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COMBINATION EFFECT OF FINERENONE AND EMPAGLIFLOZIN IN PARTICIPANTS WITH CHRONIC KIDNEY DISEASE AND TYPE 2 DIABETES USING A UACR ENDPOINT STUDY (CONFIDENCE)—BASELINE CHARACTERISTICS

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Meike Brinker
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Na Li
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Charlie Scott
Masaomi Nangaku

DISCLOSURES FOR RAJIV AGARWAL

- This work was supported by Bayer AG, who funded the CONFIDENCE study
- Received personal fees and nonfinancial support from Akebia Therapeutics, Alnylam, Bayer Healthcare Pharmaceuticals, Boehringer Ingelheim, Intercept, and Novartis
- Member of data safety monitoring committees for Chinook and Vertex
- Served as an associate editor of the *American Journal of Nephrology* and *Nephrology Dialysis and Transplantation*
- Author for UpToDate
- Received research grants from the National Institutes of Health and the US Veterans Administration

ALL AUTHOR DISCLOSURES

JBG has received funds for research, paid to her institution, from Bluedrop, Boehringer Ingelheim, Eli Lilly, Merck, and Roche; and is a consultant for Anji, AstraZeneca, Bayer, Boehringer Ingelheim, Eli Lilly, Mineralys, Novo Nordisk, Pfizer, Valo, and Vertex. **HJLH** has received consulting fees from Alexion, AstraZeneca, Bayer, Boehringer Ingelheim, Chinook, CSL Behring, Dimerix, Eli Lilly, Gilead, Janssen, Merck, Novartis, Novo Nordisk, Roche, and Travere Therapeutics; research support from AstraZeneca, Boehringer Ingelheim, Janssen, and Novo Nordisk; honoraria from AstraZeneca and Novo Nordisk; and travel expenses from Eli Lilly. **JFEM** has received grants from McMaster University (Hamilton, Canada), Novo Nordisk, and the European Union; consulting fees from AstraZeneca, Bayer, Boehringer Ingelheim, and Novo Nordisk; honoraria from AstraZeneca, Bayer, Novartis, and Novo Nordisk; has participated on a data safety monitoring board or advisory board for AstraZeneca, Bayer, Boehringer Ingelheim, and Sanofi; and had a leadership role in the KDIGO group. **JBM** has received personal fees from Bayer, Eli Lilly, Mannkind, and Novo Nordisk; and is the principal investigator on grants to Washington University from Biomea, Diamyd, Juvenile Diabetes Research Foundation, National Institutes of Health, and Novo Nordisk. **AKM** has received research support and personal fees from Bayer, Chinook Therapeutics, and Novartis; personal fees from Novo Nordisk and Otsuka; and research support from Alexion and Boehringer Ingelheim. **JR** has received research grants from Applied Therapeutics, Biomea Fusion, Boehringer Ingelheim, Carmot, Corcept, Eli Lilly, Hanmi, Merck, Novartis, Novo Nordisk, Oramed, Regeneron, Pfizer, and Sanofi; served on scientific advisory boards and received honorarium or consulting fees from Applied Therapeutics, Biomea Fusion, Boehringer Ingelheim, Eli Lilly, Hanmi, Novo Nordisk, Oramed, Regeneron, Roche, Sanofi, Structure Therapeutics, and Zealand; and received honoraria for lectures from Boehringer Ingelheim, Eli Lilly, Novo Nordisk, and Sanofi. **PR** has received research support and personal fees from AstraZeneca and Novo Nordisk; and personal fees from Abbott, Astellas, Bayer, Boehringer Ingelheim, Eli Lilly, Gilead, Mundipharma, Sanofi, and Vifor. **MV** has received research grant support, served on advisory boards, or had speaker engagements with American Regent, Amgen, AstraZeneca, Bayer AG, Baxter Healthcare, Boehringer Ingelheim, Bristol Myers Squibb, Chiesi, Cytokinetics, Fresenius Medical Care, Idorsia Pharmaceuticals, Lexicon Pharmaceuticals, Merck, Milestone Pharmaceuticals, Novartis, Novo Nordisk, Pharmacosmos, Relypsa, Roche Diagnostics, Sanofi, and Tricog Health; and participates on clinical trial committees for studies sponsored by AstraZeneca, Bayer AG, Galmed, Impulse Dynamics, Novartis, and Occlutech. **MB** is an employee of Bayer AG, Germany. **RE** was an employee of Bayer AG, Germany at the time the study initiated. **NL** is an employee of Bayer Healthcare, China. **MFS** is an employee of Bayer AG, Germany; and a shareholder of AstraZeneca, Bayer, Eli Lilly, and Novo Nordisk. **CS** is an employee of Bayer Corp., USA. **MN** has received research grants from Astellas, Bayer, Boehringer Ingelheim, Chga, Daiichi-Sankyo, JT, Kyowa-Kirin, Takeda, Tanabe-Mitsubishi, and Torii; consulting fees from Astellas, Boehringer Ingelheim, Daiichi-Sankyo, JT, Kyowa-Kirin, and Tanabe-Mitsubishi; and honoraria from Astellas, Astra Zeneca, Boehringer Ingelheim, Chugai, Daiichi-Sankyo, GSK, Kyowa-Kirin, and Tanabe-Mitsubishi

INTRODUCTION

Despite available interventions, people with CKD associated with T2D remain at risk of kidney failure and cardiovascular complications

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; MRA, mineralocorticoid receptor antagonist; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

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The COmbinatioN effect of FInerenone anD EmpaglifloziN in participants with CKD and T2D using a UACR Endpoint study (CONFIDENCE) explored the efficacy and safety associated with simultaneous initiation of finerenone and empagliflozin therapy compared with either agent alone[6]

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RATIONALE FOR USE OF FINERENONE + SGLT2 INHIBITOR COMBINATION

Finerenone and SGLT2 inhibitors[1]:
Shared and distinct physiological effects

Finerenone[1]:
↓ Oxidative stress, ↓ inflammation, ↓ fibrosis, improves endothelial function

SGLT2 inhibitor[1]:
Kidney hemodynamic effect
→ glucosuria and natriuresis,
↓ intraglomerular hypertension

Complementary MoA[1]:
→ potential for additive beneficial effect in CKD + T2D and CVD

CKD, chronic kidney disease; CVD, cardiovascular disease; ENaC, epithelial sodium channel; MoA, mechanism of action; MR, mineralocorticoid receptor; Na^+, sodium; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes.
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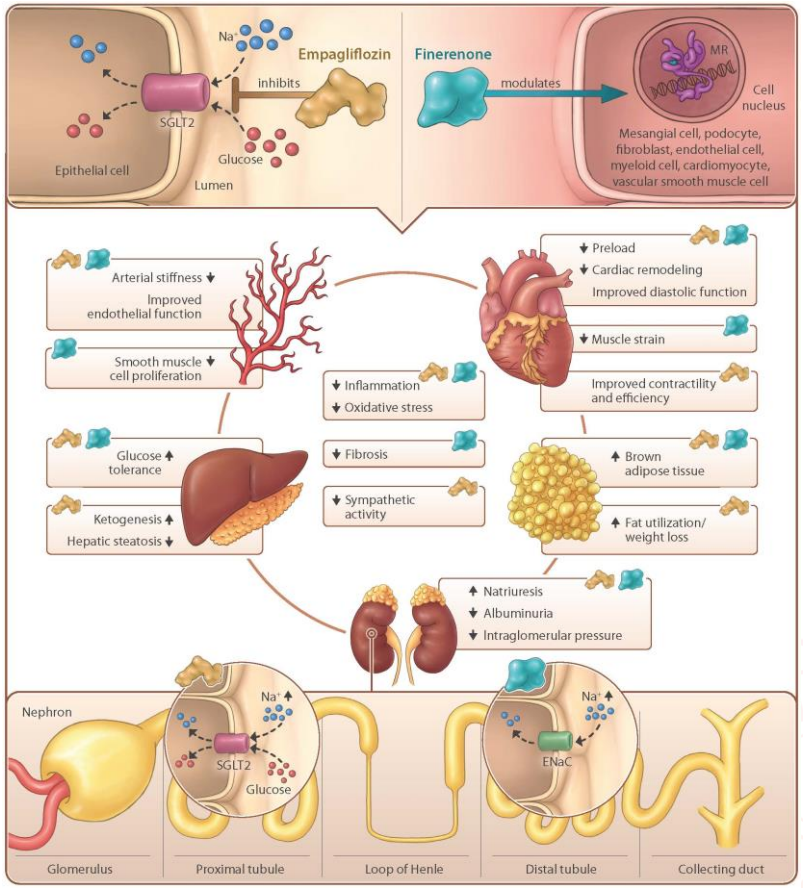

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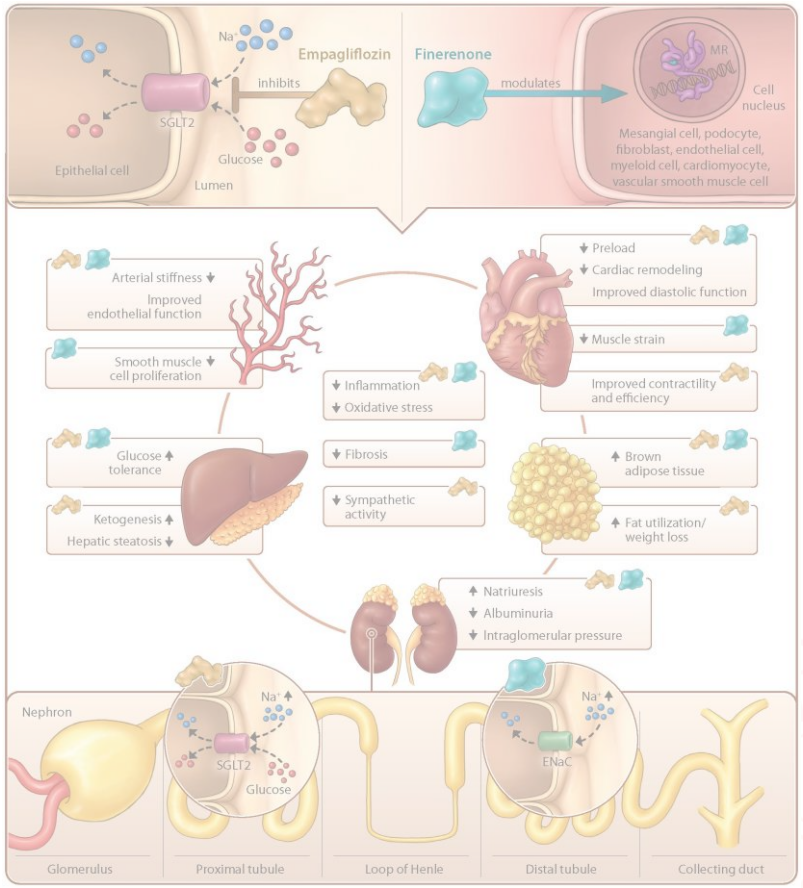

