Aldosterone Inhibition in Kidney Diseases: the Old, the New, and the Promise

12/6 (Sat.) 10:00-10:15

Dr. Tai-Shuan Lai

National Taiwan University Hospital, Taiwan

Disclosure

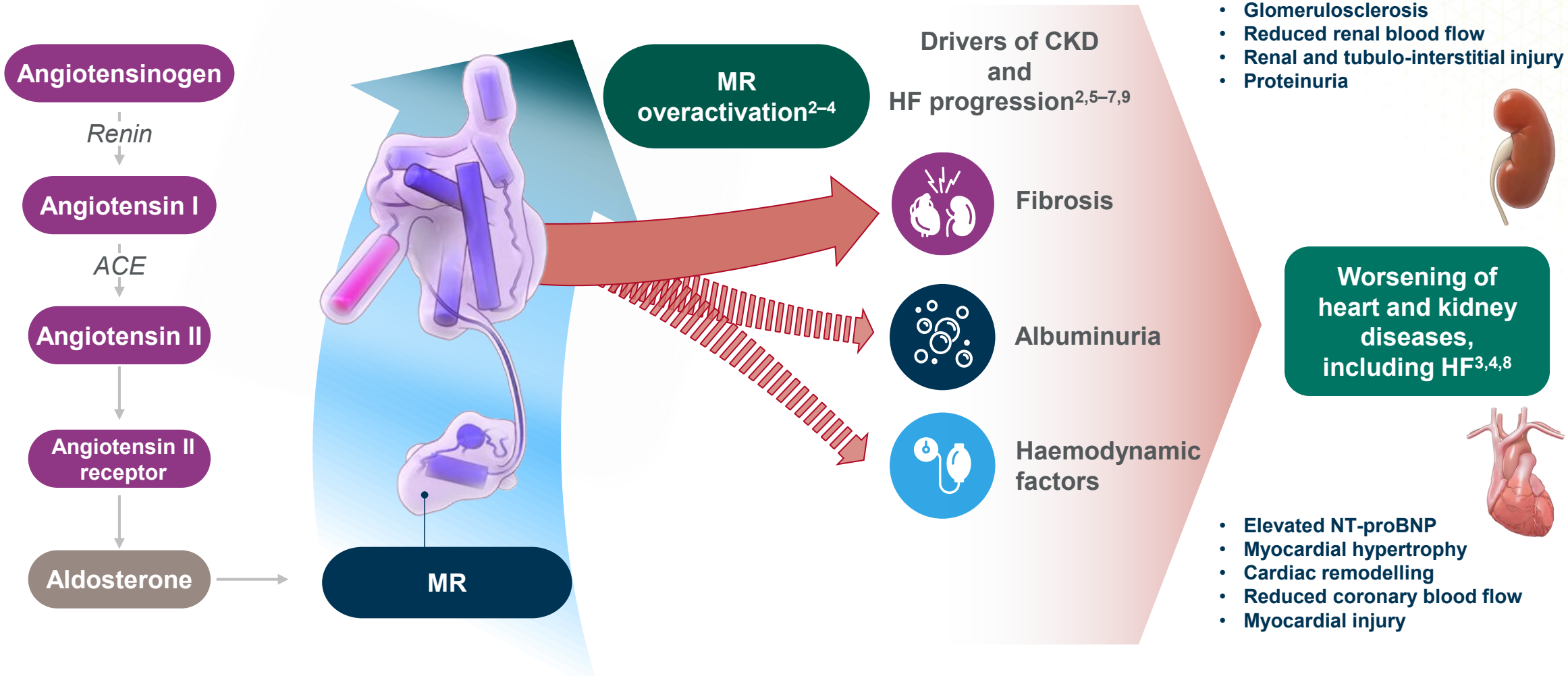
- I have nothing to disclose

Outlines

- MR Overactivation in CKD and MoA of nsMRA
- Current evidence of nsMRA, finerenone
- ASI, a new weapon for aldosterone inhibition?
- Ongoing clinical trials of nsMRAs and ASis in CKD management

