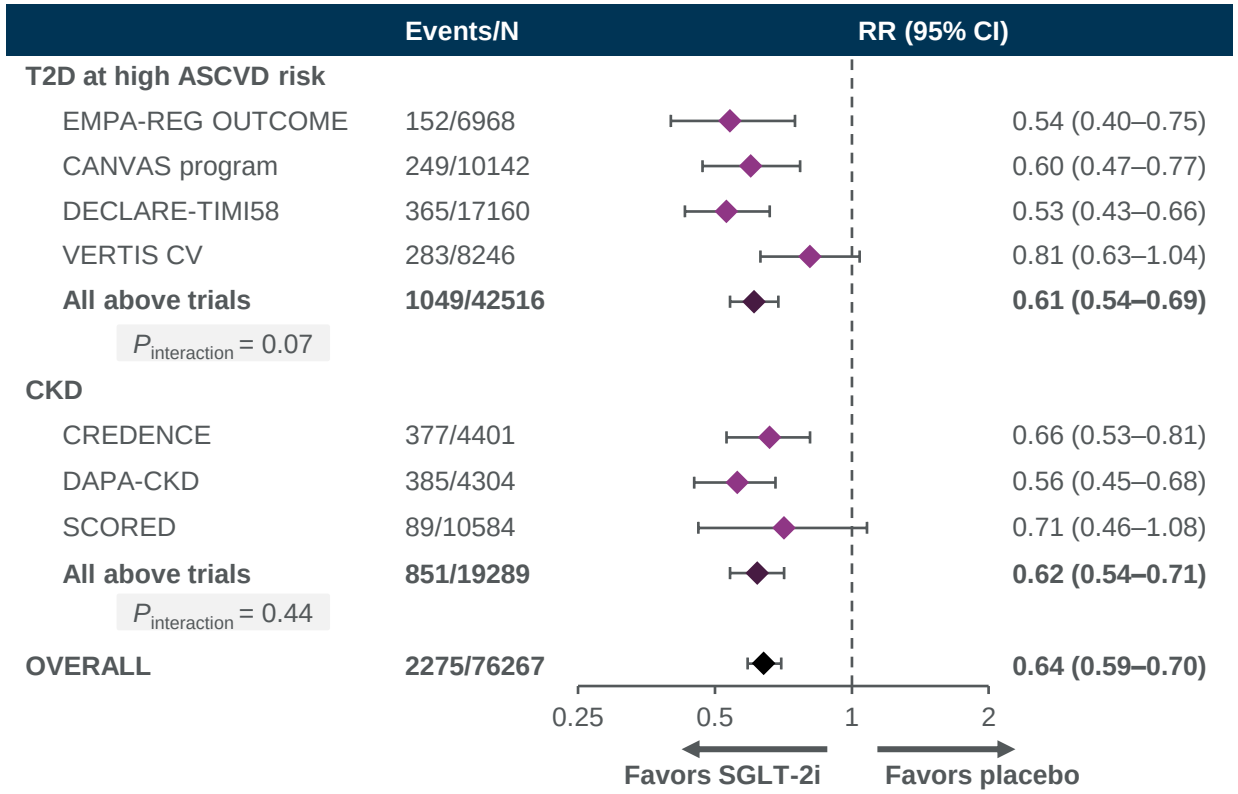
CKD, chronic kidney disease; CVD, cardiovascular disease; MoA, mechanism of action; MR, mineralocorticoid receptor; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes.

Green JB, et al. *Nephrol Dial Transplant.* 2023;38(4):894–903.

The beneficial effects of SGLT-2is on kidney outcomes are widely considered to be a class effect

A comprehensive meta-analysis across different patient groups, including three trials in CKD, showed **no heterogeneity between different SGLT-2is** on a range of efficacy and safety outcomes[1]

Kidney disease progression by patient group and trial[1]



The UK Kidney Association (UKKA) suggest that the beneficial effects of SGLT-2is on kidney disease progression or risk of heart failure hospitalization are **likely to be a class effect**[2]

They also note increasing evidence for **similarities in cardiac and kidney benefits with different SGLT-2is**[2]

SGLT-2is also have similar:[3,4]

- Chemical structures
- Mechanisms of action
- Pharmacokinetics
- Safety profiles

ASCVD, Atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CI, confidence interval; CV, cardiovascular; RR, relative risk; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes.

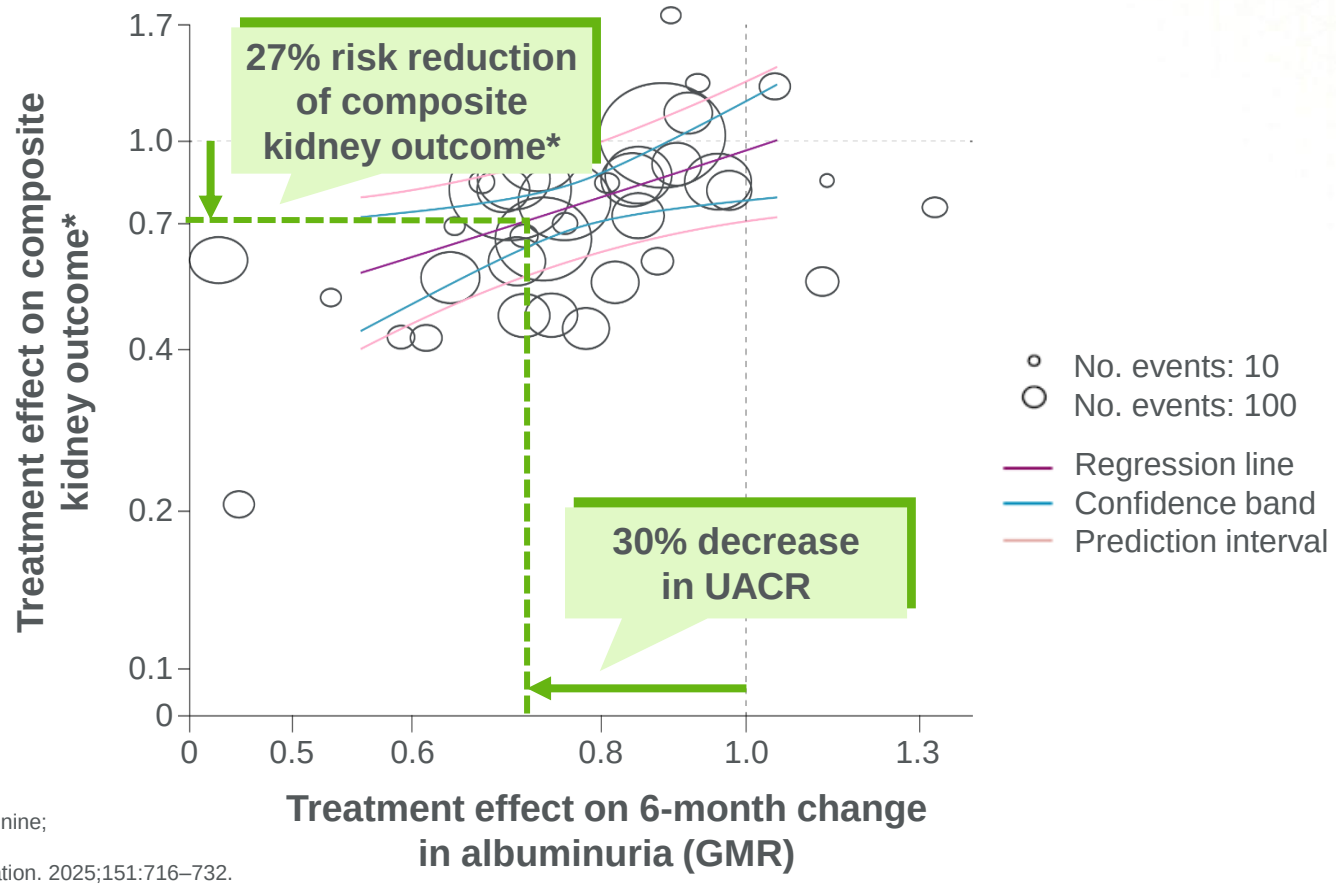
1. Staplin N, et al. *EClinicalMedicine.* 2021;41:101163; 2. Roddick AJ, et al. *BMC Nephrol.* 2023;24:310; 3. Giugliano D, Esposito K. *Cardiovasc Diabetol.* 2019;18:94; 4. Scheen AJ. *Clin Pharmacokinet.* 2015;54:691–708.

UACR is an important surrogate marker of kidney disease progression and a predictor of adverse CV outcomes

A **30% fall in geometric mean UACR** over 6 months has been associated with a **27% reduction in risk of the composite kidney outcome*** in patients with baseline UACR ≥30 mg/g *[≥3.4mg/mmol]*[1]

Albuminuria is also **associated with CV death** among patients with T2D, hypertension, CKD, and HF, demonstrating the value of using UACR as a biomarker to identify and monitor disease[2]

Meta-analysis: Association between treatment effects on change in UACR and treatment effects on composite kidney outcome* in patients with baseline UACR ≥30 mg/g *[≥3.4mg/mmol]* (N=22,544)[1]

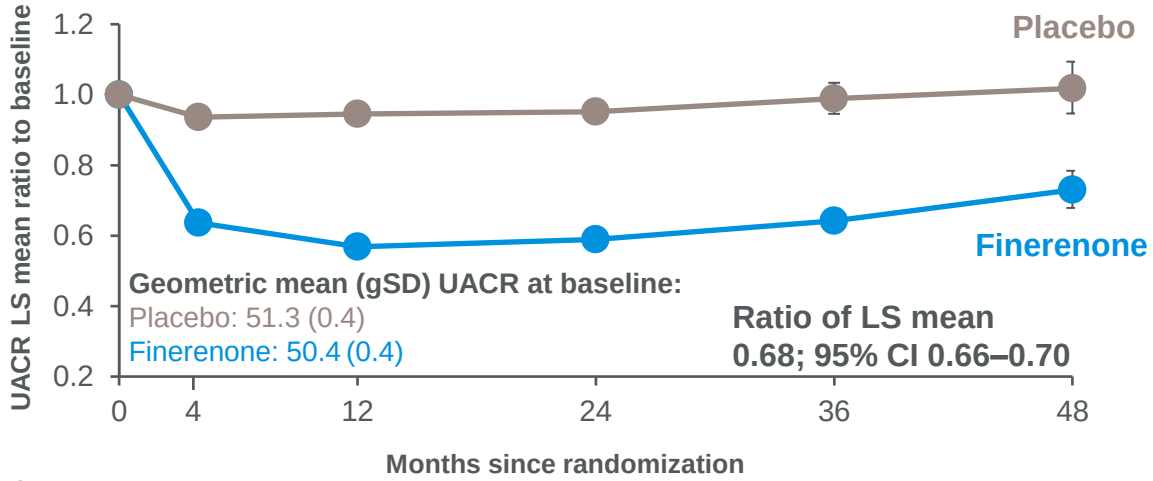


*Time to treatment of ESKD (initiation of chronic treatment with dialysis or kidney transplantation), eGFR <15 mL/min/1.73 m^2, or doubling of SCr sustained at the next visit.
CKD, chronic kidney disease; CV, cardiovascular; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HF, heart failure; GMR, geometric mean ratio; SCr, serum creatinine; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Heerspink HJL, et al. *Lancet Diabetes Endocrinol.* 2019;7:128–139; 2. Claudel SE, et al. Circulation. 2025;151:716–732.

In FIDELITY and EMPA-KIDNEY, both finerenone and empagliflozin led to decreases in UACR versus placebo[1–3]

A lower mean UACR with finerenone versus placebo was maintained throughout the study[1]



No. of patients						
Finerenone	6517	6273	5988	4867	2745	899
Placebo	6504	6239	5973	4829	2706	872

A lower geometric mean UACR was observed with empagliflozin versus placebo[3]

Empagliflozin		Placebo
22.8±0.5 mg/mmol (202±4 mg/g)	versus	28.3 ± 0.6 mg/mmol (250 ± 5 mg/g)

Overall decrease: **-19%** (95% CI: -23 to -15)

In FIDELITY, **finerenone reduced UACR by 32% between baseline and month 4 versus placebo[1]**

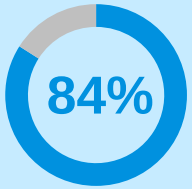
In EMPA-KIDNEY, **empagliflozin reduced UACR by 19% between baseline and year 2 versus placebo*[3]**

*Based on a linear mixed model repeated measures (MMRM) approach.
BL, baseline; CI, confidence interval; CV, cardiovascular; gSD, geometric standard deviation; LS, least-squares; UACR, urine albumin-to-creatinine ratio.
1. Agarwal R, *et al. Eur Heart J* 2022;43:474–484 (including supplementary material); 2. Agarwal R, *et al. Ann Intern Med* 2023;176:1606–1616; 3. The EMPA-KIDNEY Collaborative Group, et al. *N Engl J Med* 2023;388(2):117–127 (including supplement).