Post hoc analyses[2]:
Beneficial effects of finerenone appear to be independent of baseline SGLT2 inhibitor use

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Secondary analyses of FIDELITY (a pooled analysis of the FIGARO-DKD and FIDELIO-DKD trials) suggested a potential additive effect of finerenone and SGLT2 inhibitors on kidney and CV outcomes[1]

CV, cardiovascular; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

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Using population pharmacokinetics and pharmacodynamics in FIDELITY, there is evidence for a potential additive effect of finerenone with an SGLT2 inhibitor on UACR-lowering and chronic eGFR slope[2]

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However, no trial has yet evaluated the safety and efficacy of simultaneously initiating an SGLT2 inhibitor and finerenone in people with T2D and albuminuria

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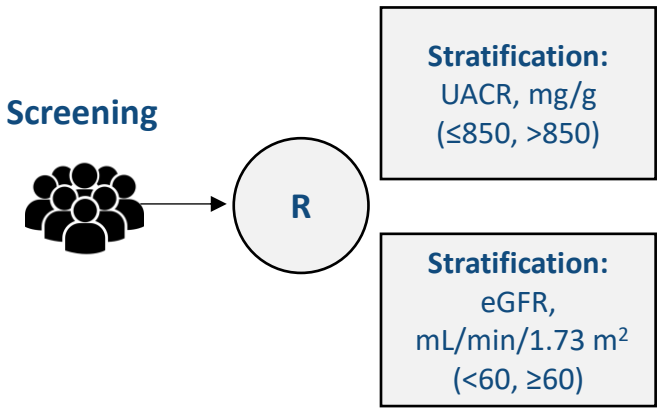
CONFIDENCE STUDY DESIGN: A RANDOMIZED, CONTROLLED, DOUBLE-BLIND, DOUBLE-DUMMY, INTERNATIONAL, MULTICENTER, THREE-ARMED, PARALLEL-GROUP, PHASE 2 STUDY

CONFIDENCE STUDY DESIGN

Randomized participants were stratified by eGFR and UACR at screening



†Participants with an eGFR of 40–90 mL/min/1.73 m^2 were recruited (Part A) prior to recruiting participants with an eGFR of 30–90 mL/min/1.73 m^2 (Part B). The number of participants will be capped in parts A and B as follows: <80% with an eGFR of ≤75 mL/min/1.73 m^2 and <20% with an eGFR of >75 mL/min/1.73 m^2. Up/down titration based on eGFR, serum/plasma potassium or potassium, safety, and tolerability.

ABPM, ambulatory blood pressure monitoring; eGFR, estimated glomerular filtration rate; R, randomization; UACR, urinary albumin-to-creatinine ratio.

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CONFIDENCE STUDY DESIGN

Participants were randomized in a 1:1:1 ratio to one of three parallel groups

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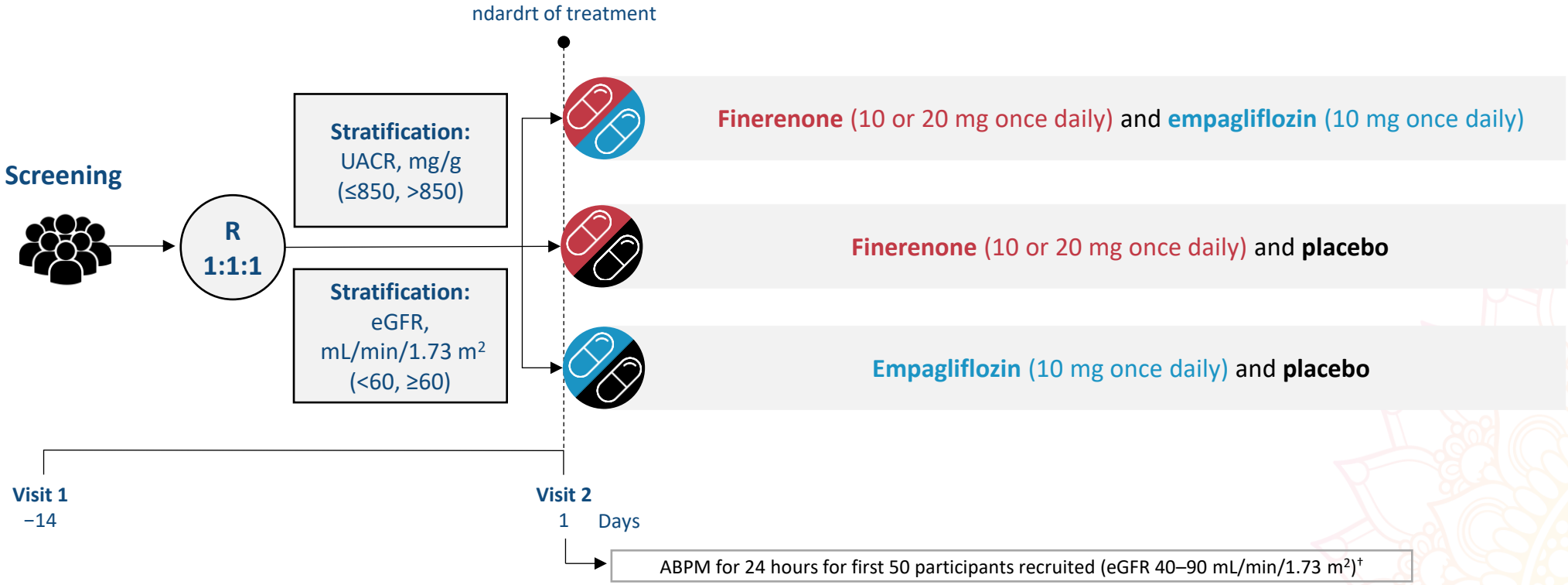
CONFIDENCE STUDY DESIGN

CONFIDENCE comprised two consecutive parts. In Part A, participants with an eGFR of 40–90 mL/min/1.73 m^2 were enrolled and underwent ABPM for 24 hours after administration of their first study drug dose on Day 1. A decision to extend enrolment to participants with an eGFR as low as 30 mL/min/1.73 m^2 (Part B) was made following analysis of safety findings for the participants in Part A



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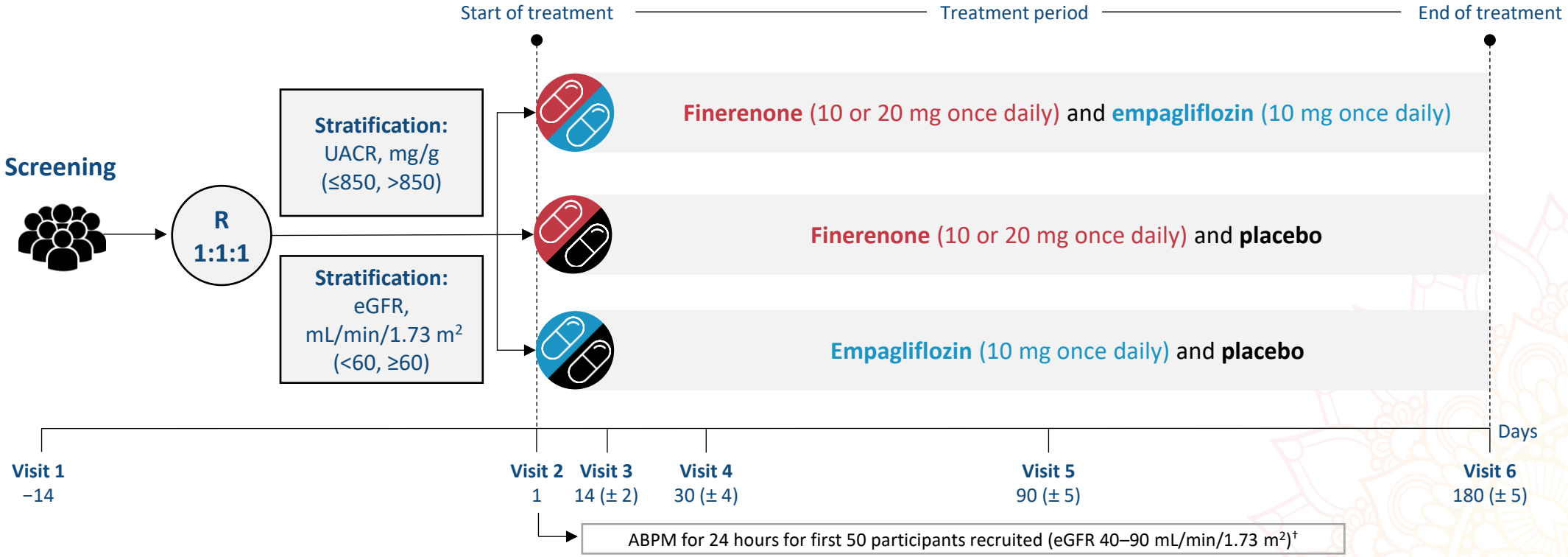
The treatment period spans from Day 1 to Day 180, with study visits on Days 1, 14, 30, 90, and 180