MR Overactivation in CKD

Drivers of CKD progression include fibrosis, albuminuria and haemodynamic factors, all associated with MR overactivation[1–9]



1. Fountain JH, *et al*. Physiology, renin angiotensin system. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2023;
2. Bauersachs J, *et al*. *Hypertension* 2015;65:257–263; 3. Kolkhof P, *et al. Handb Exp Pharmacol* 2017;243:271–305; 4. Barrera-Chimal J, *et al. Kidney Int* 2019;96:302–319;
5. Alicic RZ, *et al*. *Clin J Am Soc Nephrol* 2017;12:2032–2045; 6. Mora-Fernández C, *et al*. *J Physiol* 2014;592:3997–4012; 7. Hahn VS, *et al. JACC Heart Fail* 2020;8:712–724;
8. Buonafine M, *et al. Am J Hypertens* 2018;31:1165–1174; 9. Khan MS, *et al. JACC Rev* 2023; 81:270–282

MR signalling has adverse effects on inflammation and kidney fibrosis

MR activation promotes inflammation and fibrosis via different mechanisms

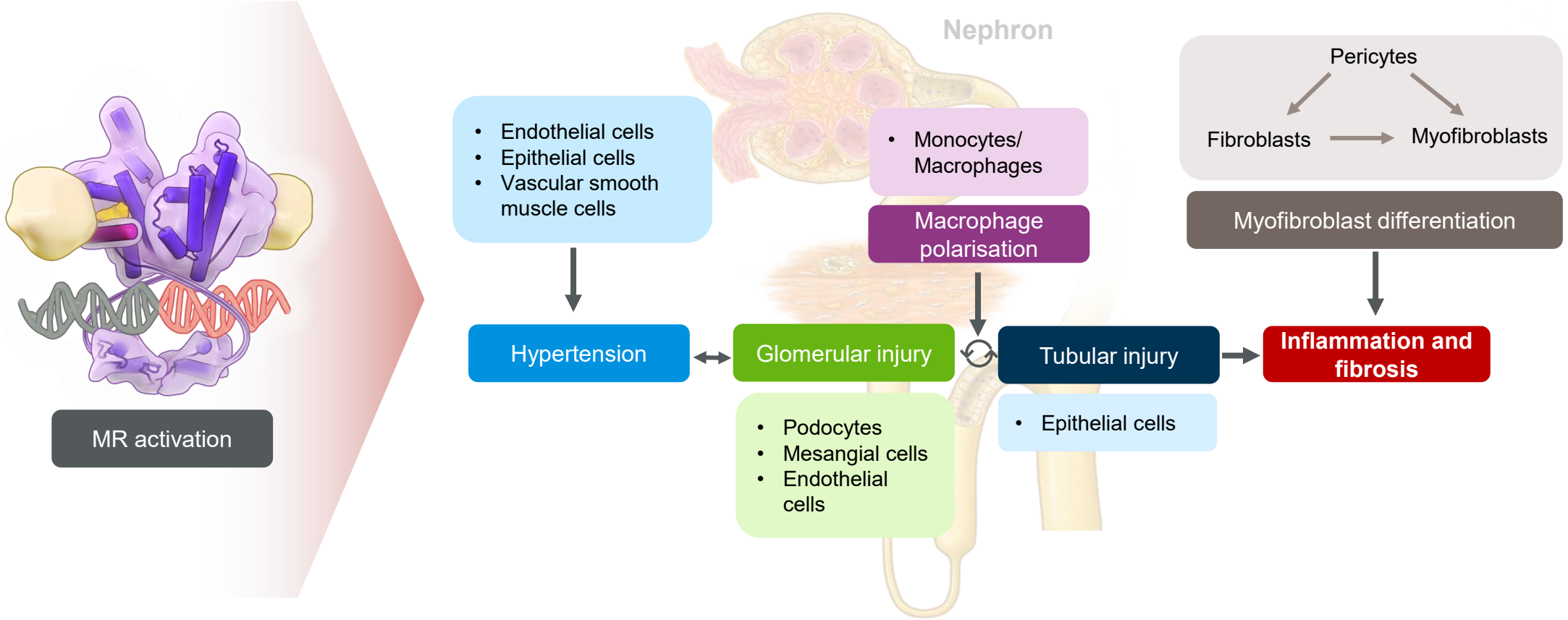
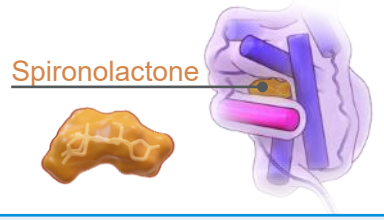
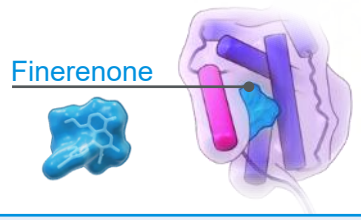