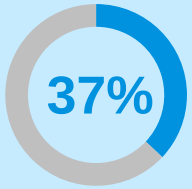
In clinical trials of finerenone and SGLT-2is, UACR reduction was strongly associated with improved kidney and CV outcomes

Finerenone

In FIDELITY (CKD and T2D), **UACR** mediated:[1*]



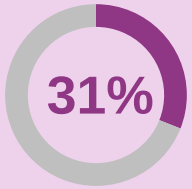
of finerenone's treatment effect on the **composite kidney outcome**



of finerenone's treatment effect on the **composite CV outcome**

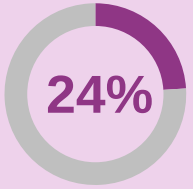
SGLT-2is

In patients with T2D and CVD, **UACR** mediated:[2†]



of empagliflozin's treatment effect on the **composite kidney outcome**

In patients with T2D and increased CVD risk, **UACR** mediated:[3‡]



of canagliflozin's treatment effect on the **composite kidney outcome**

Please see slide notes for the kidney and CV composite endpoint definitions.

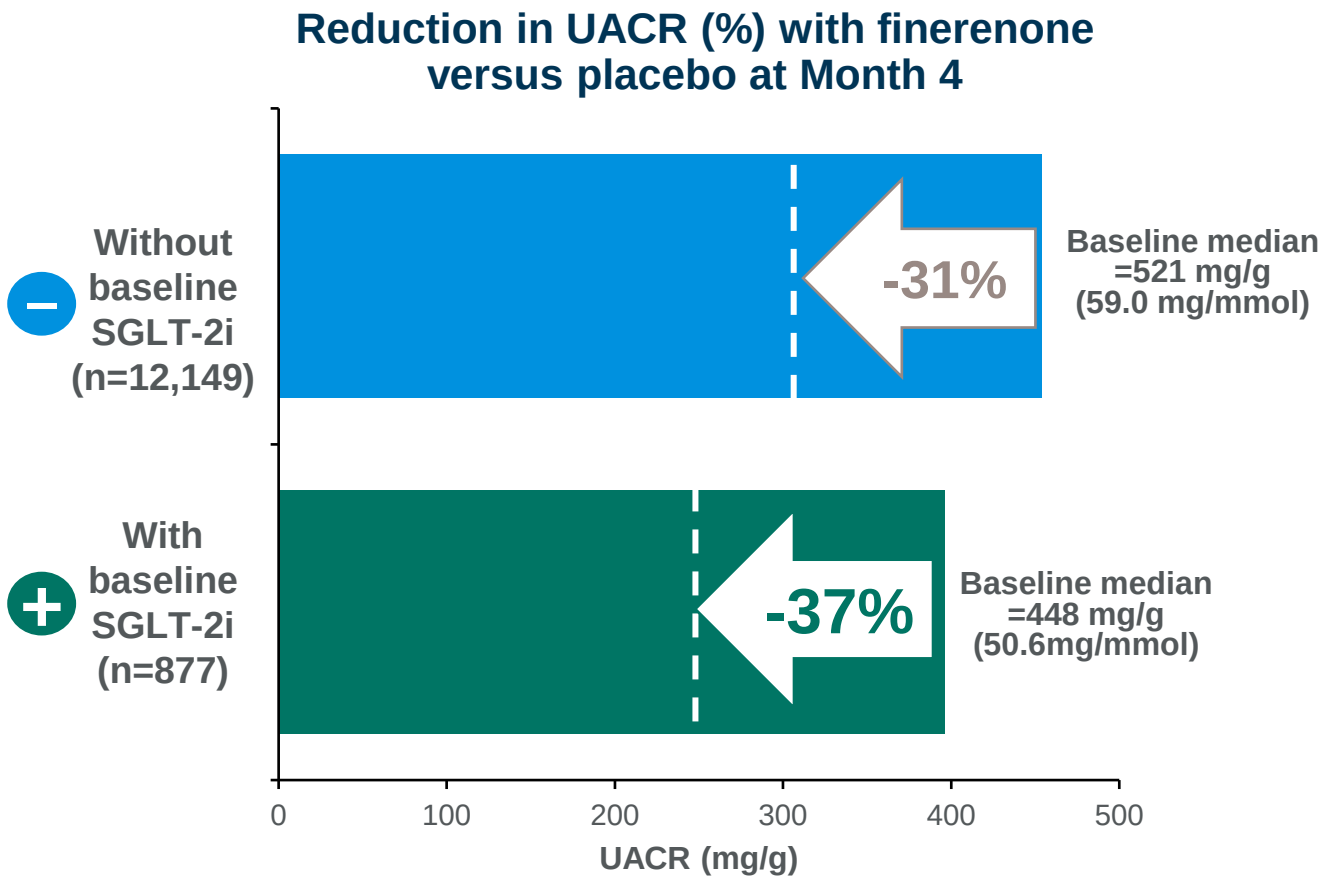
*The FIDELITY study included 12,512 patients; †The EMPA-REG OUTCOME trial analysis included 6968 participants; ‡The CANVAS Program UACR analysis included 9660 participants.

CKD, chronic kidney disease; CV, cardiovascular; CVD, cardiovascular disease; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

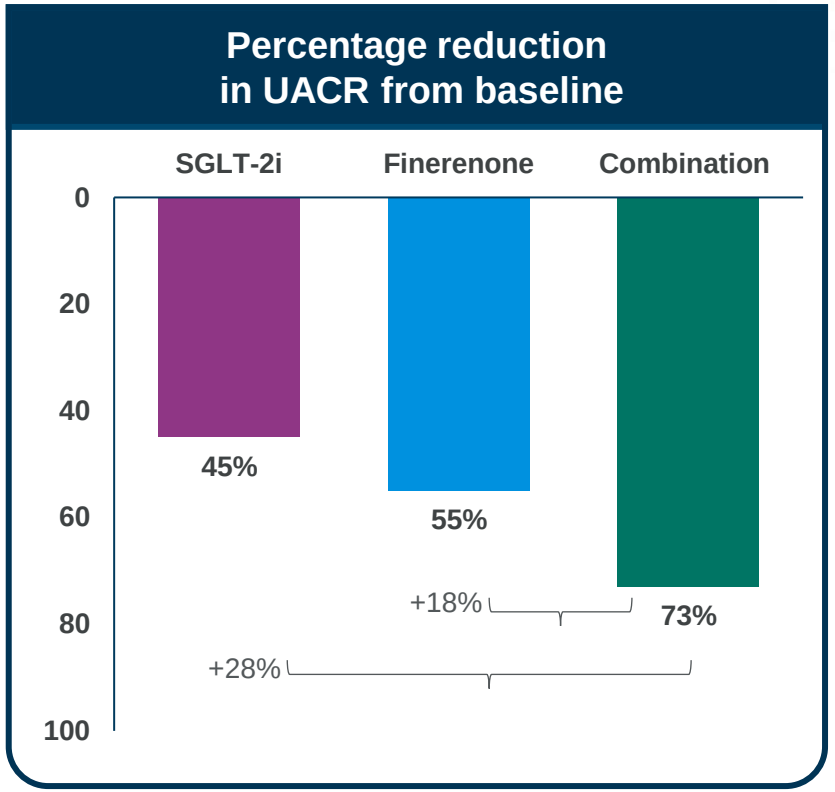
1. Agarwal R, et al. *Ann Intern Med.* 2023;176:1606−1616; 2. Wanner C, et al. *Nephrol Dial Transplant.* 2024;39:1504−1513; 3. JingWei L, et al. *Kidney Int.* 2020;98:769−777.

Combined use of finerenone and SGLT-2i therapy can lead to substantial UACR reductions in patients with CKD

FIDELITY subgroup analysis (CKD and T2D)[1]



RWE from a retrospective analysis of patients from a US specialty CKD clinic confirm the results from FIDELITY[2]



CKD, chronic kidney disease; RWE, real-world evidence; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Rossing P, et al. *Diabetes Care.* 2022;45:2991–2998; 2. Hanouneh M, et al. *Diagnostics (Basel).* 2024;14(13):1357.

Guidelines have recommended the addition of finerenone in patients previously receiving SGLT-2i

ABCD-UKKA 2024 guidelines[1]

Suggestion to **add finerenone** in patients with persistent albuminuria (ACR >30 mg/mmol) **despite the use of maximum tolerated doses of RASI and SGLT-2i**[1]

KDIGO 2024 guidelines[2]

A **non-steroidal MRA** may be **added to a RASi and an SGLT-2i** for treatment of T2D and CKD in adults (prioritizing agents with documented kidney or CV benefits)[2]

Diabetes Canada CKD guidelines[5]

Grade A, Level 1A recommendation for nsMRA for **adults with type 2 diabetic nephropathy** to improve kidney and cardiovascular outcomes[5]

ADA 2025 Standards of Care[3]

Notes that **finerenone and SGLT-2i may be used interchangeably or together** for the goal of **slowing the progression of CKD**[3]

ESC 2023 Guidelines[4]

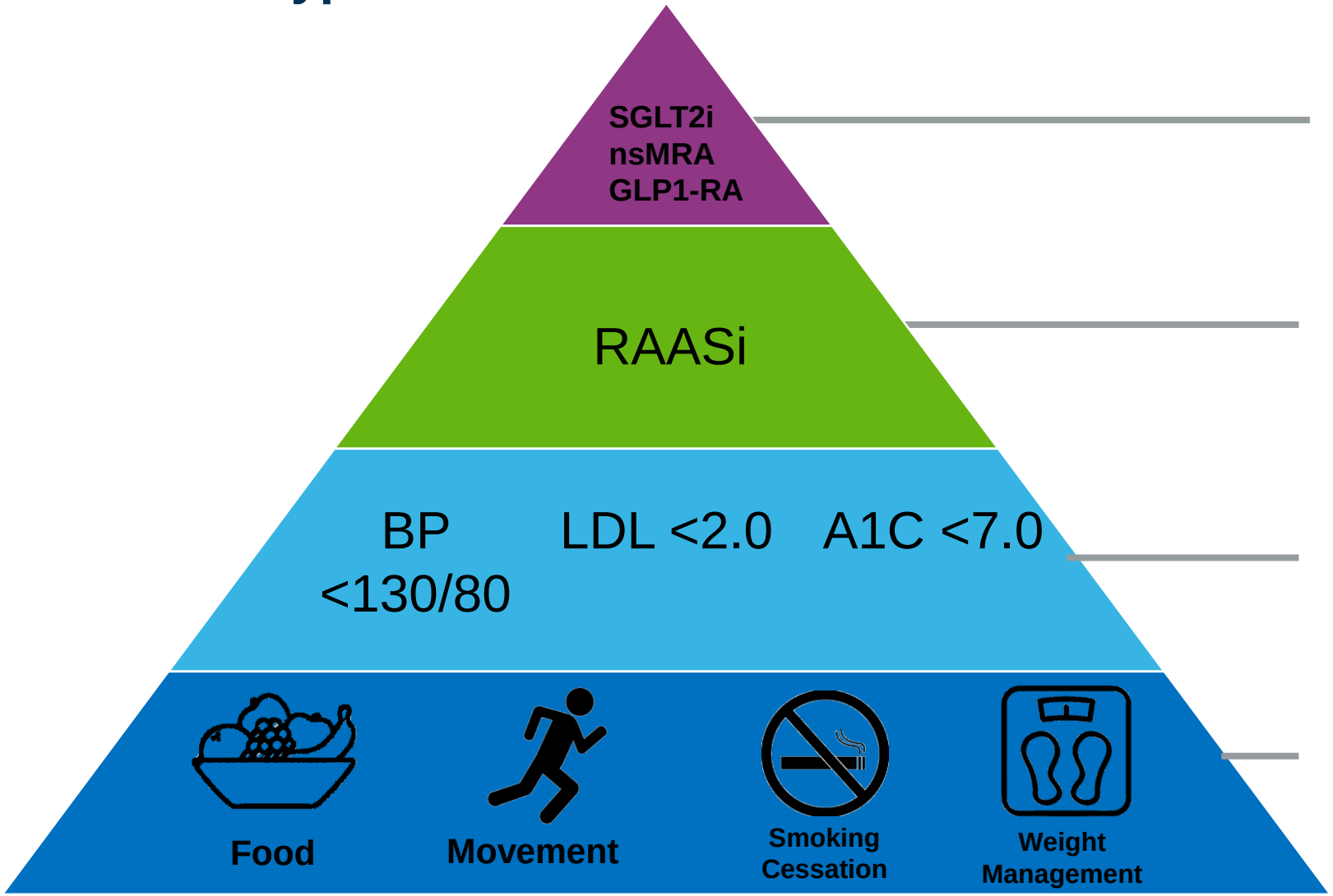
Recommend that **patients with CKD and diabetes should be treated with an SGLT-2i and/or finerenone**, as these agents reduce CV and kidney failure risk in addition to standard of care[4]

More data are needed to **elucidate the role of finerenone and SGLT-2i combination** in patients with T2D and CKD

ABCD, Association of British Clinical Diabetologists; ACR, albumin-creatinine ratio; ADA, American Diabetes Association; CKD, chronic kidney disease; CV, cardiovascular; ESC, European Society of Cardiology; KDIGO, Kidney Disease Improving Global Outcomes; RASI, renin-angiotensin system inhibitor; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UKKA, UK Kidney Association.