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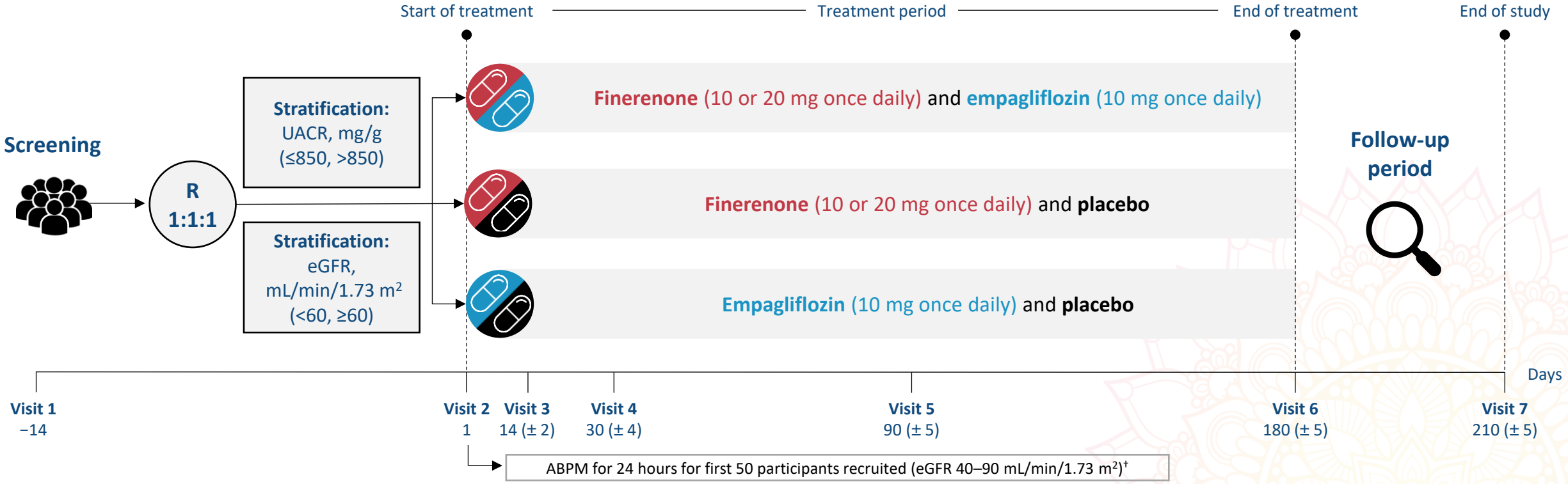
A follow-up/end-of-study visit is scheduled 30 days after the last dose of study drug



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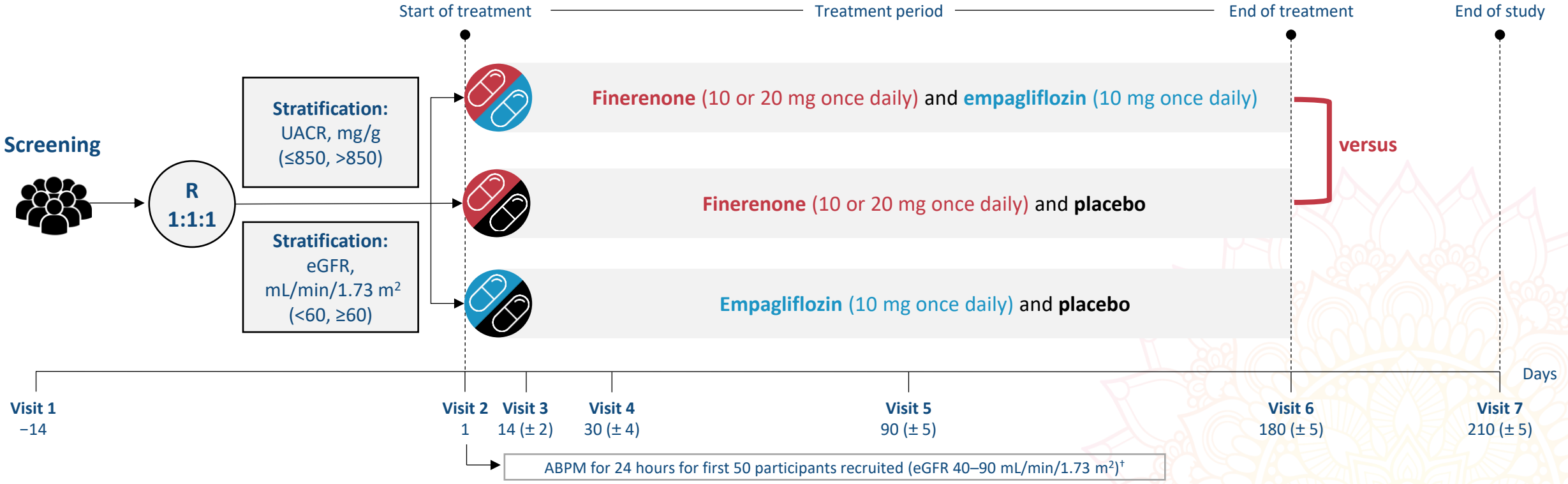
PRIMARY ENDPOINT: RELATIVE CHANGE FROM BASELINE IN UACR AT 180 DAYS



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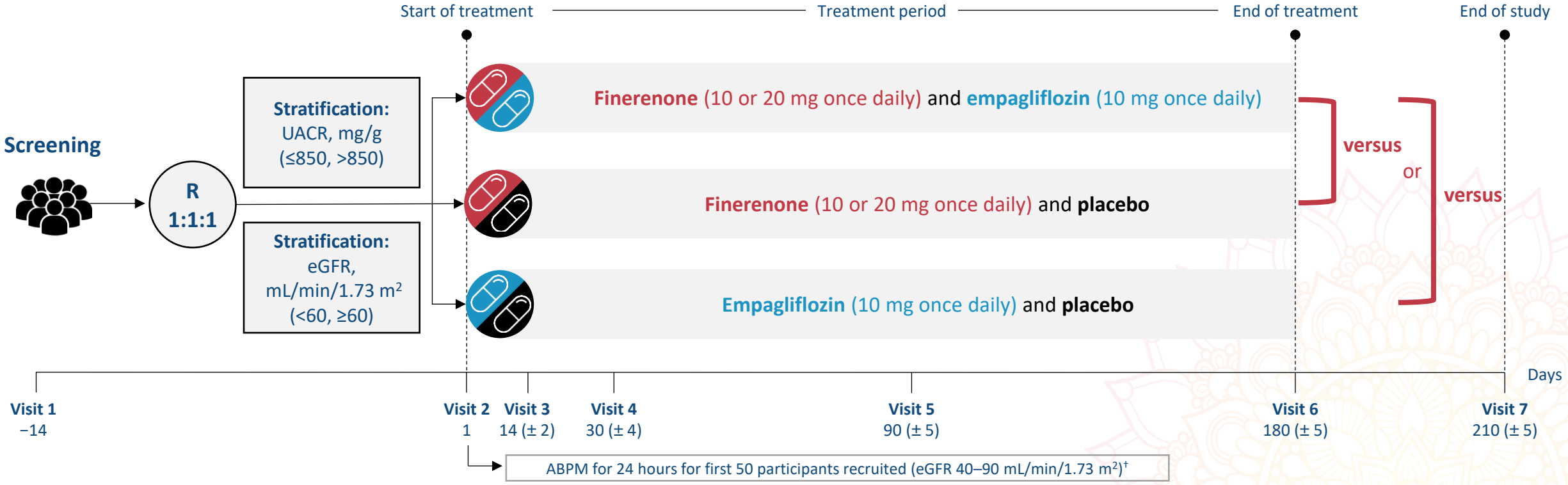

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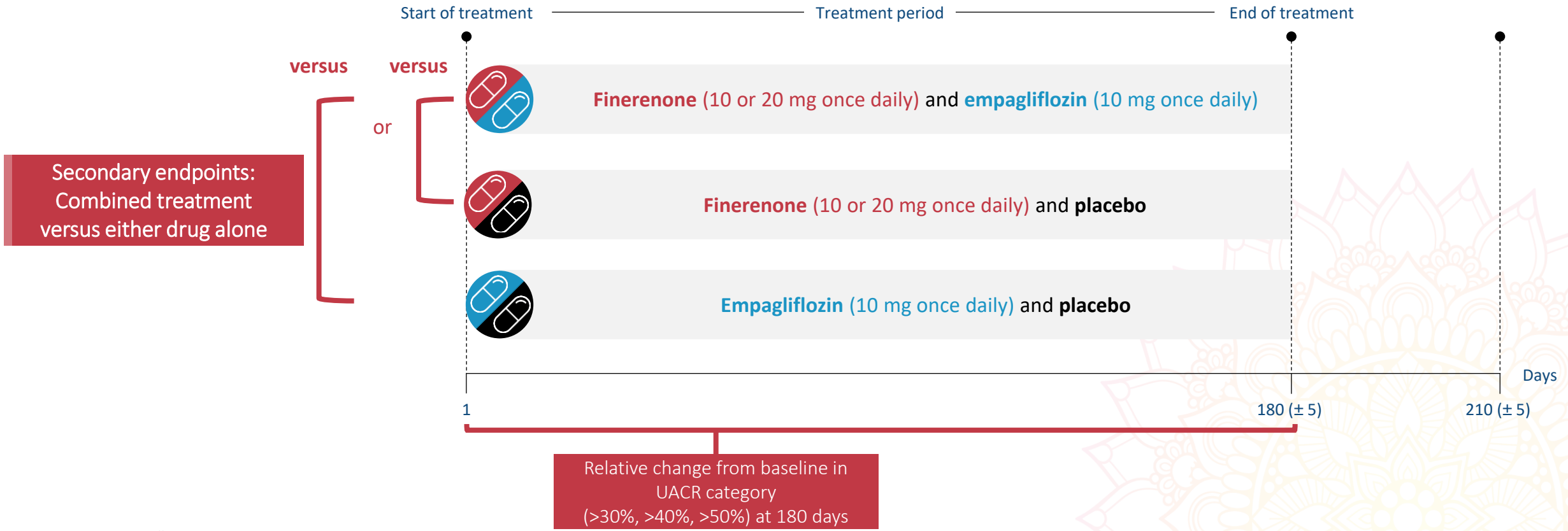
SECONDARY UACR ENDPOINTS



UACR, urinary albumin-to-creatinine ratio.