Figure adapted from Luther JM & Fogo AB. *Kidney Int Suppl* 2022;12:63–68

MRAs: steroidal versus nonsteroidal

	Steroidal MRAs[1]		Kerendia (finerenone)[1]
			
Structural properties	Flat (steroidal)	Flat (steroidal)	Bulky (nonsteroidal)
Potency to MR	+++	+	+++
Selectivity to MR	+	++	+++
CNS penetration	+	+	–
Half-life	**Long (>20 h)#**	**Medium/short (4–6 h)#**	**Short (2–3 h)‡**
Active metabolites	++	–	–
Sexual side effects	++	(+)	–
Effect on BP	+++	++	+
Tissue distribution	Kidney > heart (at least 6-fold)[2,3]	Kidney > heart (~3-fold)[2,3]	Balanced kidney : heart (1:1)[2,3]
Indication (TFDA)	**Edema, hypertension, PA[4]**	**HFrEF post-AMI, chronic HFrEF[5]**	**CKD associated with T2D[6]**

*Most of the available evidence exploring these differences is available for the nonsteroidal MRA finerenone. Other nonsteroidal MRAs have different physicochemical and pharmacological properties, but corresponding comparisons within this class are pending due to missing data; #observed in HF patients; ‡in healthy volunteers

BP, blood pressure; CKD, chronic kidney disease; CNS, central nervous system; HF, heart failure; LVEF, left ventricular ejection fraction; MR, mineralocorticoid receptor; MRA, mineralocorticoid receptor antagonist; T2D, type 2 diabetes; TFDA, Taiwan Food and Drug Administration

1. Kintscher U, *et al. Br J Pharmacol* 2022;179:3220–3234; 2. Kolkhof P, *et al. Curr Opin Nephrol Hypertens* 2015;24:417–424; 3. Kolkhof P, *et* al. *Handb Exp Pharmacol*. 2017;243:271-305; 4. Pfizer Pharmaceuticals Co., Ltd. ALDACTONE® (spironolactone) Prescription Information. 2021. https://info.fda.gov.tw/MLMS/H0001D3.aspx?LicId=02022610 [accessed 14 November 2022]; 5. Pfizer Pharmaceuticals Co., Ltd. INSPRA® (eplerenone). Prescription Information. 2020. https://info.fda.gov.tw/MLMS/H0001D3.aspx?LicId=02024305 [accessed 14 November 2022]; 6. Bayer Taiwan Co., Ltd. KERENDIA® (finerenone) Prescription Information. 2023. https://mcp.fda.gov.tw/im_detail_1/%E8%A1%9B%E9%83%A8%E8%97%A5%E8%BC%B8%E5%AD%97%E7%AC%AC028325%E8%99%9F and https://mcp.fda.gov.tw/im_detail_1/%E8%A1%9B%E9%83%A8%E8%97%A5%E8%BC%B8%E5%AD%97%E7%AC%AC028326%E8%99%9F [accessed 20 April 2023]