1. Dasgupta I, et al. *Diabet Med* 2025;42(2):e15450; 2. KDIGO. 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Available from: https://kdigo.org/wp-content/uploads/2024/03/KDIGO-2024-CKD-Guideline.pdf [accessed May 2025]; 3. ADA. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes – 2025. Available at: https://diabetesjournals.org/care/article/48/Supplement_1/S239/157554/11-Chronic-Kidney-Disease-and-Risk-Management [accessed May 2025]; 4. Marx N, et al. *Eur Heart J* 2023;44(39):4043–4140 [published correction appears in *Eur Heart J.* 2023;44(48):5060]. 5. Tobe S et al., *Canadian Journal of Diabetes* 2025,49(2);73-86

Diabetes Canada CKD Guidelines: Holistic management of patients with CKD and type 2 diabetes



Add More Kidney Heart Protection

Add Kidney Heart Protection

BP Control, Lipid management, Blood Glucose Control

Foundational Health Behaviours Change

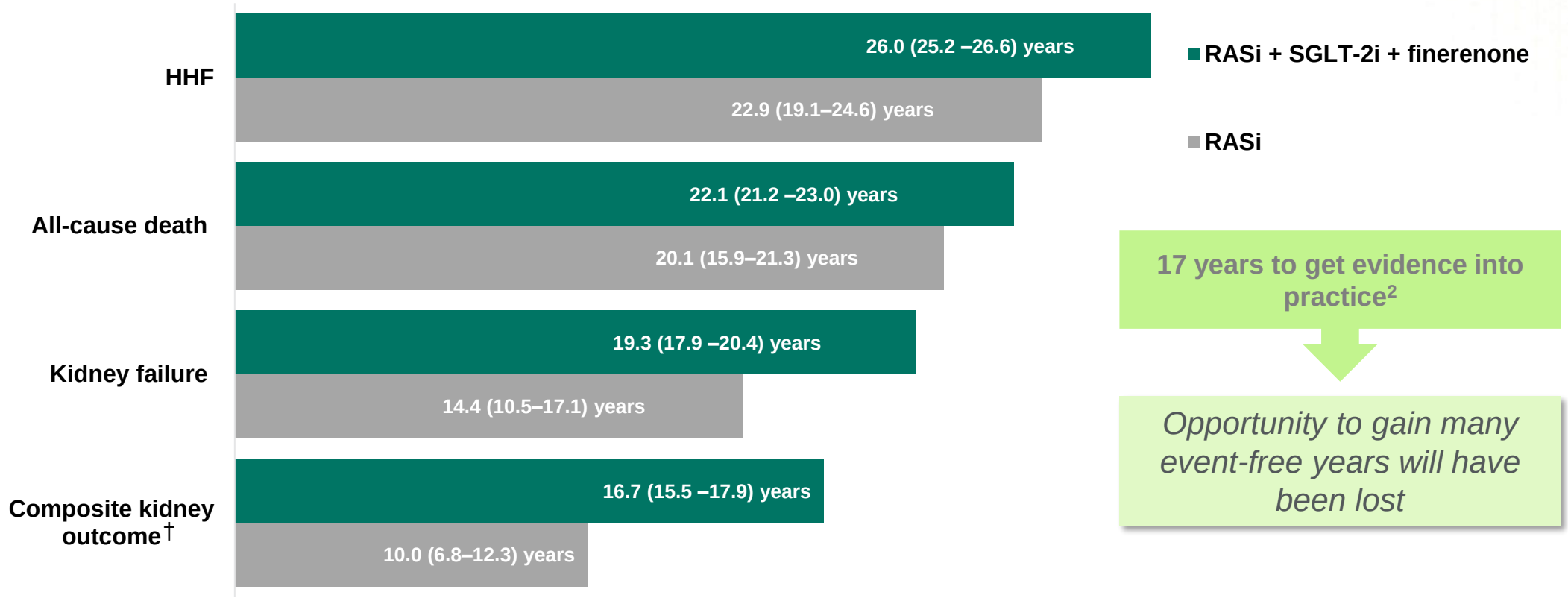
Diabetes with Chronic Kidney Disease

1. Tobe S et al., *Canadian Journal of Diabetes* 2025,49(2);73-86

A1C – glycated hemoglobin, BP – Blood Pressure, LDL - low-density lipoprotein , GLP1-RA – glucagon-like peptide receptor agonist, nsMRA – non-steroidal mineralocorticoid receptor antagonist, SGLT2i – sodium-glucose cotransporter-2 inhibitor

Theoretical effect of combination therapy on risk of progression to kidney failure, HF, and death

Anticipated event-free survival* with optimal kidney therapeutics in people with diabetes and CKD[1,3]



17 years to get evidence into practice[2]

Opportunity to gain many event-free years will have been lost

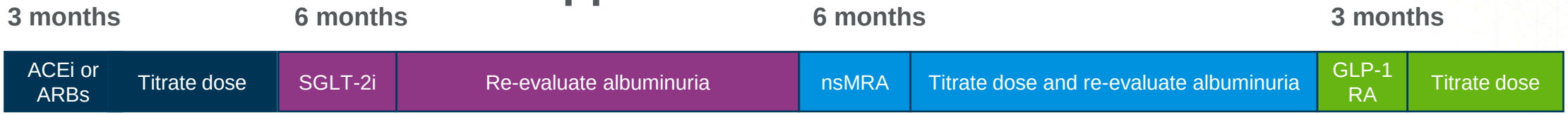
*Estimated event-free survival for various outcomes if indicated therapies were initiated at age 50 years in subjects with diabetes and CKD (eGFR <60 mL/min/1.73 m^2).
†Composite kidney outcome = doubling of serum creatinine, kidney failure, and death from kidney failure.
Data derived from Heerspink H, et al (2023)[3]
CKD, chronic kidney disease; HF, heart failure; HHF, hospitalization for heart failure; RASI, renin-angiotensin system inhibitor; SGLT-2i, sodium-glucose co-transporter-2 inhibitor.

Figure adapted from Luyckx VA, et al. Am J Nephrol 2024;55(3):298–315.

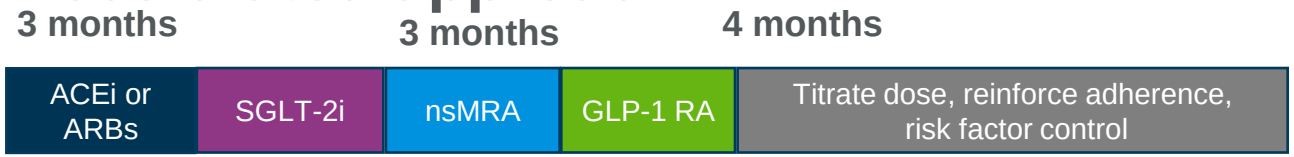
1. Luyckx VA, et al. *Am J Nephrol.* 2024;55(3):298–315; 2. Rubin R. *JAMA.* 2023;329(16):1333–1336; 3. Heerspink H, et al. *Diabetes Obes Metab.* 2023;25(11):3327–3336.

A more rapid approach to initiating combination therapy has been proposed for the management of CKD and T2D[1,2]

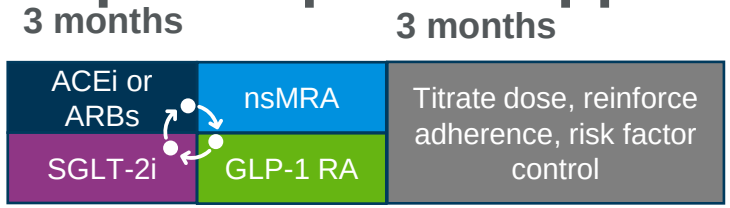
Traditional/conservative approach



Accelerated approach



Rapid sequence approach



Sequence individualized based on dominant clinical priorities

Match intensity of treatment to risk
Prioritize patients at high or very high kidney/cardiovascular risk (especially those with severely increased albuminuria) for accelerated or rapid sequence approach*

In addition, simultaneous initiation of GDMT is a promising approach to reduce the risk of CV events and kidney disease progression in patients with CKD[2]

*Based on KDIGO heat map, Kidney Failure Risk Equation, or other validated risk score.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; CKD, chronic kidney disease; CV, cardiovascular; GDMT, guideline-directed medical therapy; GLP-1 RA, glucagon-like peptide 1 receptor agonist; KDIGO, Kidney Disease Improving Global Outcomes; nsMRA, non-steroidal mineralocorticoid receptor–antagonist; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; T2D, type 2 diabetes.

1. Neuen BL, et al. *Clin J Am Soc Nephrol*. 2024;19:1209–1211; 2. Rashid AM, et al. *J Am Soc Nephrol*. 2025; doi:10.1681/ASN.0000000752.

Background to the CONFIDENCE trial: Key conclusions

The complementary MoAs of finerenone and SGLT-2is may translate to additive clinical benefits, with the effect of SGLT-2is on kidney outcomes widely considered to be a class effect[1,2]

Both finerenone and SGLT-2is are associated with reductions in UACR,[3–5] an important surrogate marker of kidney disease progression and a predictor of adverse CV outcomes[6,7]

Combined use of finerenone and an SGLT-2i can lead to substantial UACR reductions in patients with CKD[8,9] and guidelines recommend finerenone in patients previously receiving SGLT-2i[10–13]

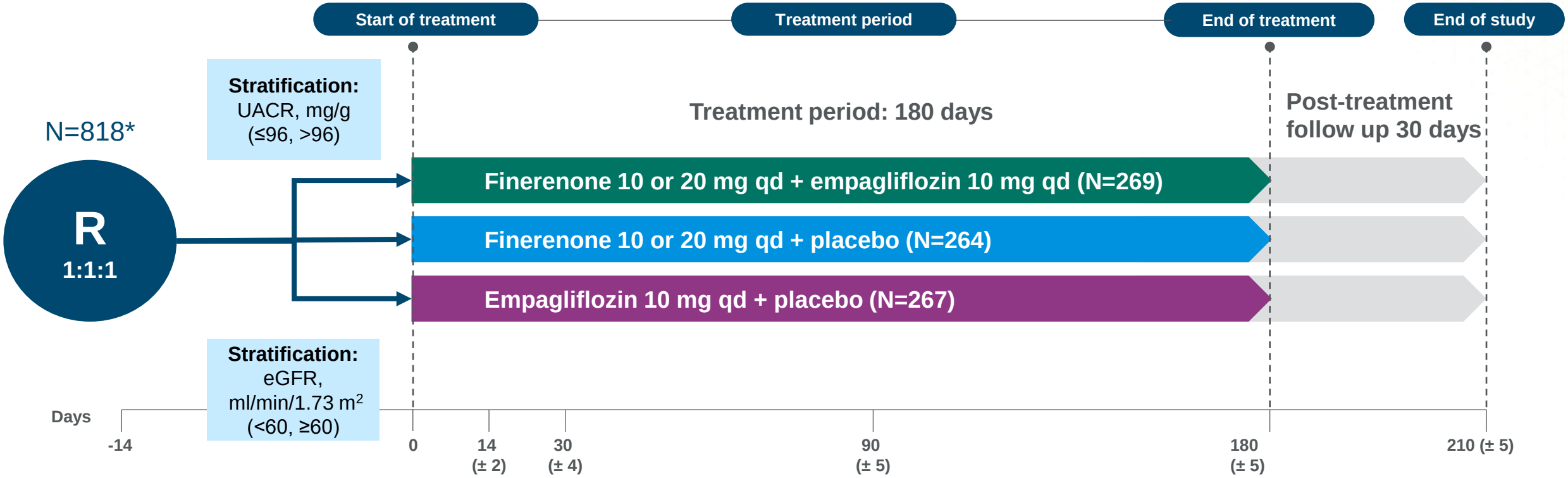
Adverse clinical events could be reduced with combination therapy and an accelerated or rapid approach to initiating combination therapy has been proposed for the management of CKD and T2D[14,15]

CKD, chronic kidney disease; CV, cardiovascular; MoA, mechanism of action; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.
See slide notes for references.

CONFIDENCE trial design

CONFIDENCE was a randomized, double-blind, double-dummy, multicenter, three-armed, parallel-group, phase II study[1–3]

Participants enrolled from 185 sites across multiple countries/regions: Belgium, Canada, Denmark, France, Germany, India, Israel, Italy, Japan, Republic of Korea, the Netherlands, Spain, Taiwan, and the USA



*Four participants underwent randomization twice in error and 14 participants from one site were excluded owing to historic violations of Good Clinical Practice guidelines not related to this study, and their data were not included. Therefore, 800 participants were included in the full analysis set for the efficacy analyses.[3]
eGFR, estimated glomerular filtration rate; qd, once daily; R, randomization; UACR, urine albumin-creatinine ratio.