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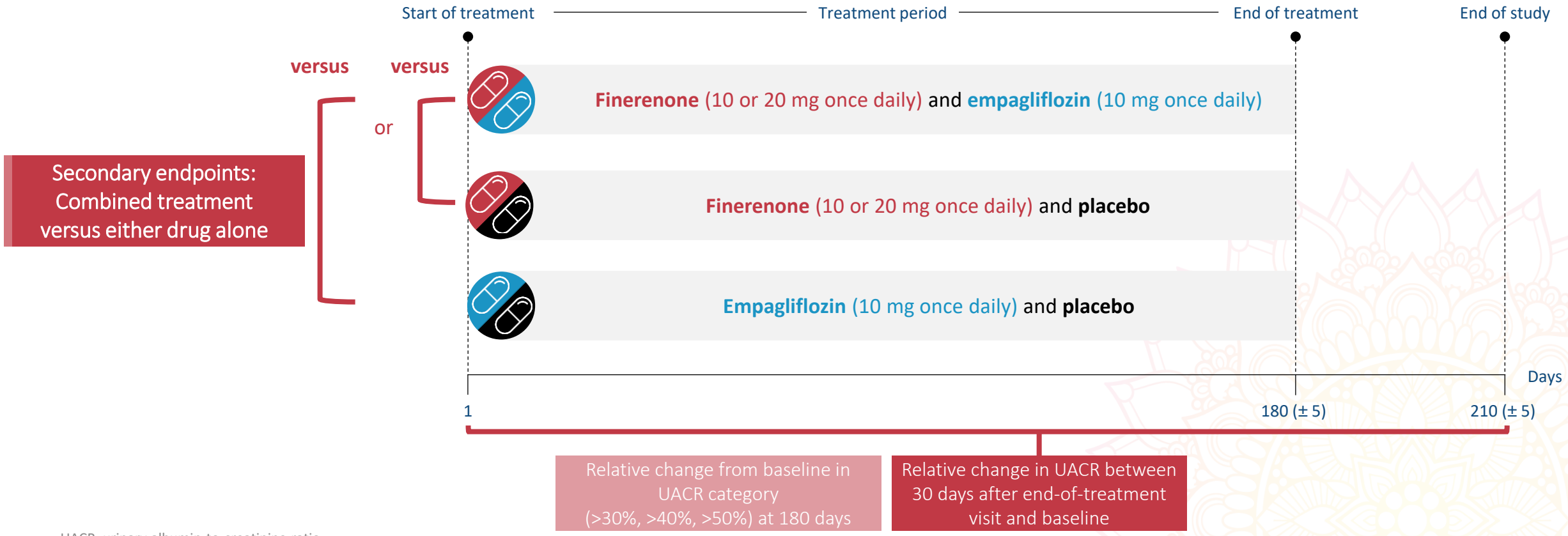

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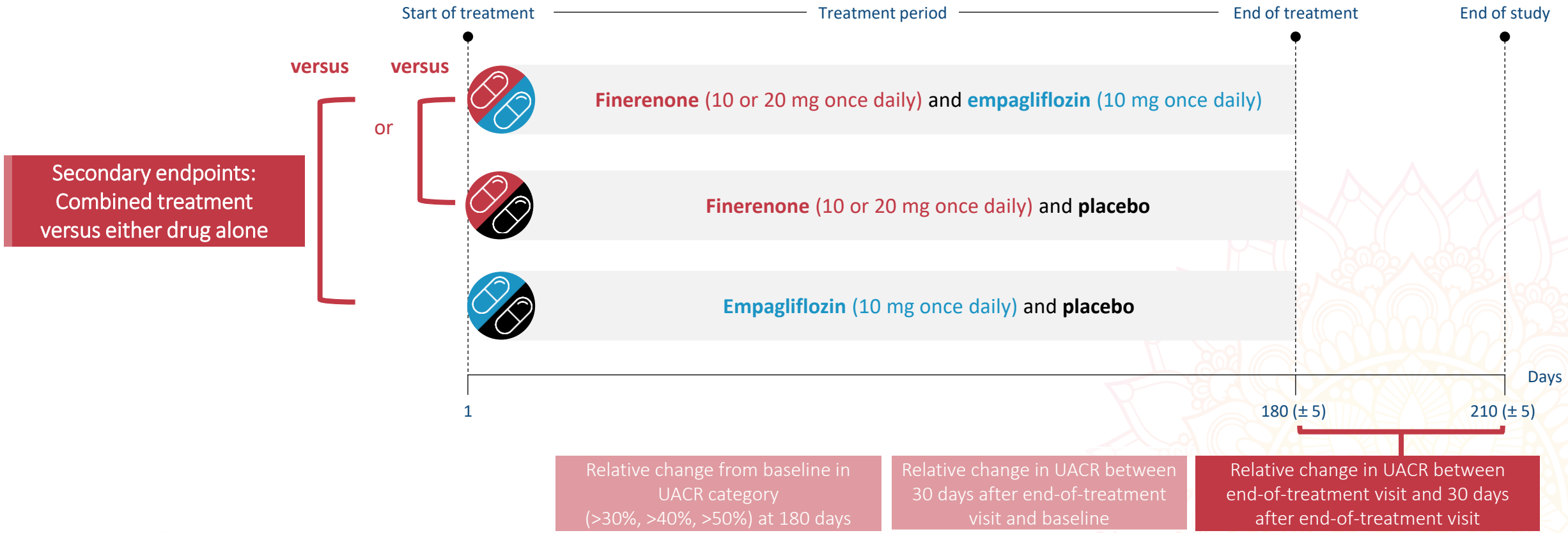

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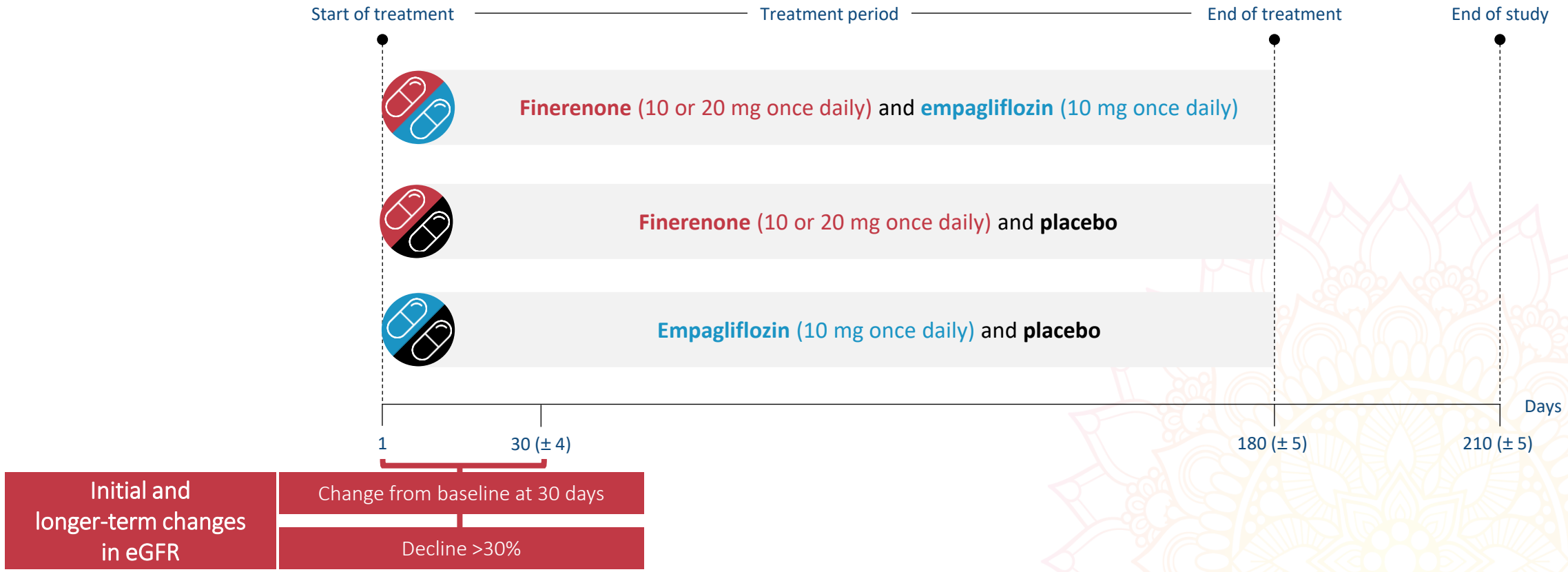
eGFR SAFETY ENDPOINTS



eGFR, estimated glomerular filtration rate.

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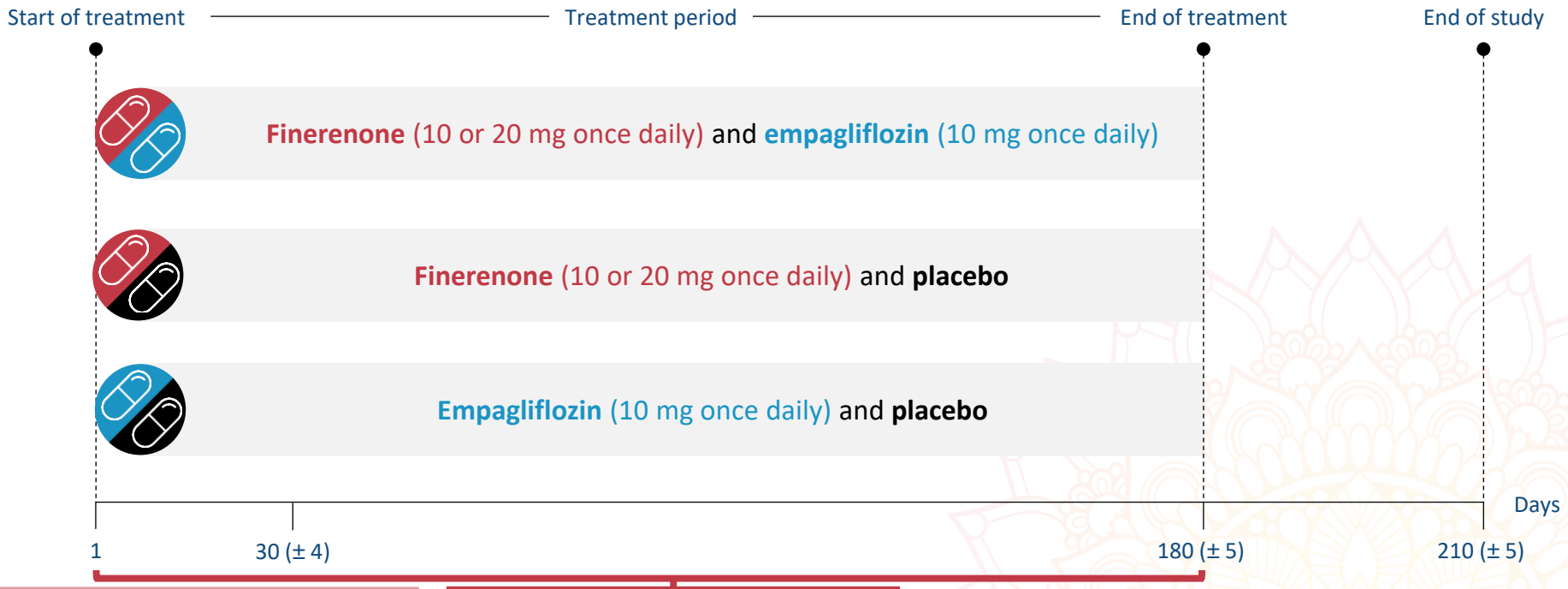

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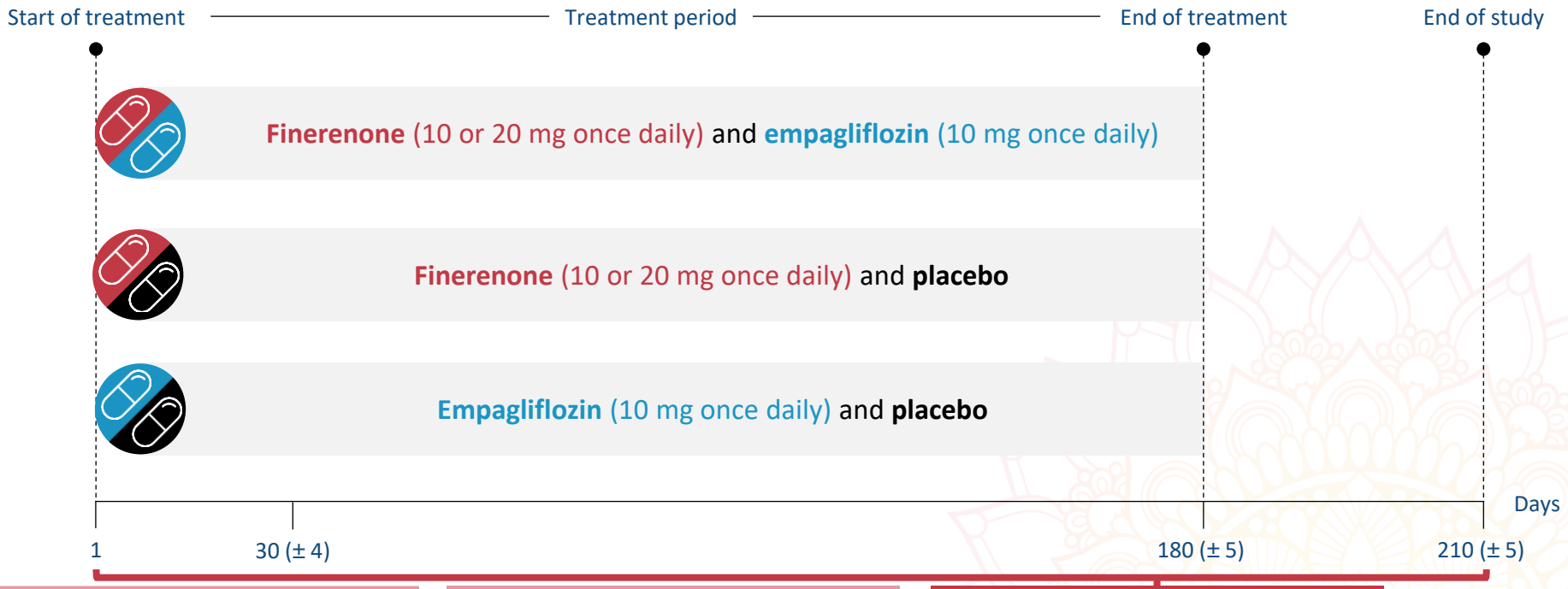

Initial and longer-term changes in eGFR	Change from baseline at 30 days	Change from baseline at 180 days	Change from baseline at 210 days
	Decline >30%		

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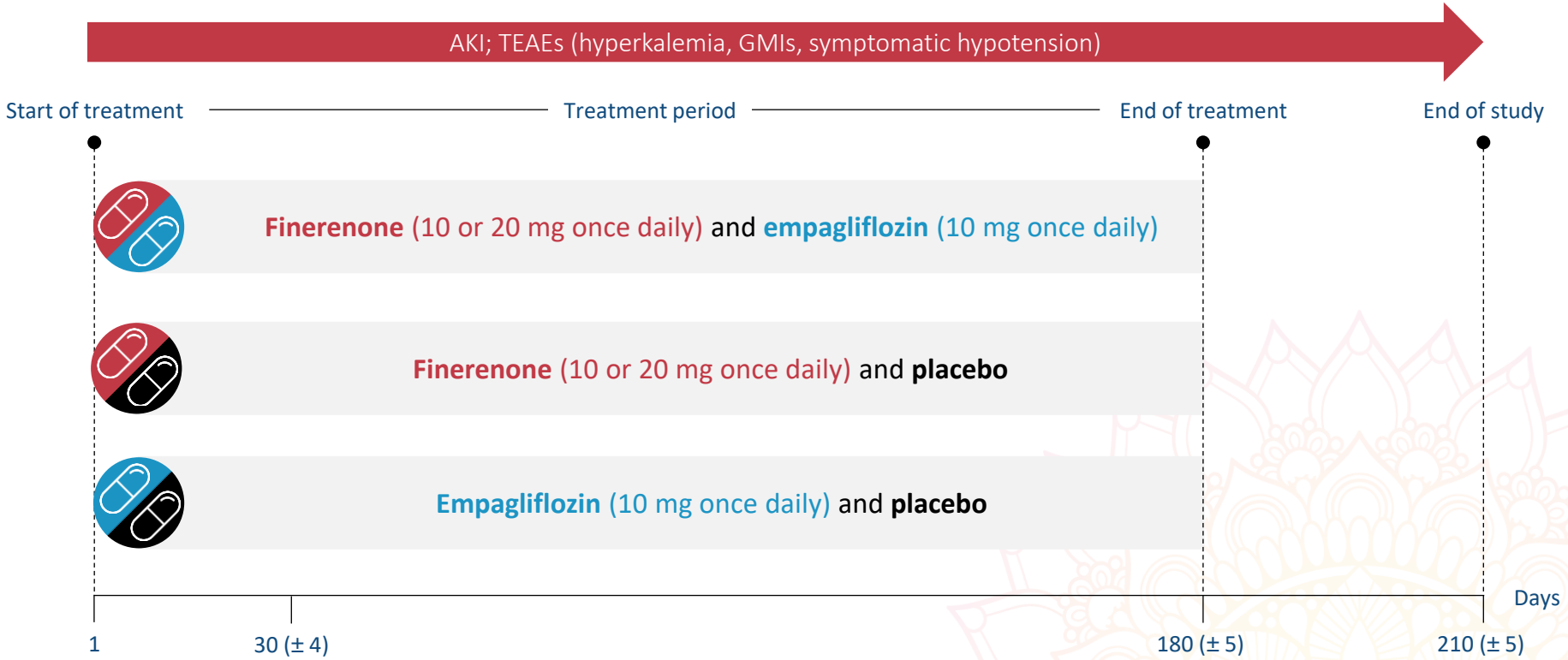
Green JB, et al. *Nephrol Dial Transplant.* 2023;38:894–903. This figure is adapted from Green JB, et al. under the terms of the Creative Commons Attribution-Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0/).

OTHER SAFETY ENDPOINTS



AKI, acute kidney injury; GMI, genital mycotic infection; TEAE, treatment-emergent adverse event.

COMPARISON OF CONFIDENCE INCLUSION CRITERIA WITH OTHER KIDNEY OUTCOME TRIALS OF SGLT2 INHIBITORS AND FINERENONE

INCLUSION CRITERIA: COMPARISON WITH SGLT2 INHIBITOR STUDIES

Criteria	CONFIDENCE[1,2]	CREDENCE[3] (Canagliflozin)	DAPA-CKD[4] (Dapagliflozin)	EMPA-KIDNEY[5] (Empagliflozin)
eGFR (mL/min/1.73 m^2) and/or UACR (mg/g)	eGFR 30 to 90 with a **UACR ≥100** to <5000	eGFR 30 to <90 with a UACR >300 to 5000[†]	eGFR 25 to 75 with a UACR 200 to 5000	eGFR ≥20 to <45 (irrespective of level of albuminuria) or eGFR ≥45 to <90 with a UACR ≥200
With/without T2D	With T2D	With T2D	With or without T2D	With or without T2D
Background therapy	Clinically maximum-tolerated dose of an ACEi or ARB	Stable dose of an ACEi or ARB for at least 4 weeks before randomization	Stable dose of an ACEi or ARB for at least 4 weeks before screening[‡]	Clinically appropriate dose of a single-agent RASi[§]

[†]There was a prespecified plan to include approximately 60% of patients with an eGFR of 30 to <60 mL/min/1.73 m^2; [‡]Participants who were documented to be unable to take ACEIs or ARBs were allowed to participate; [§]Patients could be included, as specified in the protocol, if an investigator judged that a RASi was not indicated or would not be not tolerated.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; RASi, renin–angiotensin system inhibitor; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

1. Green JB, et al. *Nephrol Dial Transplant.* 2023;38:894–903 (supplementary appendix); 2. Clinicaltrials.gov. Available at: https://clinicaltrials.gov/study/NCT05254002 (accessed December 10, 2024);
3. Perkovic V, et al. *N Engl J Med.* 2019;380:2295–2306; 4. Heerspink HJL, et al. *N Engl J Med.* 2020;383:1436–1446; 5. The EMPA-KIDNEY Collaborative Group. *N Engl J Med.* 2023;388:117–127.