CONFIDENCE

CONFIDENCE aimed to determine the role of simultaneous finerenone and SGLT-2i initiation in people with CKD and T2D[1–3]

Key inclusion criteria

- Aged ≥18 years
- eGFR 30–90 mL/min/1.73m^{2*}
- UACR ≥11.3 – <565 mg/mmol
- T2D with HbA1c <11%
- Clinically maximum tolerated dose of ACEi/ARB for >1 month

Key exclusion criteria

- T1D
- Day 1 BP >160/100 or SBP <90 mmHg
- Serum K^+ >4.8 mmol/L
- HFrEF with NYHA Class II–IV
- Current treatment with finerenone and an SGLT-2i

Primary endpoint

Relative change in UACR from baseline to Day 180:

- **Combination** versus **empagliflozin**
- **Combination** versus **finerenone**

Secondary endpoints

Secondary efficacy outcomes

Relative change in UACR:

- Between end of treatment visit to 30 days after end of treatment visit
- Between 30 days after end of treatment visit and baseline
- Category (>30%, >40%, and >50%) at 180 days

Secondary safety outcomes

- Initial and longer-term changes in eGFR
- Acute kidney injury
- Treatment-related AEs: hyperkalemia, symptomatic hypotension, genital mycotic events

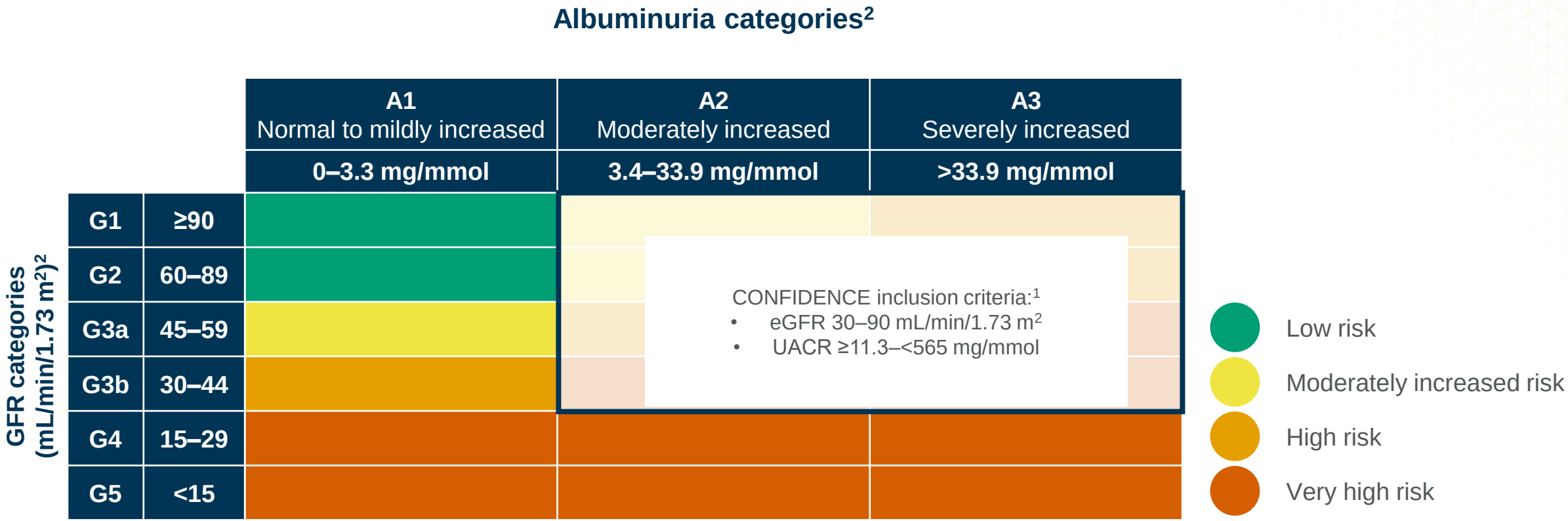
*Patients will require at least one value of eGFR <60 mL/min/1.73 m^2 within the previous 3 months or have registered diagnosis of CKD. Patients with an eGFR >75–90 mL/min/1.73 m^2 will be capped at 20%. Patients in Part A required to have eGFR 40–90 mL/min/1.73 m^2, expanded to 30–90 mL/min/1.73 m^2 in Part B following feedback from DMC and safety analysis.

ACEi, angiotensin-converting enzyme inhibitor; AE, adverse event; ARB, angiotensin receptor blocker; BP, blood pressure; CKD, chronic kidney disease; DMC, data monitoring committee; eGFR, estimated glomerular filtration rate; HbA1c, glycated hemoglobin; HFrEF, heart failure with reduced ejection fraction; NYHA, New York Heart Association; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T1D, type 1 diabetes; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Green JB, et al. *Nephrol Dial Transplant.* 2023;38(4):894–903; 2. NCT05254002. Available at: https://clinicaltrials.gov/study/NCT05254002 [accessed May 2025]; 3. Agarwal R, et al. *Nephrol Dial Transplant.* 2025; https://doi.org/10.1093/ndt/gfaf022.

CONFIDENCE

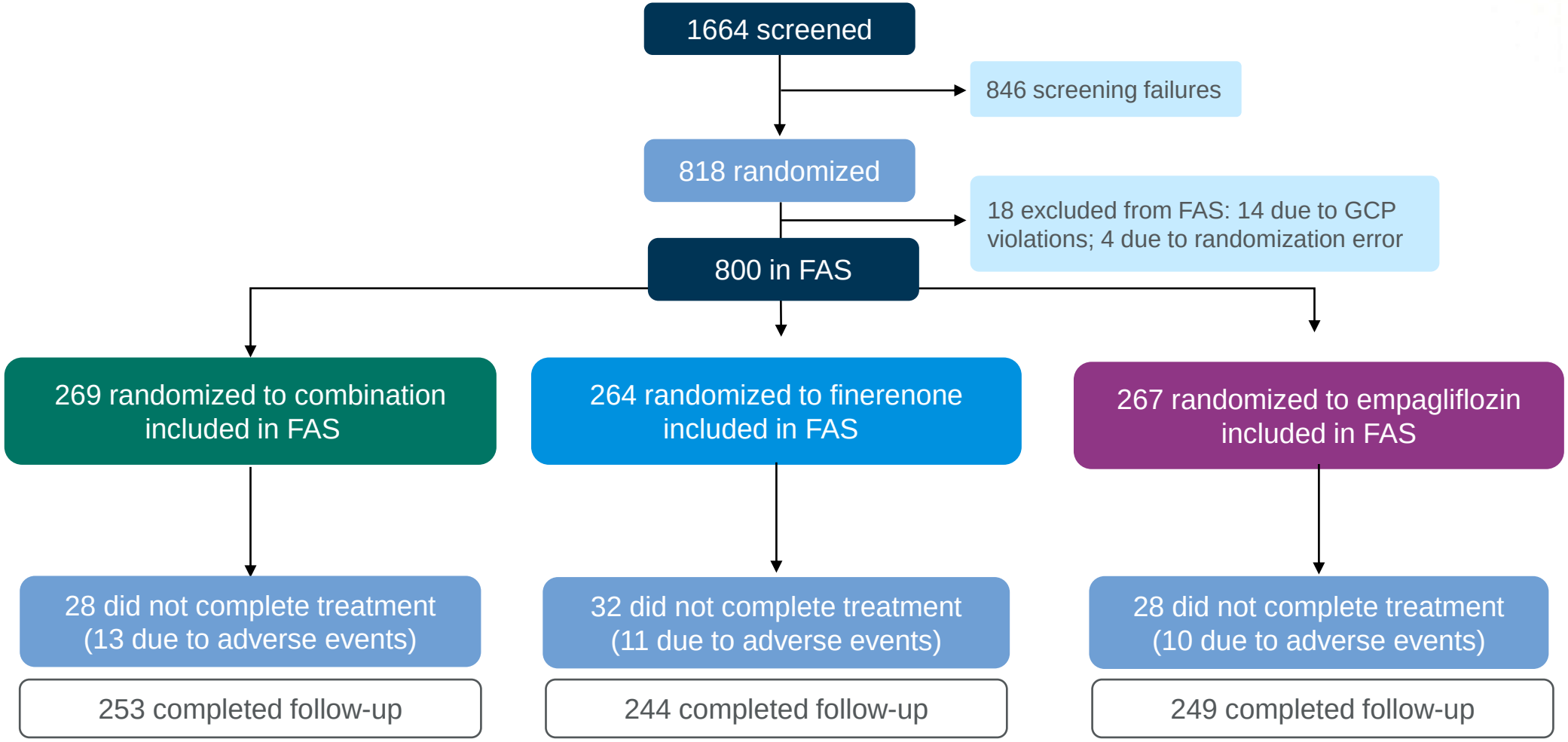
CONFIDENCE included patients with CKD and T2D at risk of kidney disease progression and CV events[1]



CKD, chronic kidney disease; CV, cardiovascular; eGFR, (estimated) glomerular filtration rate; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Agarwal R, et al. *Nephrol Dial Transplant.* 2025; doi: 10.1093/ndt/gfaf022; 2. Kidney Disease: Improving Global Outcomes. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int.* 2022;102:S1–S127.

87% of randomized patients completed the treatment period in the CONFIDENCE study



87% of randomized patients completed the treatment period, with a similar proportion in each treatment group

FAS, full analysis set; GCP, Good Clinical Practice.

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

CONFIDENCE

CONFIDENCE trial design: Key conclusions

CONFIDENCE was a randomized, double-blind, double-dummy, multicenter, three-armed, parallel-group, phase II study[1–3]

The trial aimed to determine the efficacy and safety of simultaneous finerenone and SGLT-2i initiation in people with CKD and T2D using UACR as the primary endpoint[4]

CONFIDENCE included patients with CKD and T2D at risk of kidney disease progression and 87% of randomized patients completed the treatment period[3,4]

CKD, chronic kidney disease; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Green JB, et al. *Nephrol Dial Transplant.* 2023;38(4):894–903; 2. NCT05254002. Available at: https://clinicaltrials.gov/study/NCT05254002 [accessed May 2025]; 3. Agarwal R, et al. *Nephrol Dial Transplant.* 2025; https://doi.org/10.1093/ndt/gfaf022; 4. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

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CONFIDENCE:
Key baseline data

CONFIDENCE included a diverse range of patients with CKD and T2D with a high comorbidity burden

Patients: N=800*

Sex

75% 25%

Mean age

66.5 years

BMI

29 kg/m^2

Mean eGFR

54 mL/min/1.73 m^2

Median UACR

65.4 mg/mmol

HbA1c %

7.3%

Serum [K$^+$]

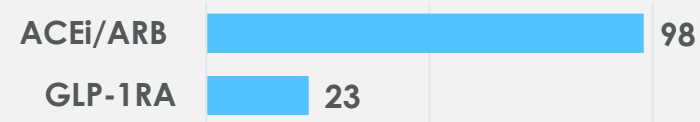
4.5 mmol/L, mean

Race (%)

Medical history (%)

Hypertension	88
ASCVD	28
Diabetic retinopathy	16

Comedications (%)



*Full analysis set.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; [K$^+$], potassium concentration; UACR, urine albumin-creatinine ratio.

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

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Demographics and baseline characteristics in the CONFIDENCE trial were well balanced across treatment groups

	Combination N=269	Finerenone N=264	Empagliflozin N=267	Total N=800
Age, years, mean (SD)	67.7 (10.0)	65.5 (10.7)	66.2 (10.1)	66.5 (10.3)
Female, n (%)	67 (24.9)	61 (23.1)	70 (26.2)	198 (24.8)
Race, n (%)				
White	130 (48.3)	105 (39.8)	116 (43.4)	351 (43.9)
Asian	114 (42.4)	132 (50.0)	125 (46.8)	371 (46.4)
Black/African American	22 (8.2)	21 (8.0)	24 (9.0)	67 (8.4)
eGFR, mL/min/1.73 m^2, mean (SD)*	**53.9 (16.9)**	**54.3 (17.8)**	**54.2 (16.6)**	**54.2 (17.1)**
UACR, mg/mmol, median (IQR)	**64.9 (31.0–112.9)**	**65.2 (33.0–145.6)**	**65.8 (34.0–126.9)**	**65.4 (33.0–123.4)**
SBP, mmHg, mean (SD)	135.0 (13.7)	135.1 (13.7)	135.4 (12.6)	135.2 (13.3)
HbA1c, % (SD)	7.3 (1.2)	7.3 (1.2)	7.3 (1.2)	7.3 (1.2)
Serum potassium, mmol/L, mean (SD)	**4.4 (0.4)**	**4.5 (0.5)**	**4.5 (0.4)**	**4.5 (0.4)**
Medical history, n (%)				
Hypertension	239 (88.8)	234 (88.6)	229 (85.8)	702 (87.8)
ASCVD	75 (27.9)	71 (26.9)	78 (29.2)	224 (28.0)
Diabetic retinopathy	43 (16.0)	36 (13.6)	48 (18.0)	127 (15.9)
Concomitant medication, n (%)				
ACEi/ARB	267 (99.3)	260 (98.5)	260 (97.4)	787 (98.4)
GLP-1RA	68 (25.3)	52 (19.7)	62 (23.2)	182 (22.8)

Selected baseline data shown. *Calculated by the CKD-EPI equation with a modification to the equation for Japanese participants. See slide notes for abbreviations.