INCLUSION CRITERIA: COMPARISON WITH FINERENONE STUDIES

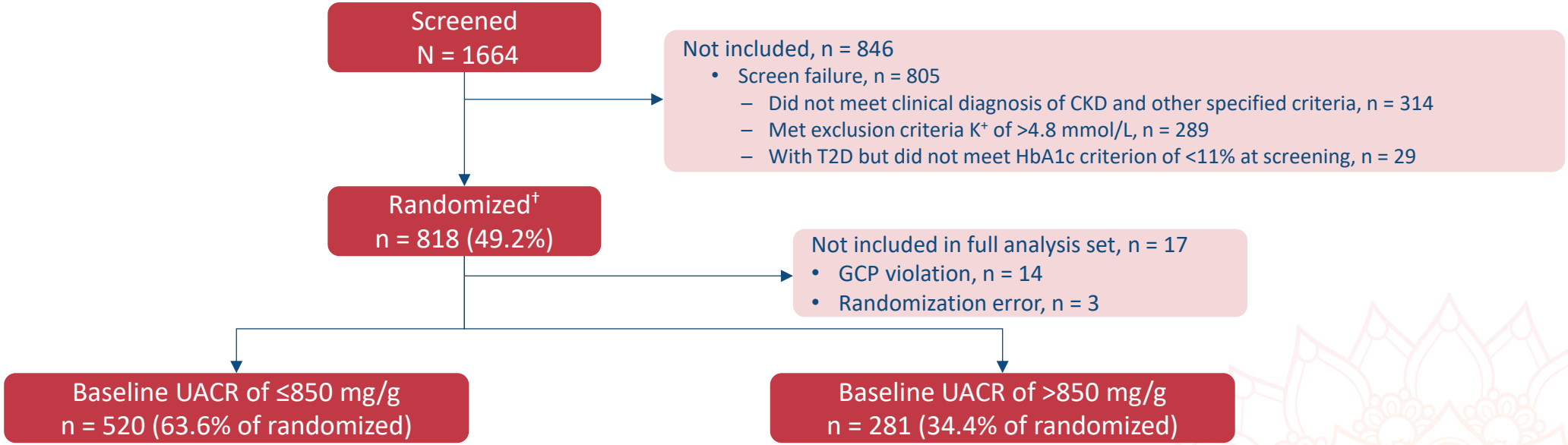
Criteria	CONFIDENCE[1,2]	FIDELIO-DKD[3]	FIGARO-DKD[4]
eGFR (mL/min/1.73 m^2) and/or UACR (mg/g)	eGFR 30 to 90 with a **UACR ≥100** to <5000	eGFR 25 to <60 with a UACR of 30 to <300 or eGFR 25 to <75 with a UACR 300 to 5000	eGFR 25 to 90 with a UACR of 30 to <300 or eGFR ≥60 with a UACR 300 to 5000
With/without T2D	With T2D	With T2D	With T2D
Background therapy	Clinically maximum-tolerated dose of an ACEi or ARB	Stable dose of an ACEi or ARB at the maximum dose on the manufacturer's label that did not cause unacceptable side effects	Stable dose of an ACEi or ARB at the maximum dose on the manufacturer's label that did not cause unacceptable side effects

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

1. Green JB, et al. *Nephrol Dial Transplant.* 2023;38:894–903 (supplementary appendix); 2. Clinicaltrials.gov. Available at: https://clinicaltrials.gov/study/NCT05254002 (accessed December 10, 2024); 3. Bakris GL, et al. *N Engl J Med*. 2020; 383:2219–2229; 4. Pitt B, et al. *N Engl J Med.* 2021; 385:2252–2263.

PARTICIPANT DISPOSITION AND BASELINE DEMOGRAPHICS IN CONFIDENCE

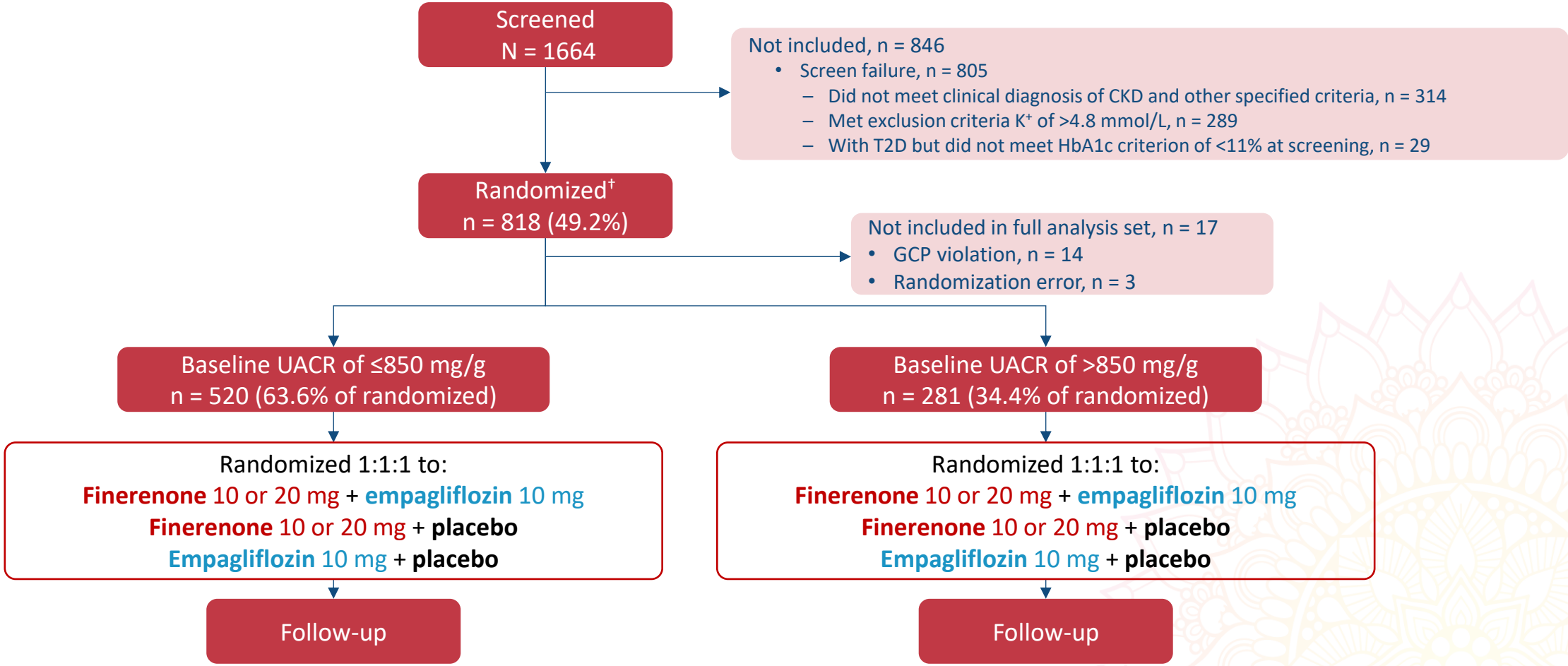
PARTICIPANT DISPOSITION



†Participants were also stratified by eGFR (< or ≥60 mL/min/1.73 m²).

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GCP, Good Clinical Practice; HbA1c, glycated hemoglobin; K+, potassium; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

PARTICIPANT DISPOSITION



†Participants were also stratified by eGFR (< or ≥60 mL/min/1.73 m²).

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; GCP, Good Clinical Practice; HbA1c, glycated hemoglobin; K+, potassium; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

BASELINE DEMOGRAPHICS

Characteristic	Total (N = 801)†
Age, mean years	66.5
Female, %	25
Race, %‡	
Asian	46
Asian Indian	17
White	44
Black/African American	8
Other	<1
Ethnicity, %§	
Hispanic or Latino	10
Not Hispanic or Latino	89
Region, %	
Asia	45
North America	28
Europe	27

Characteristic	Total (N = 801)†
Smoking history, %	
Current smoker	15
BMI, mean kg/m^2	29
Body weight, mean kg	82
SBP, mean mmHg	135
DBP, mean mmHg	77
Hemoglobin, mean g/dL	12.9
HbA1c, %	7.3
Serum potassium, mean mmol/L	4.5

†There were 17 randomized participants excluded from the full analysis set due to GCP violations or randomization errors; ‡Race was not reported for 5 (<1%) participants; §Ethnicity was not reported for 5 (<1%) participants.
BMI, body mass index; DBP, diastolic blood pressure; GCP, Good Clinical Practice; HbA1c, glycated hemoglobin; SBP, systolic blood pressure.

BASELINE DEMOGRAPHICS BY UACR SUBGROUP

Characteristic	UACR subgroup	
	≤850 mg/g (n = 520)	>850 mg/g (n = 281)
Age, mean years	68	**64**
Race, %		
Asian	41	**56**
Asian Indian	14	**22**
White	48	37
Black/African American	10	6
Other	<1	1
Region, %		
Asia	40	**55**
North America	30	24
Europe	30	21
HbA1c, %	7.2	**7.5**

HbA1c, glycated hemoglobin; UACR, urinary albumin-to-creatinine ratio.

COMPARISON OF CONFIDENCE BASELINE CHARACTERISTICS WITH OTHER KIDNEY OUTCOME TRIALS OF SGLT2 INHIBITORS AND FINERENONE

SGLT2, sodium-glucose co-transporter-2.

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS IN PARTICIPANTS WITH CKD AND T2D BY STUDY

Characteristic	CONFIDENCE (N = 801)
Age, mean years	67
Women, %	25
Current smoker, %	15
BMI, mean kg/m^2	29
Body weight, mean kg	82
SBP, mean mmHg	135
DBP, mean mmHg	77
HbA1c, %	7.3

BMI, body mass index; CKD, chronic kidney disease; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; T2D, type 2 diabetes.