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

CONFIDENCE

CONFIDENCE baseline data: Key conclusions

CONFIDENCE included a diverse range of patients with CKD and T2D, including a high proportion of Asian participants

Patients in the CONFIDENCE trial had a high comorbidity burden, particularly hypertension or ASCVD, and moderately to severely increased albuminuria

Based on average HbA1c and BMI, patients had controlled diabetes and were overweight

The majority of patients were on concomitant medications at baseline, with 98% of patients using ACEi/ARB and 23% using a GLP-1RA

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; CKD, chronic kidney disease; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes.

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

CONFIDENCE

CONFIDENCE: Key efficacy and safety data

CONFIDENCE: Overview of key efficacy and safety findings[1,2]

Simultaneous initiation of finerenone and an SGLT-2i led to an early and additive reduction in UACR

Both primary endpoints were achieved

greater reduction in UACR at Day 180 with combination therapy than finerenone alone (*p*<0.001)

greater reduction in UACR at Day 180 with combination therapy than empagliflozin alone (p<0.001)

Absolute reduction in UACR with combination therapy from baseline:

52% at Day 180

30% at Day 14

When initiated simultaneously, the safety profile of finerenone and an SGLT-2i was largely consistent with that of either agent alone

The incidence of serious AEs and AEs leading to drug discontinuation was low across all treatment groups

The greater initial eGFR decline following simultaneous initiation of finerenone and an SGLT-2i was expected and likely hemodynamic

No serious AKI events were reported

Simultaneous initiation of finerenone and an SGLT-2i led to an expected additive reduction in SBP

The incidence of symptomatic hypotension was low

Hyperkalemia rates were numerically lower in patients simultaneously initiated on finerenone and an SGLT-2i versus finerenone alone

The clinical impact was minimal

These data provide strong support for early, simultaneous initiation of finerenone and SGLT-2i therapy in patients with CKD and T2D

AE, adverse event; AKI, acute kidney injury; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

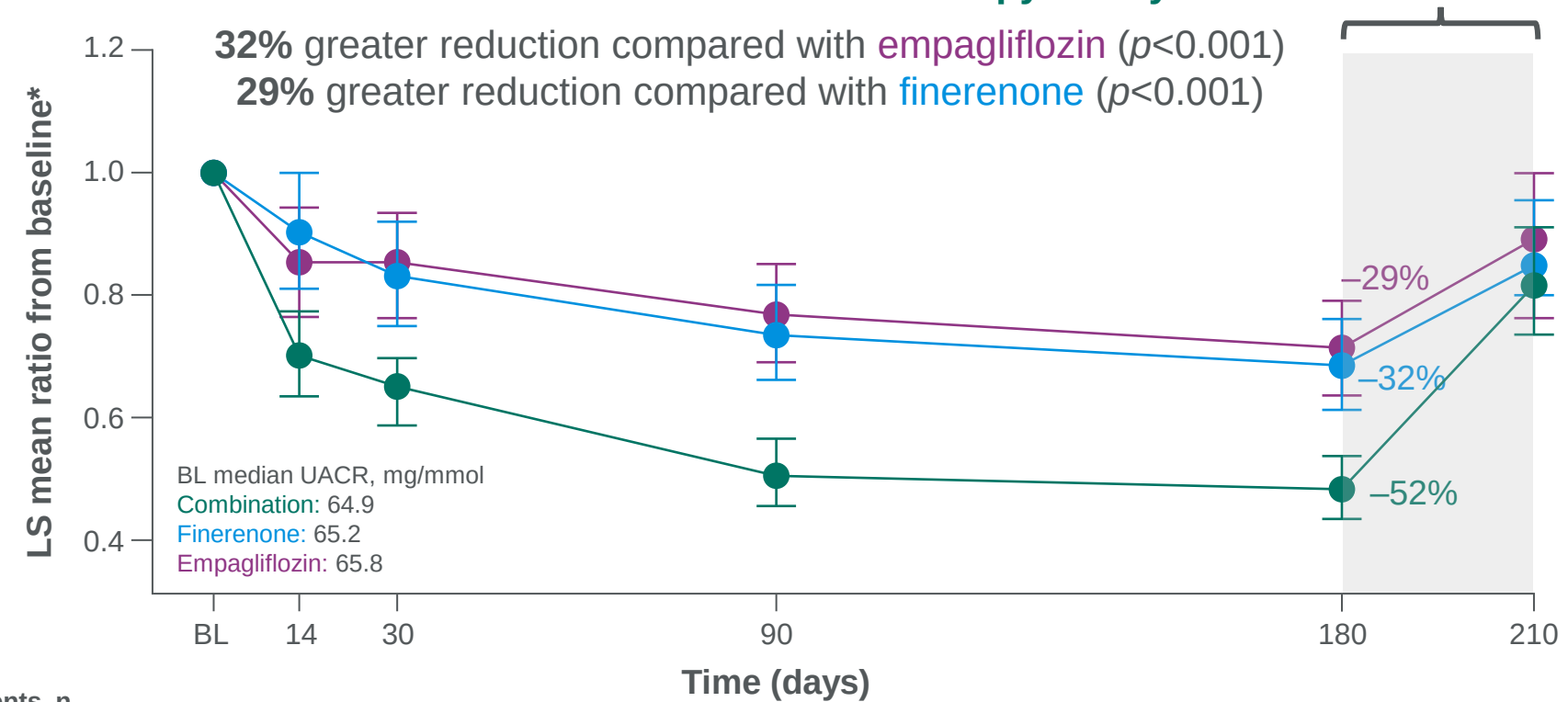
1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659; 2. Agarwal R, et al. *ERA* 2025; LBCT oral presentation.

CONFIDENCE

Simultaneous initiation of finerenone and an SGLT-2i led to an additive reduction in UACR of up to 52% from baseline in patients with CKD and T2D

Primary endpoint: UACR reduction with combination therapy at Day 180

32% greater reduction compared with empagliflozin ($p<0.001$)
29% greater reduction compared with finerenone ($p<0.001$)



Patients, n	BL	14	30	90	180	210
Combination	265	248	253	248	240	238
Finerenone	258	247	248	237	236	227
Empagliflozin	261	254	252	246	238	232

LS mean ratio (95% CI)
0.68 (0.59–0.79)
0.71 (0.61–0.82)

Consistent benefit: Combination therapy generally resulted in a **greater reduction in UACR from baseline to Day 180** compared with either treatment alone **across prespecified subgroups**

*LS means (95% CI) for the ratio to baseline of UACR under "missing at random" in the full analysis set.
BL, baseline; CI, confidence interval; CKD, chronic kidney disease; LS, least-squares; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659.

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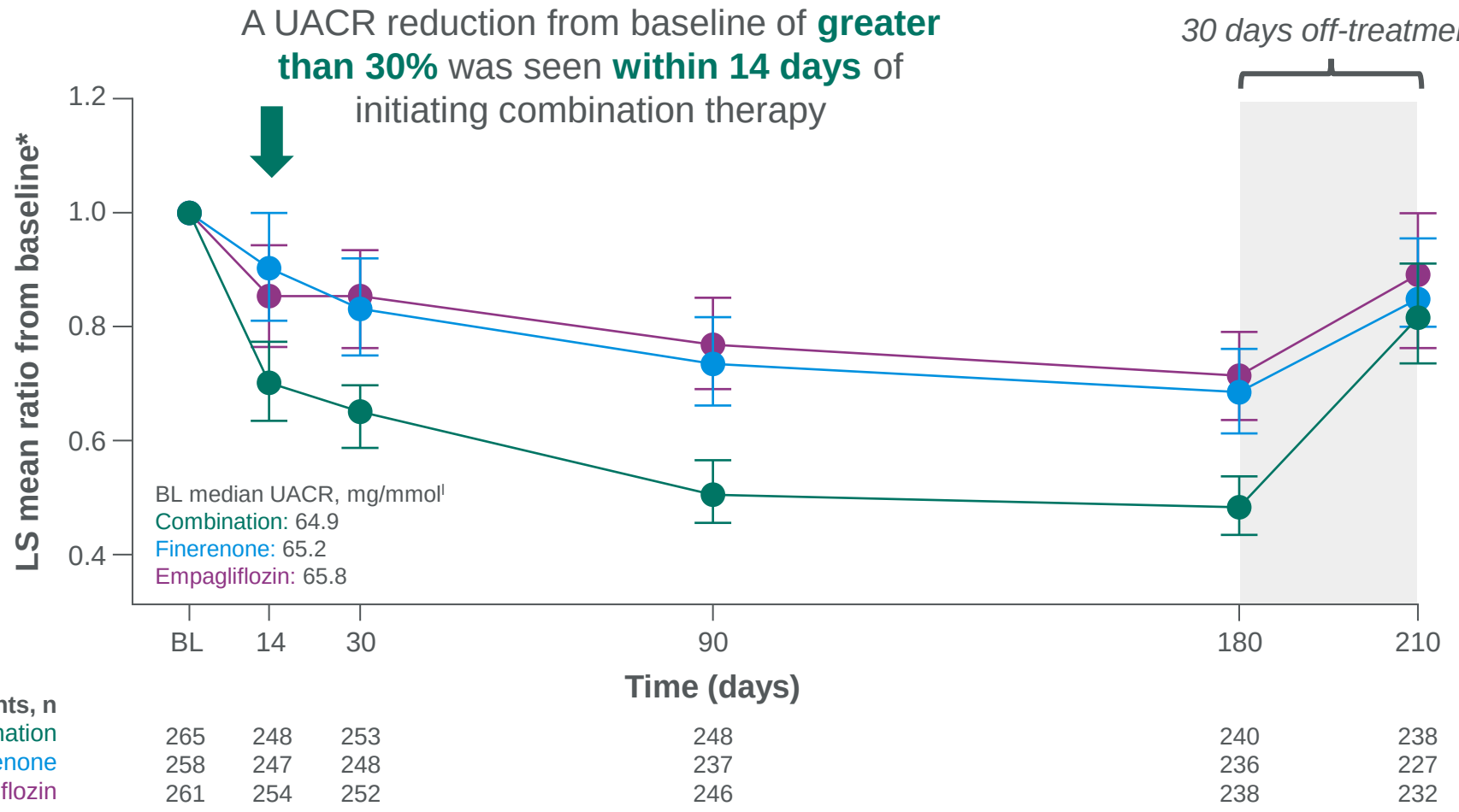
An early reduction in UACR was seen following simultaneous initiation of finerenone and an SGLT-2i



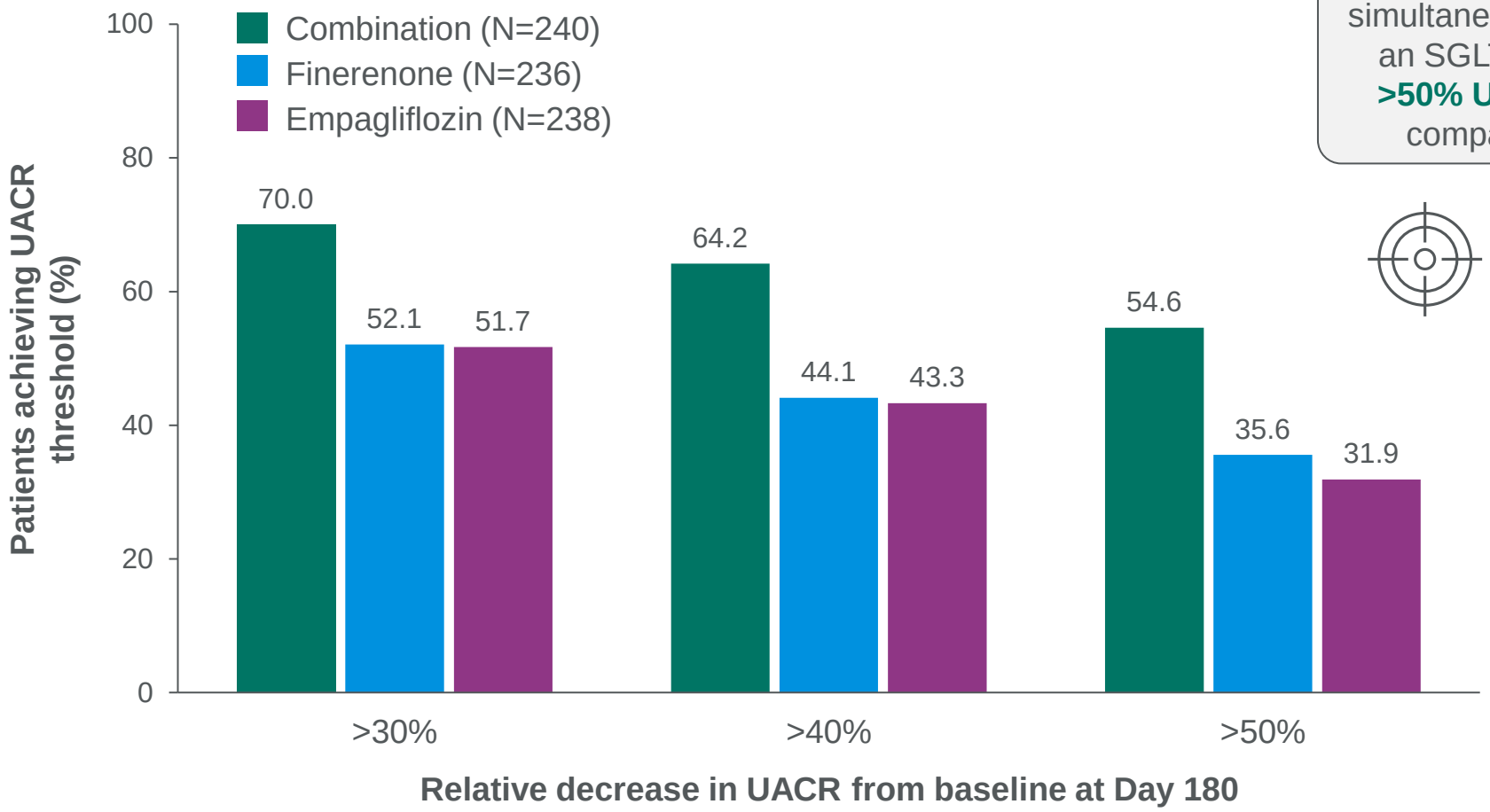
After stopping therapy, UACR levels increased but remained below baseline for all treatment groups

*LS means (95% CI) for the ratio to baseline of UACR under "missing at random" in the full analysis set.
BL, baseline; CI, confidence interval; LS, least-squares; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659.

CONFIDENCE

70% of patients simultaneously initiated on finerenone and an SGLT2i achieved the ADA-recommended target of >30% reduction in UACR[1,2]



Almost **20% more patients** simultaneously initiated on finerenone and an SGLT-2i achieved **>30%, >40%, or >50% UACR reduction** from baseline compared with either agent alone[1]

Clinical relevance: A reduction in UACR of 30% or greater is recommended by the ADA to slow kidney disease progression in patients with CKD*[2]

*For patients with UACR ≥300 mg/g.

ADA, American Diabetes Association; CKD, chronic kidney disease; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.

1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659. 2. Draznin B, et al. *Diabetes Care.* 2022;45:S175–S184.

CONFIDENCE

When initiated simultaneously, the overall AE profile of finerenone and an SGLT-2i was similar to that of either agent alone

	Combination N=268	Finerenone N=264	Empagliflozin N=266
Type of TEAE	**n (%)**	**n (%)**	**n (%)**
Any AE	144 (53.7)	136 (51.5)	135 (50.8)
Leading to discontinuation of study drug	12 (4.5)	9 (3.4)	9 (3.4)
Any SAE	19 (7.1)	16 (6.1)	17 (6.4)
Leading to discontinuation of study drug	3 (1.1)	3 (1.1)	2 (0.8)
TEAE leading to death	3 (1.1)	0	3 (1.1)
Acute kidney injury	5 (1.9)	3 (1.1)	0
Symptomatic hypotension events	3 (1.1)	0	0
Genital mycotic events	4 (1.5)	0	4 (1.5)

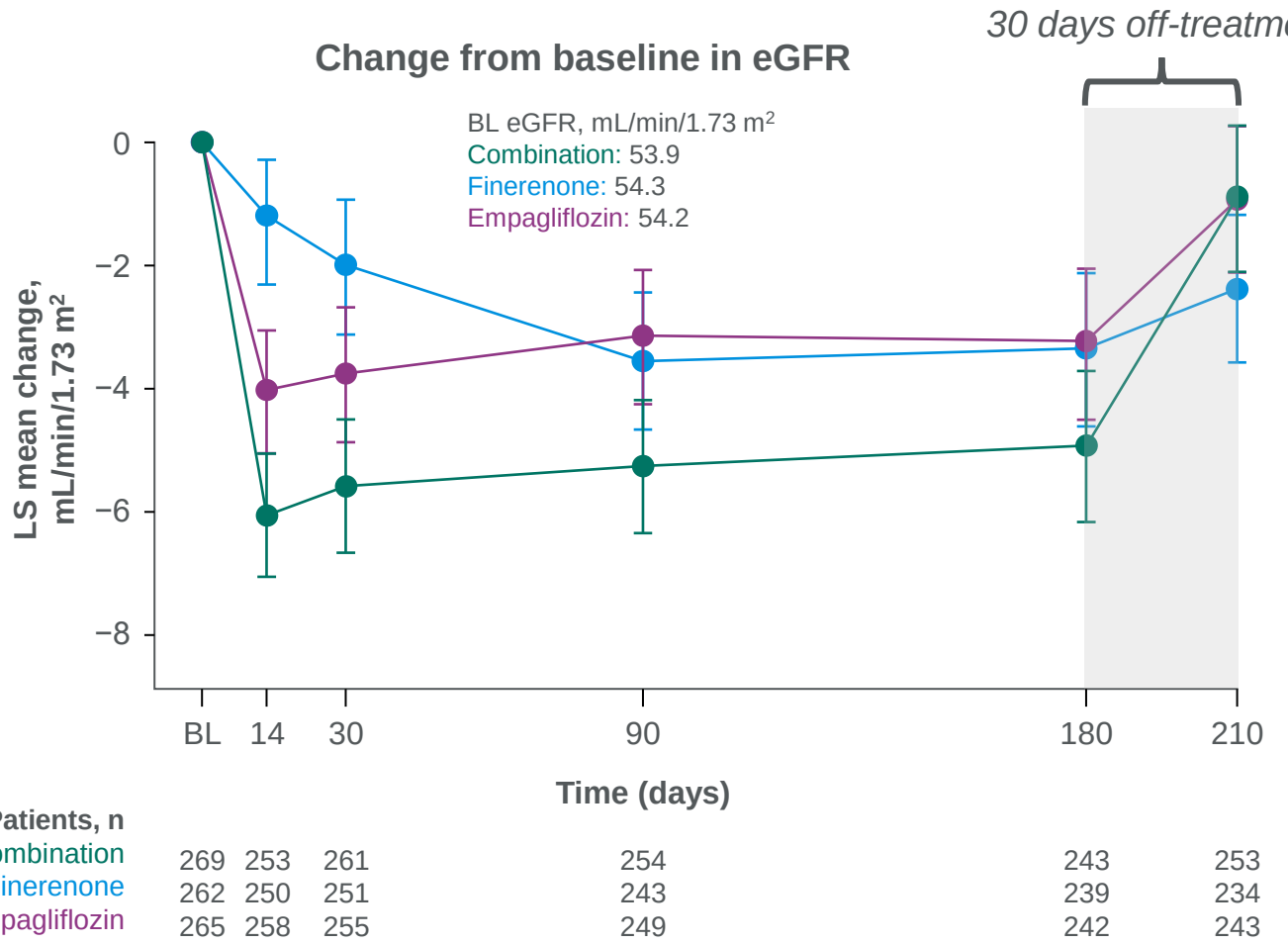
Fewer than 5% of AEs led to treatment discontinuation

The **incidence of SAEs**, including those leading to death, **was low**

AEs were defined as TEAEs if they occurred in patients who had received at least one dose of study treatment and that started or worsened after the first dose of study treatment and up to 3 days after any temporary or permanent interruption of study treatment.
AE, adverse event; SAE, serious adverse event; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; TEAE, treatment-emergent adverse event.
Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

CONFIDENCE

As expected, initial eGFR decline following simultaneous initiation of finerenone and an SGLT-2i was greater than with either agent alone[1]



The **incidence of acute kidney injury was low** in the combination therapy group (1.9%), with **no serious events** of acute kidney injury reported[1,2]

eGFR decline >30% at 30 days from baseline, n (%)[1]

Combination N=268	Finerenone N=264	Empagliflozin N=266
17 (6.3)	10 (3.8)	3 (1.1)

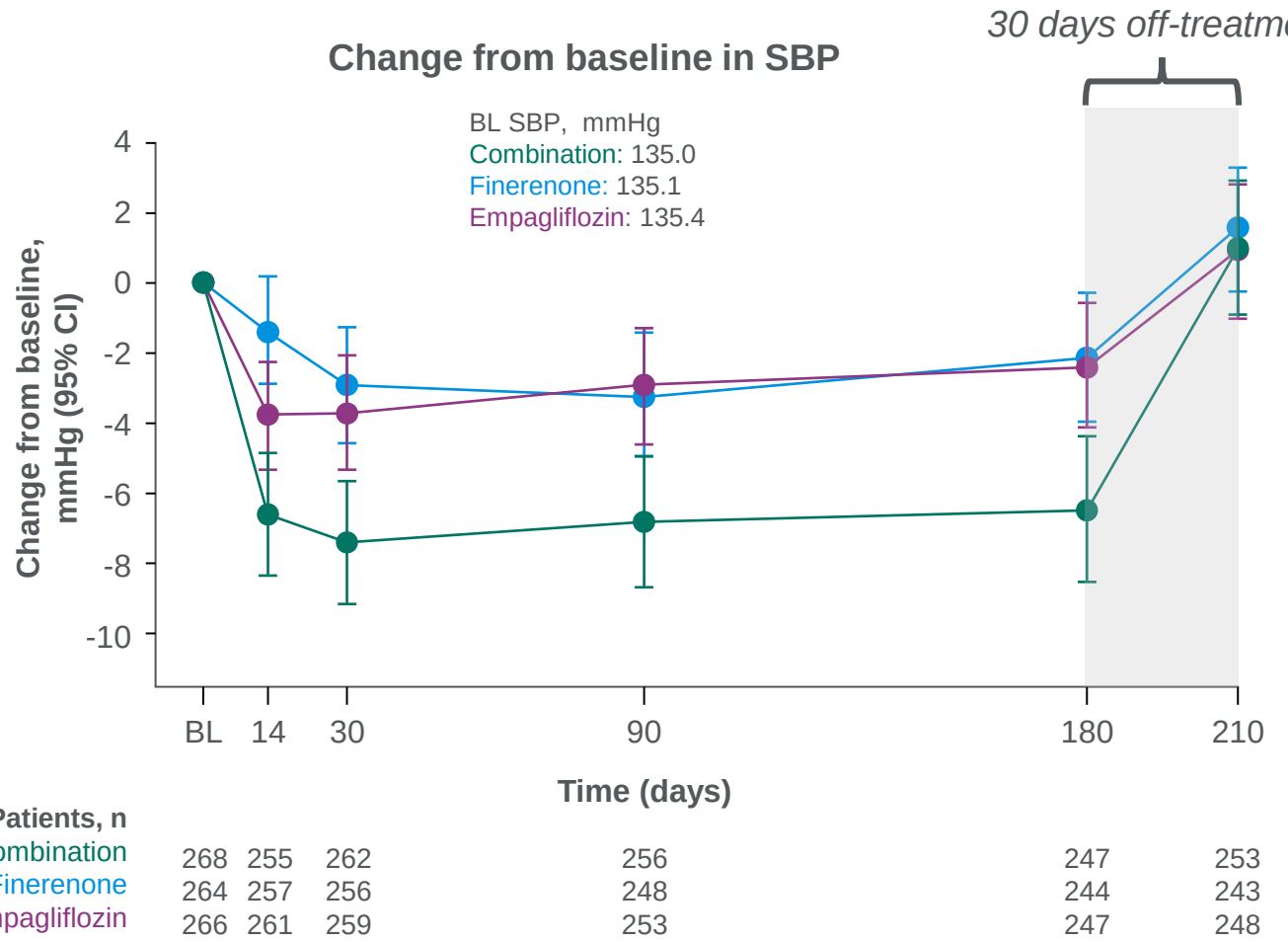
The initial eGFR decline returned to near baseline levels* after stopping therapy, suggesting the changes seen were **likely hemodynamic**[1,2]

*At day 210 (30 days after end of treatment), there was no significant difference in mean eGFR change from baseline between the combination group and either monotherapy group.
eGFR, estimated glomerular filtration rate; LS, least-squares; SGLT-2i, sodium-glucose co-transporter-2 inhibitor.

1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement); 2. Agarwal R, et al. *ERA* 2025; LBCT oral presentation.