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS: COMPARISON WITH SGLT2 INHIBITOR STUDIES

Characteristic	CONFIDENCE (N = 801)	CREDENCE[1] (Canagliflozin) (N = 4401)	DAPA-CKD[2] (Dapagliflozin) (N = 2906)†	EMPA-KIDNEY[3] (Empagliflozin) (N = 3039)†
Age, mean years	67	63	64	69
Women, %	25	34	33	33
Current smoker, %	15	15	-	-
BMI, mean kg/m^2	29	31	30	32
Body weight, mean kg	82	87	-	-
SBP, mean mmHg	135	140	139	139
DBP, mean mmHg	77	78	77	76
HbA1c, %	7.3	8.3	7.8	7.2

†Data are shown for participants with T2D only.

BMI, body mass index; CKD, chronic kidney disease; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; SBP, systolic blood pressure; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes.

1. Perkovic V, et al. *N Engl J Med.* 2019;380:2295–2306 (supplementary appendix); 2. Wheeler DC, et al. *Nephrol Dial Transplant*. 2020;35:1700–1711; 3. The EMPA-KIDNEY Collaborative Group. *Nephrol Dial Transplant.* 2022;37:1317–1329.

BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS: COMPARISON WITH FINERENONE STUDIES

Characteristic	CONFIDENCE (N = 801)	FIDELIO-DKD[1] (N = 5674)	FIGARO-DKD[2] (N = 7352)
Age, mean years	67	66	64
Women, %	25	30	31
Current smoker, %	15	14	18
BMI, mean kg/m^2	29	31	31
Body weight, mean kg	82	87	89
SBP, mean mmHg	135	138	136
DBP, mean mmHg	77	76	77
HbA1c, %	7.3	7.7	7.7

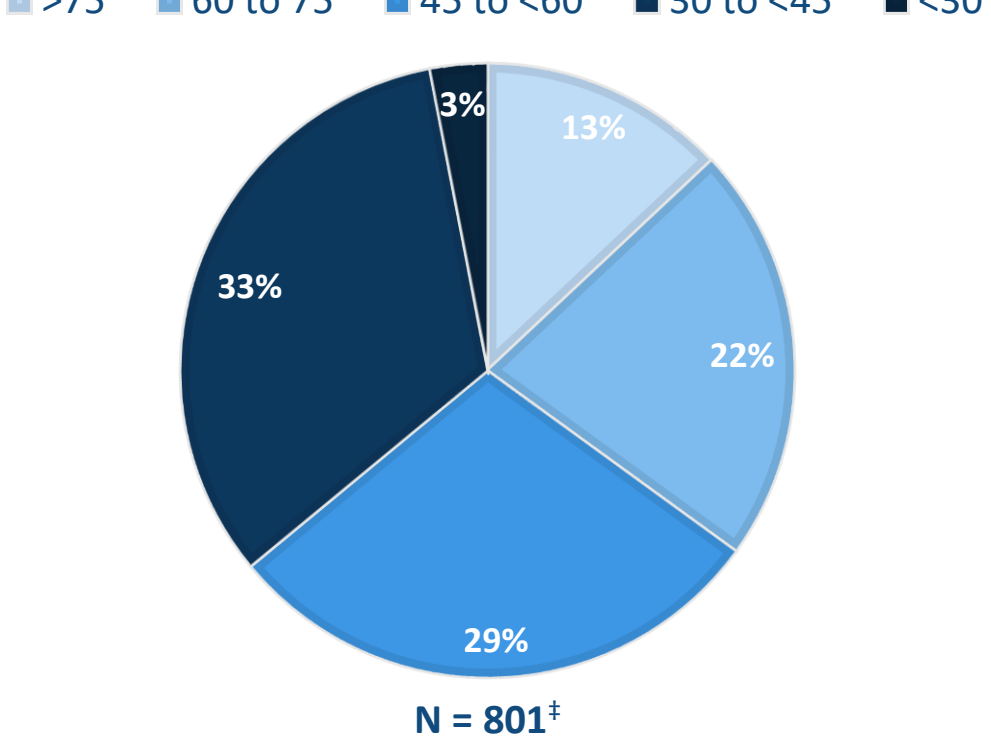
BMI, body mass index; DBP, diastolic blood pressure; DKD, diabetic kidney disease; HbA1c, glycated hemoglobin; SBP, systolic blood pressure.

1. Bakris GL, et al. *N Engl J Med*. 2020;383:2219–2229; 2. Pitt B, et al. *N Engl J Med.* 2021;385:2252–2263.

KIDNEY DISEASE CHARACTERISTICS IN CONFIDENCE

Mean eGFR[†]: 54 mL/min/1.73 m^2

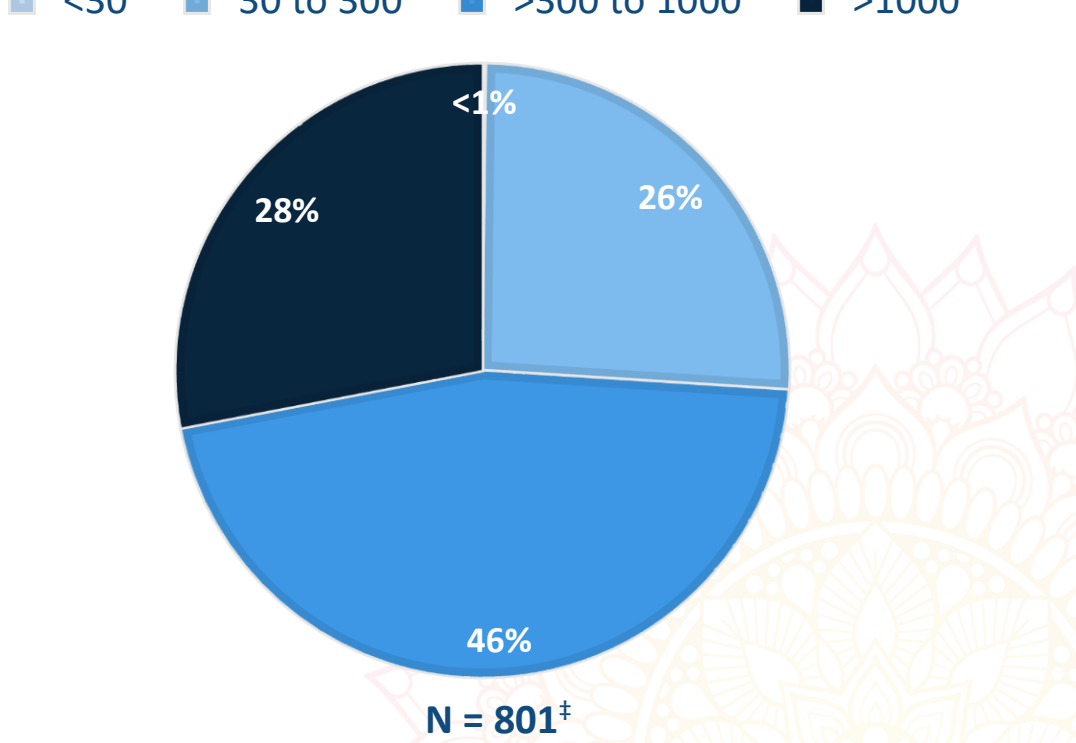
Distribution of eGFR categories



N = 801[‡]

Median UACR[§]: 583 mg/g

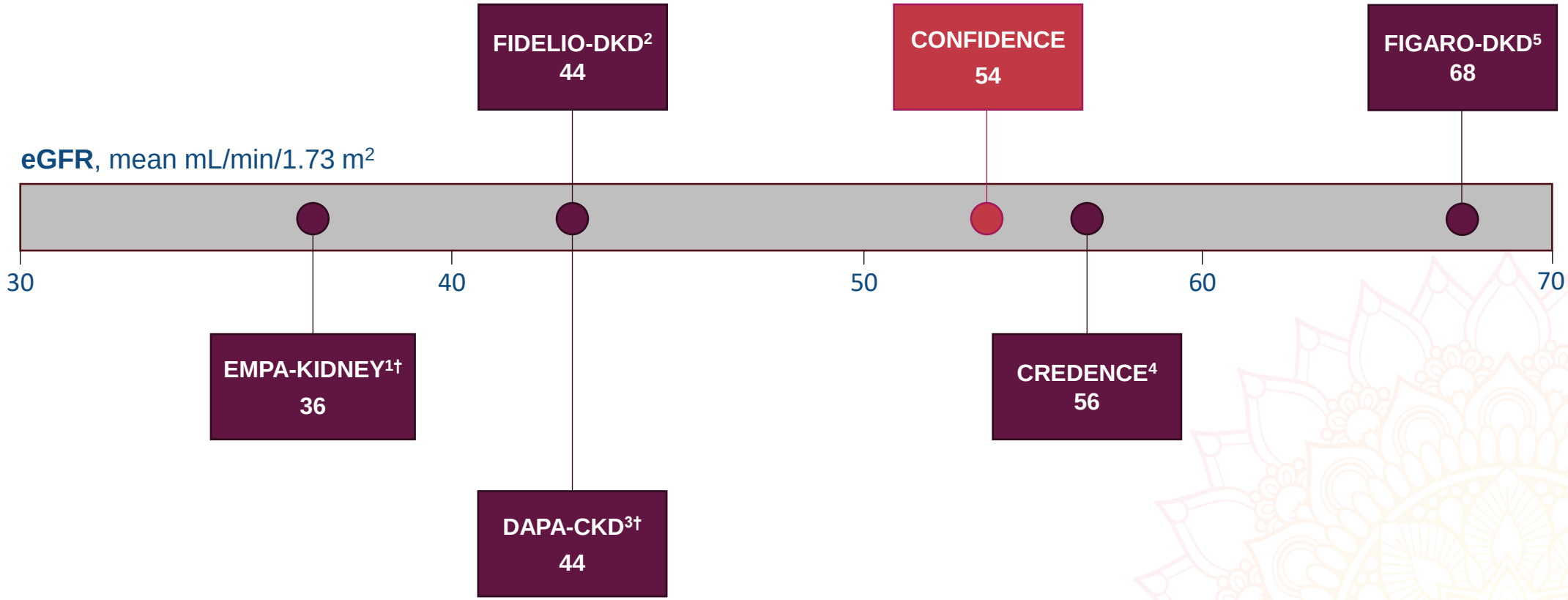
Distribution of albuminuria categories



N = 801[‡]

[†]Calculated by the CKD-EPI equation[1] with a modification for Japanese participants[2]; [‡]There were 17 randomized participants excluded from the full analysis set due to GCP violations or randomization errors;
[§]UACR may have decreased for participants between the screening and randomization visits.
CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; GCP, Good Clinical Practice; UACR, urinary albumin-to-creatinine ratio.
1. Levey AS, et al. *Am J Kidney Dis.* 2020;75:84–104; 2. Horio M, et al. *Am J Kidney Dis*. 2010;56:32–38.

eGFR IN PARTICIPANTS WITH CKD AND T2D BY STUDY

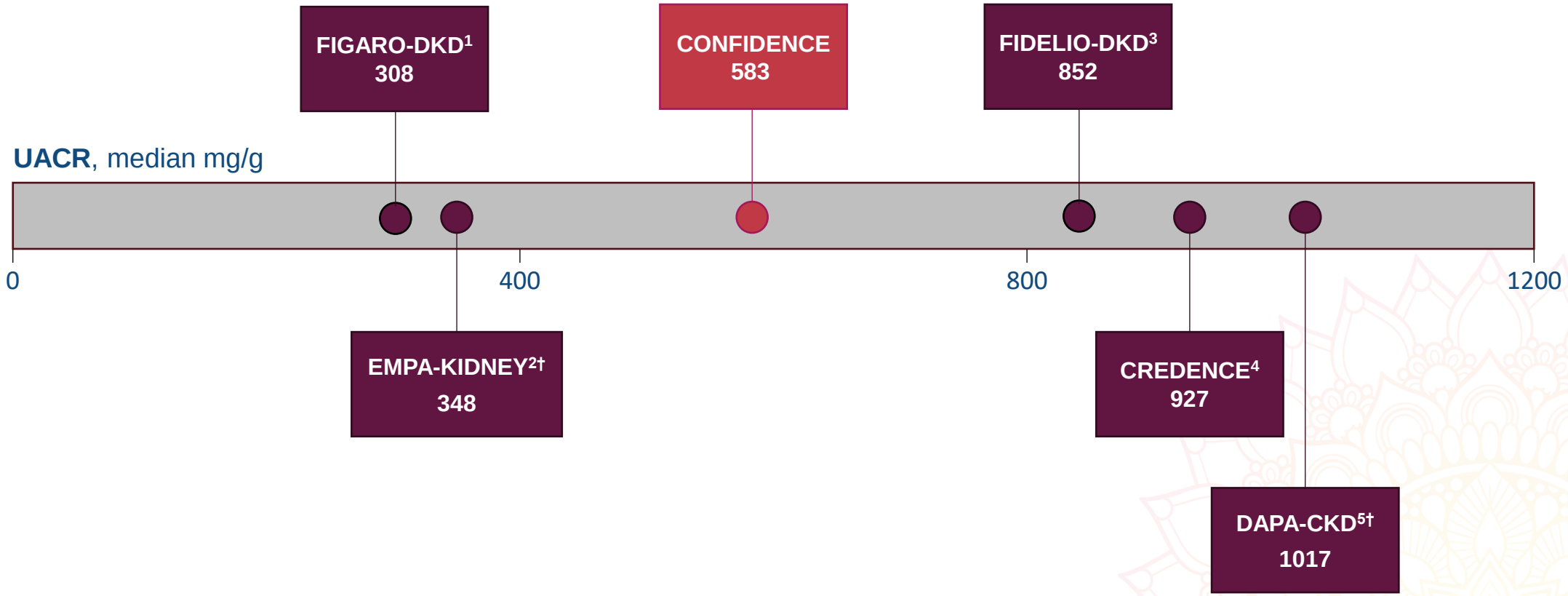


[†]Data are shown for participants with T2D only.

CKD, chronic kidney disease; DKD, diabetic kidney disease; eGFR, estimated glomerular filtration rate; T2D, type 2 diabetes.

1. The EMPA-KIDNEY Collaborative Group. *Nephrol Dial Transplant*. 2022;37:1317–1329; 2. Bakris GL, et al. *N Engl J Med*. 2020; 383:2219–2229; 3. Wheeler DC, et al. *Nephrol Dial Transplant*. 2020;35:1700–1711; 4. Perkovic V, et al. *N Engl J Med*. 2019;380:2295–2306; 5. Pitt B, et al. *N Engl J Med*. 2021;385:2252–2263.

UACR IN PARTICIPANTS WITH CKD AND T2D BY STUDY



[†]Data are shown for participants with T2D only.

CKD, chronic kidney disease; DKD, diabetic kidney disease; T2D, type 2 diabetes; UACR, urinary albumin-to-creatinine ratio.

1. Pitt B, et al. *N Engl J Med.* 2021;385:2252–2263; 2. The EMPA-KIDNEY Collaborative Group. *Nephrol Dial Transplant.* 2022;37:1317–1329; 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. Wheeler DC, et al. *Nephrol Dial Transplant*. 2020;35:1700–1711.

MEDICAL HISTORY OF CV AND MICROVASCULAR DISEASE

Characteristic	Total (N = 801)†
Medical history, %‡	
Hypertension	88
ASCVD	28
Coronary artery disease	17
Myocardial infarction	5
Stroke	8
Peripheral arterial disease	7
Diabetic retinopathy	16
Atrial fibrillation	6
Heart failure	4

†There were 17 randomized participants excluded from the full analysis set due to GCP violations or randomization errors; ‡Coded using the MedDRA dictionary.
ASCVD, atherosclerotic cardiovascular disease; CV, cardiovascular; GCP, Good Clinical Practice; MedDRA, Medical Dictionary for Regulatory Activities.

CONCOMITANT MEDICATIONS AND ANTIHYPERGLYCEMIC AGENTS

Characteristic	Total (N = 801)†
Concomitant medications, %	
ACEi/ARB‡	98
Calcium channel blockers	61
Statins	39
Antiplatelet agents	40
Beta-blockers	35
Diuretics	36
Potassium-lowering agents	<1
Potassium supplements	<1

Characteristic	Total (N = 801)†
Antihyperglycemic agents, %	
Insulin	39
GLP-1 RAs	23
Oral hypoglycemic agents	
Metformin	60
DPP-4 inhibitors	31
Sulfonylureas	24

†There were 17 randomized participants excluded from the full analysis set due to GCP violations or randomization errors; ‡According to the protocol, all patients were required to use an ACEi or ARB at the clinically maximum-tolerated dose.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; DPP-4, dipeptidyl peptidase-4; GCP, Good Clinical Practice; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

MEDICAL HISTORY AND CONCOMITANT MEDICATIONS: COMPARISON WITH OTHER STUDIES

Characteristic	CONFIDENCE[1] (N = 801)
Medical history, %	
ASCVD or CVD	28[†]
Heart failure	4
Diabetic retinopathy	16
Concomitant medications, %	
ACEis/ARBs	98
GLP-1 RAs	23
Insulin and analogues	39
DPP-4 inhibitors	31
Metformin	60
Statins	39
Antiplatelets	40

[†]ASCVD; [‡]Data are shown for participants with T2D only.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DPP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; T2D, type 2 diabetes.

1. Green JB, et al. *Nephrol Dial Transplant.* 2023;38:894–903; 2. Perkovic V, et al. *N Engl J Med.* 2019;380:2295–2306 (supplementary appendix); 3. Wheeler DC, et al. *Nephrol Dial Transplant*. 2020;35:1700–1711;
4. The EMPA-KIDNEY Collaborative Group. *Nephrol Dial Transplant.* 2022;37:1317–1329 (supplementary appendix); 5. Agarwal R, et al. *Eur Heart J*. 2022;43:474–484.

MEDICAL HISTORY AND CONCOMITANT MEDICATIONS: COMPARISON WITH OTHER STUDIES

Characteristic	CONFIDENCE[1] (N = 801)	CREDENCE[2] (N = 4401)	DAPA-CKD[3] (N = 2906)‡	EMPA-KIDNEY[4] (N = 3039)‡	FIDELITY[5] (N = 13,026)
Medical history, %					
ASCVD or CVD	28†	50	44	36	46
Heart failure	4	15	12	14	8
Diabetic retinopathy	16	43	-	-	38
Concomitant medications, %					
ACEis/ARBs	98	>99	98	85	>99
GLP-1 RAs	23	4	4	10	7
Insulin and analogues	39	66	55	55	59
DPP-4 inhibitors	31	17	26	26	25
Metformin	60	58	43	22	58
Statins	39	69	-	-	72
Antiplatelets	40	-	53	48	56

†ASCVD; ‡Data are shown for participants with T2D only.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; CVD, cardiovascular disease; DPP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; T2D, type 2 diabetes.

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CONFIDENCE STUDY: CONCLUSIONS

The high rates of morbidity and mortality associated with CKD in T2D highlight the unmet need for additional effective treatments for slowing CKD progression. People with both CKD and T2D are at high risk of adverse clinical outcomes because of the additive, detrimental effects of these conditions[1]

CKD, chronic kidney disease; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes.

1. Afkarian M, et al. *J Am Soc Nephrol*. 2013;24:302–308.

CONFIDENCE STUDY: CONCLUSIONS

The high rates of morbidity and mortality associated with CKD in T2D highlight the unmet need for additional effective treatments for slowing CKD progression. People with both CKD and T2D are at high risk of adverse clinical outcomes because of the additive, detrimental effects of these conditions[1]

CONFIDENCE, the first randomized trial to examine combination therapy comprising finerenone and an SGLT2 inhibitor in people with CKD and T2D, will provide the evidence to determine the potential role of simultaneous initiation of finerenone and SGLT2 inhibitors to better inform the care of people in this population

CKD, chronic kidney disease; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes.

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Full details on the baseline characteristics of the CONFIDENCE study are published here:

CKD, chronic kidney disease; SGLT2, sodium–glucose cotransporter 2; T2D, type 2 diabetes.

1. Afkarian M, et al. *J Am Soc Nephrol*. 2013;24:302–308.

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