CONFIDENCE

As expected, simultaneous initiation of finerenone and an SGLT-2i led to an additive reduction in SBP compared with either agent alone



The **incidence of symptomatic hypotension was low,** with only three cases (1.1%) reported in the combination therapy group and none reported with finerenone or empagliflozin monotherapy

Mean SBP change at 30 days from baseline, mmHg (SD)

Combination N=268	Finerenone N=264	Empagliflozin N=266
-7.4 (14.3)	-2.9 (13.7)	-3.7 (13.1)

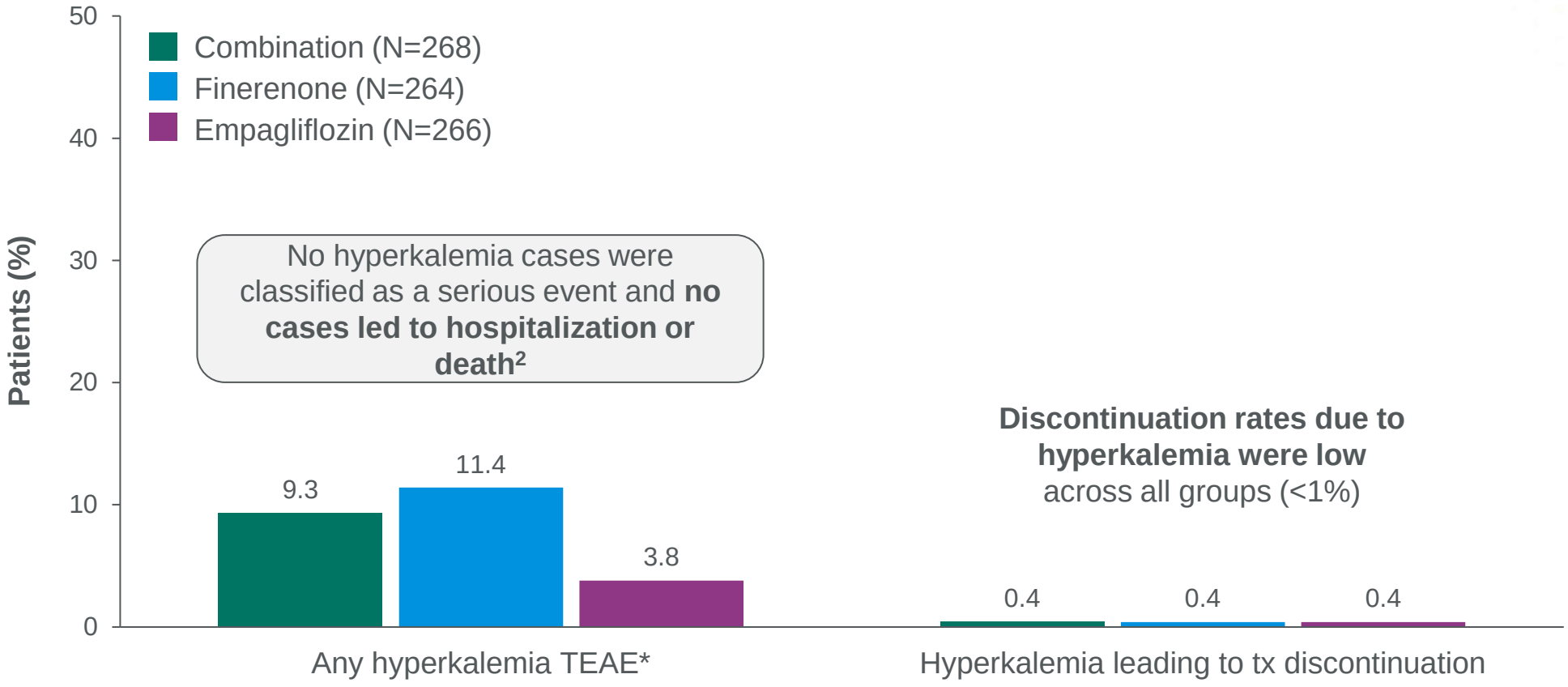
The initial SBP decline returned to near baseline levels* after stopping therapy

*At day 210 (30 days after end of treatment), there was no significant difference in mean SBP change from baseline between the combination group and either monotherapy group.
BL, baseline; CI, confidence interval; SD, standard deviation; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor

Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659 (including supplement).

CONFIDENCE

The incidence of hyperkalemia was numerically lower in patients simultaneously initiated on finerenone and an SGLT-2i compared with finerenone alone, and the clinical impact was minimal[1]

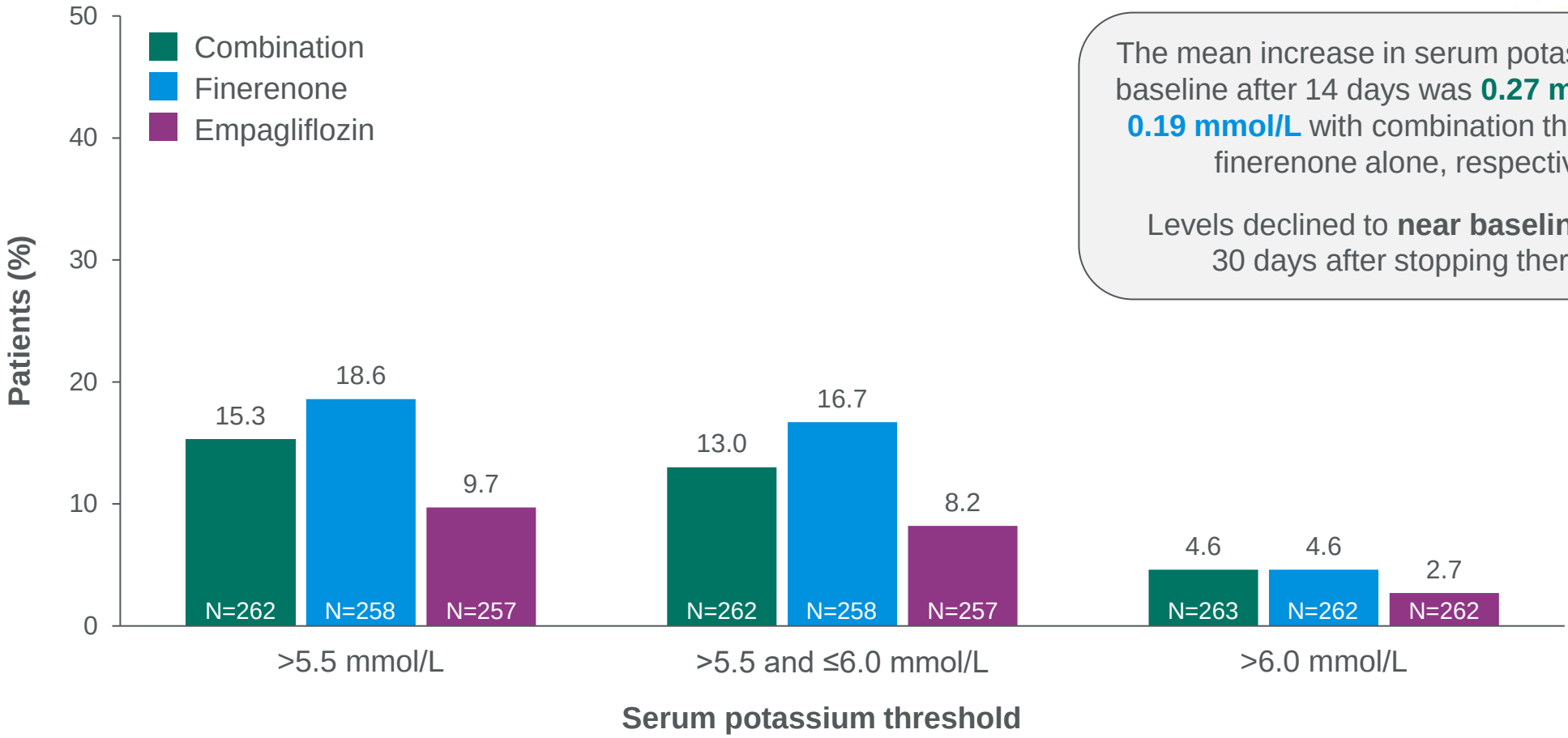


*Adverse event reported by investigators with the use of the Medical Dictionary for Regulatory Activities (MedDRA) preferred term "hyperkalemia".
SAE, serious adverse event; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; TEAE, treatment-emergent adverse event; tx, treatment.

1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659; 2. Agarwal R, et al. *ERA* 2025; LBCT oral presentation.

CONFIDENCE

Serum potassium elevations >6.0 mmol/L were uncommon in patients simultaneously initiated on finerenone and SGLT-2i combination therapy



The mean increase in serum potassium from baseline after 14 days was **0.27 mmol/L** and **0.19 mmol/L** with combination therapy and finerenone alone, respectively

Levels declined to **near baseline levels** 30 days after stopping therapy

N numbers represent all participants at risk for a treatment-emergent laboratory abnormality; participants must have had both a baseline and post-baseline treatment-emergent value while the baseline value must not have exceeded the displayed threshold.
SGLT-2i, sodium-glucose co-transporter-2 inhibitor.
Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659.

CONFIDENCE

CONFIDENCE key efficacy and safety data: Key conclusions (1/2)

1. Simultaneous initiation of finerenone and an SGLT-2i led to an early and additive reduction in UACR up to 52% in patients with CKD and T2D, significantly greater than with either agent alone[1]

2. 70% of patients initiated on both therapies achieved the ADA-recommended target of >30% UACR reduction to slow kidney disease progression[1,2]

3. Simultaneous initiation of finerenone and an SGLT-2i was associated with a low number of serious AEs and treatment discontinuations, with an overall AE profile similar to that of either agent alone[1]

ADA, American Diabetes Association; AE, adverse event; CKD, chronic kidney disease; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659; 2. Draznin B, et al. *Diabetes Care.* 2022;45:S175–S184.

CONFIDENCE

CONFIDENCE key efficacy and safety data: Key conclusions (2/2)

4. As expected, initial eGFR decline following simultaneous initiation of finerenone and an SGLT-2i was greater than with either agent alone, but this effect was likely hemodynamic and was not associated with serious kidney-related AEs[1]

5. Simultaneous initiation of finerenone and an SGLT-2i was associated with an additive reduction in SBP compared with either agent alone, and the incidence of symptomatic hypotension was low[1]

6. The incidence of hyperkalemia was numerically lower in patients simultaneously initiated on finerenone and an SGLT-2i compared with finerenone alone – no cases were serious, none led to hospitalization or death, and discontinuation rates due to hyperkalemia were low (<1%)[1,2]

AE, adverse event; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes.

1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659; 2. Agarwal R, et al. *ERA* 2025; LBCT oral presentation.

CONFIDENCE

CONFIDENCE overall takeaway

Simultaneous initiation of finerenone and an SGLT-2i led to an early and clinically meaningful reduction in UACR up to 52%, and was well tolerated in patients with CKD and T2D

CKD, chronic kidney disease; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes; UACR, urine albumin-to-creatinine ratio.

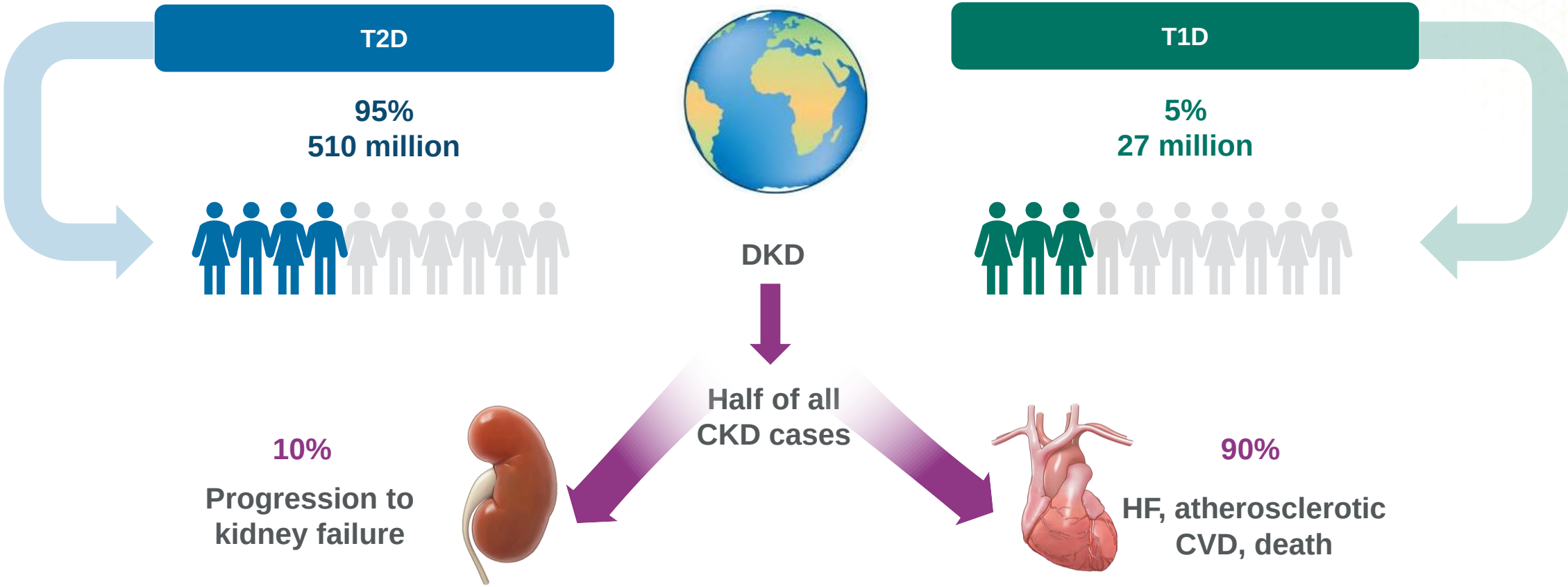
Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659.

CONFIDENCE

CONFIDENCE:
What do the results mean for clinical practice?

What problem are we trying to solve?

537 million
people live with diabetes worldwide

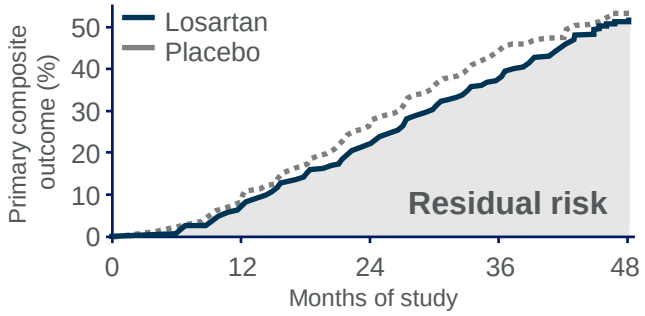


CKD, chronic kidney disease; CVD, cardiovascular disease; DKD, diabetic kidney disease; HF, heart failure; T1D, type 1 diabetes; T2D, type 2 diabetes.
Figure adapted from: Tuttle KR, et al. *Clin J Am Soc Nephrol.* 2022;17:1092–1103.

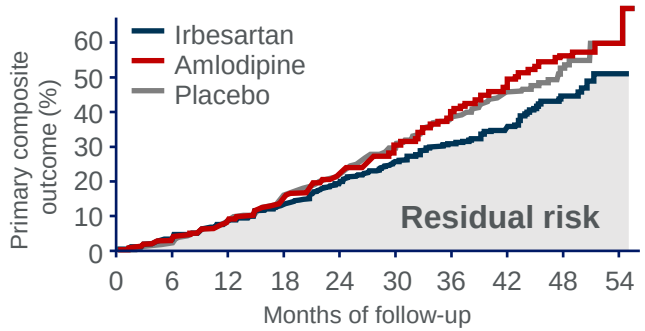
Despite available treatment options for patients with CKD and T2D, a high residual risk of adverse clinical events remains[1–6]

RAASi

RENAAL[1]

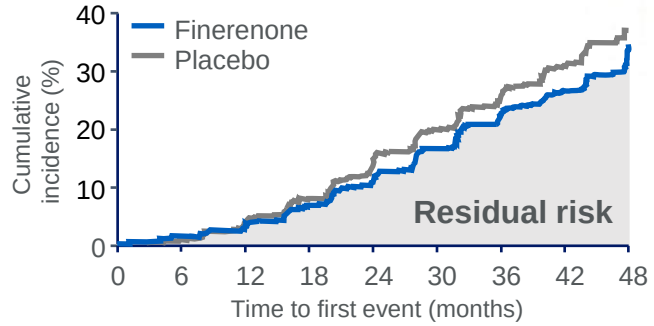


IDNT[2]



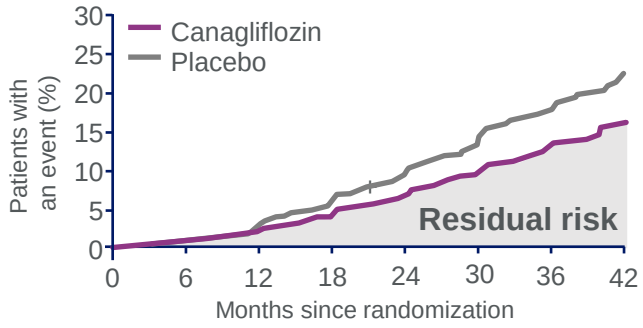
Non-steroidal MRAs (finerenone)

FIDELIO-DKD[3]

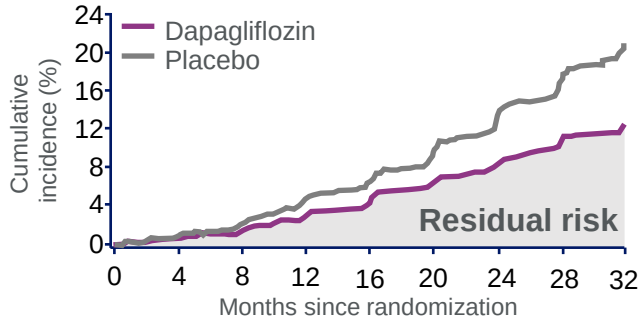


SGLT-2is

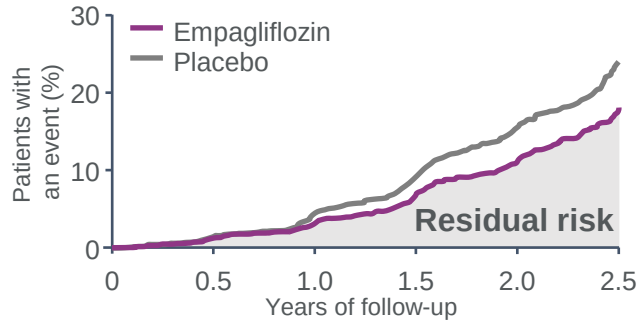
CREDENCE[4]



DAPA-CKD[5]



EMPA-KIDNEY[6]

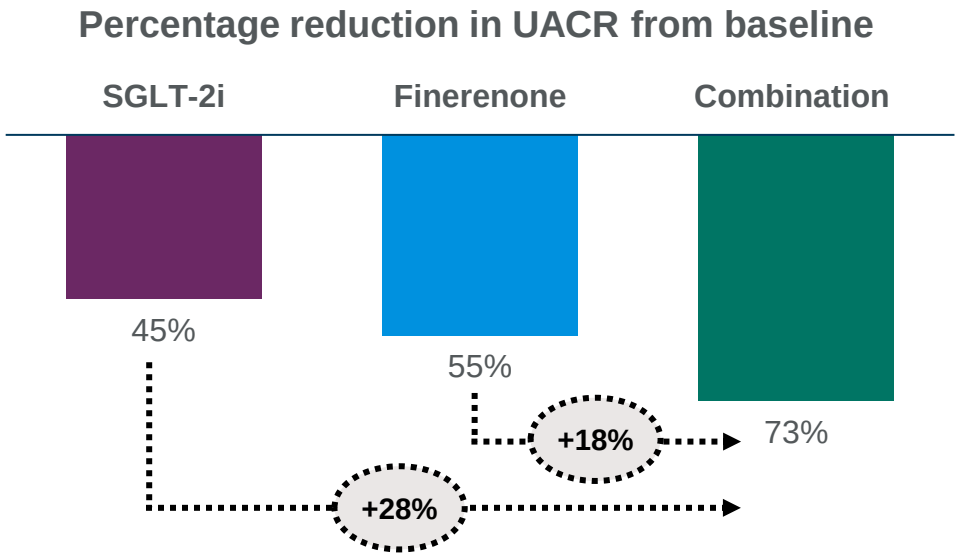


CKD, chronic kidney disease; MRA, mineralocorticoid receptor antagonist; RAASi, renin–angiotensin–aldosterone system inhibitor; SGLT-2i, sodium–glucose cotransporter-2 inhibitor; T2D, type 2 diabetes.

1. Brenner BM et al. *N Engl J Med.* 2001;345:861–869; 2. Lewis EJ et al. *N Engl J Med.* 2001;345:851–860; 3. Bakris GL et al. *N Engl J Med.* 2020;383:2219–2229; 4. Perkovic V et al. *N Engl J Med.* 2019;380:2295–2306; 5. Heerspink HJL et al. *N Engl J Med.* 2020;383:1436–1446; 6. The EMPA-KIDNEY Collaborative Group. *N Engl J Med.* 2023;388:117–127.

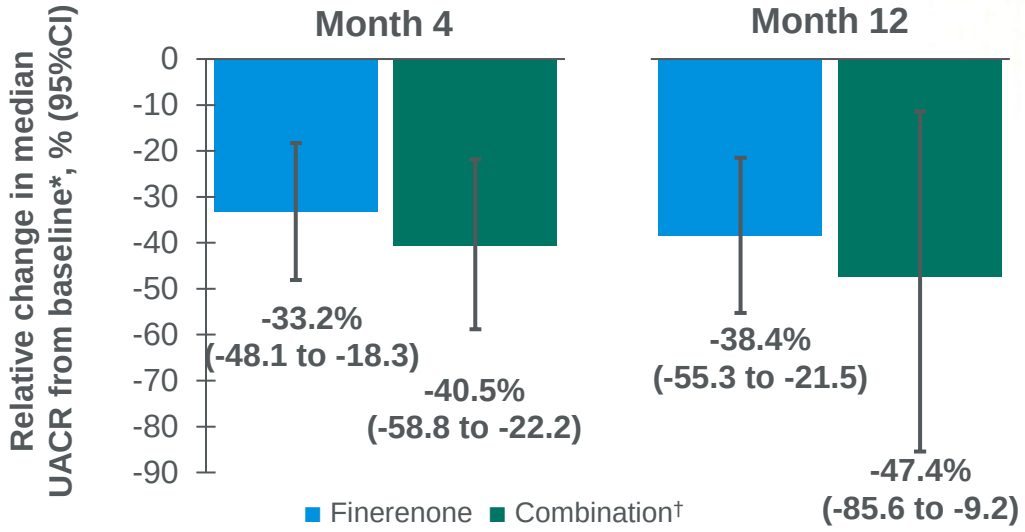
CONFIDENCE complements real-world evidence supporting the combined use of finerenone and SGLT-2i in clinical practice

US retrospective analysis of patients from a US specialty CKD clinic (N=98)[1]



Significant and clinically relevant reduction with combination

FOUNTAIN retrospective, observational study (US cohort) of finerenone initiators in clinical practice (N=15,948)[2]



Greater UACR reduction in patients with SGLT-2i use at baseline

The data shown here should not be compared with RCT data due to differences in study designs and patient populations. CONFIDENCE results reported in Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659. *The closest UACR measurement to baseline, 4 months, and 12 months, respectively, was used. This was based on the following time windows: baseline (-90 to 0 days), 4 months (32–52 days), 12 months (275–455 days); Change from baseline in UACR was evaluated at 4 and 12 months (among 913 and 443 patients, respectively, with available repeat UACR values). †Finerenone added on top of baseline SGLT-2i use.
CKD, chronic kidney disease; CI, confidence interval; RCT, randomized clinical trial; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; UACR, urine albumin-to-creatinine ratio.
1. Hanouneh M, et al. *Diagnostics (Basel).* 2024;14:1357; 2. Kovesdy C, et al. *Nephron.* 2025; doi: 10.1159/000543923.

Findings from CONFIDENCE may help alleviate common concerns around the simultaneous initiation of combination therapy

Potential concerns	What we have seen in CONFIDENCE
eGFR decline?	Expected initial eGFR decline following simultaneous initiation of combination therapy greater than with either agent alone; hemodynamic effect with no serious AKI events reported[1]
AEs?	Low incidence of SAEs and treatment discontinuations with simultaneous finerenone and SGLT-2i combination therapy; overall AE profile similar to that of either agent alone[1]
K^+ Hyperkalemia?	Hyperkalemia events lower with simultaneous finerenone and SGLT-2i combination therapy versus finerenone alone, with no hospitalizations, SAEs or deaths due to hyperkalemia[1,2]

AE, adverse event; AKI, acute kidney injury; eGFR, estimated glomerular filtration rate; K, potassium; SAE, serious adverse event; SGLT-2i, sodium-glucose co-transporter-2 inhibitor.

1. Agarwal R, et al. *N Engl J Med.* 2025; doi:10.1056/NEJMoa2410659; 2. Agarwal R, et al. *ERA* 2025; LBCT oral presentation.

CONFIDENCE

Implications of CONFIDENCE: Key conclusions

CKD associated with T2D remains a global issue and patients live with a residual risk of kidney disease progression, despite advances in treatment options[1–7]

CONFIDENCE provides support for a simultaneous approach to initiating finerenone and an SGLT-2i, complementing existing real-world evidence for finerenone and SGLT-2i combination therapy[8–10]

Findings from CONFIDENCE may help alleviate common concerns around simultaneous initiation of combination therapy and encourage earlier action to improve patient outcomes[8,11]

Finerenone is an essential treatment pillar in CKD with T2D. Its early combination with an SGLT-2i should be considered an optimal approach to rapidly reduce albuminuria and the associated risk of adverse CV and kidney outcomes[8,12,13]

CKD, chronic kidney disease; CV, cardiovascular; SGLT-2i, sodium-glucose co-transporter-2 inhibitor; T2D, type 2 diabetes.

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