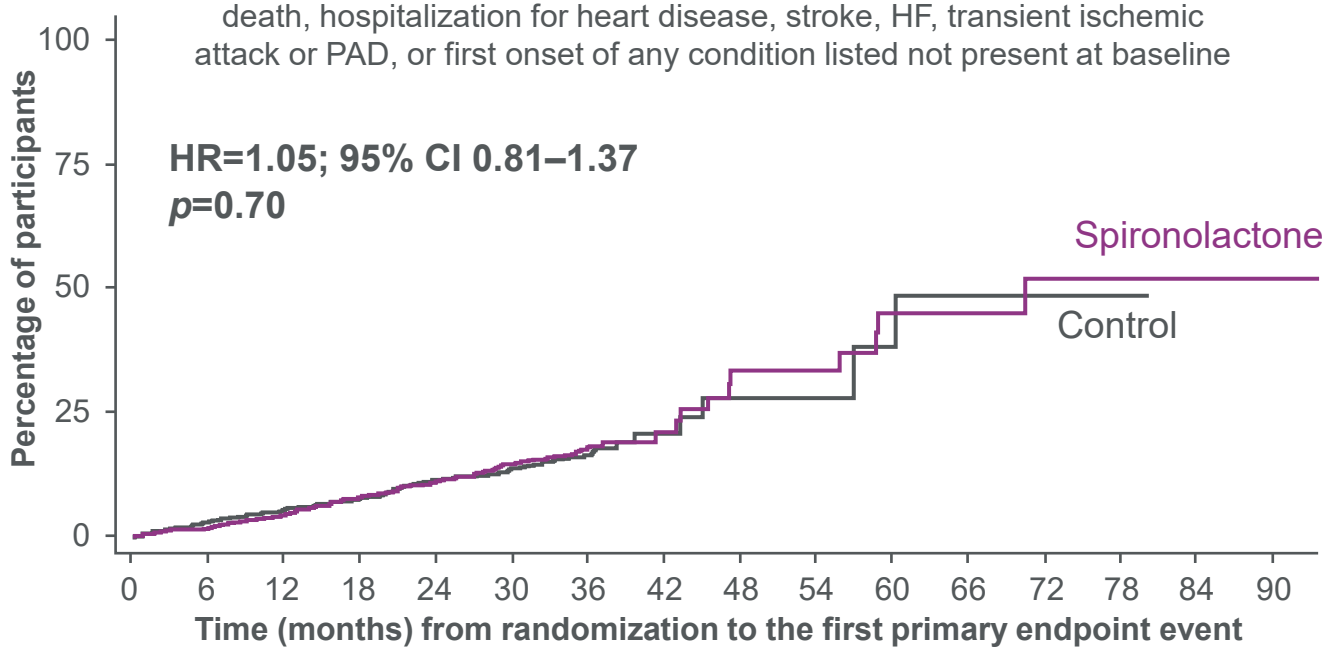
Spironolactone has failed to show kidney or CV protection in patients with CKD

BARACK-D (N=1372 patients with stage 3b CKD)*[1]

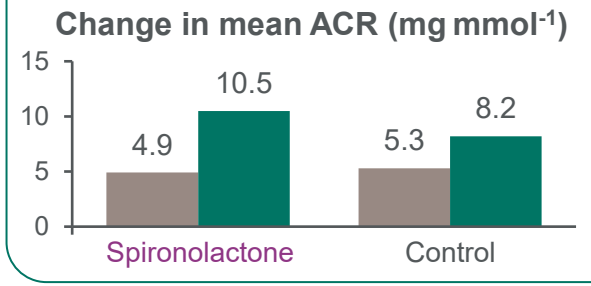
NOTE: Spironolactone also failed to prevent progression to microalbuminuria in patients with T2D at high risk of CKD[2]

No evidence was found for a reduction in adverse CV outcomes with spironolactone[1]

Primary endpoint: time from randomization until the first occurrence of death, hospitalization for heart disease, stroke, HF, transient ischemic attack or PAD, or first onset of any condition listed not present at baseline



Spironolactone was not associated with improvements in kidney function[1]



Adjusted treatment effect, mg mmol^{-1} (95% CI):
1.03 (-1.50 to -1.59)
***p*=0.897**

Spironolactone was frequently discontinued due to safety concerns[1]

455 patients randomized to spironolactone had treatment withdrawn due to safety concerns

35.4% (n=239) = decrease in eGFR meeting stop criteria

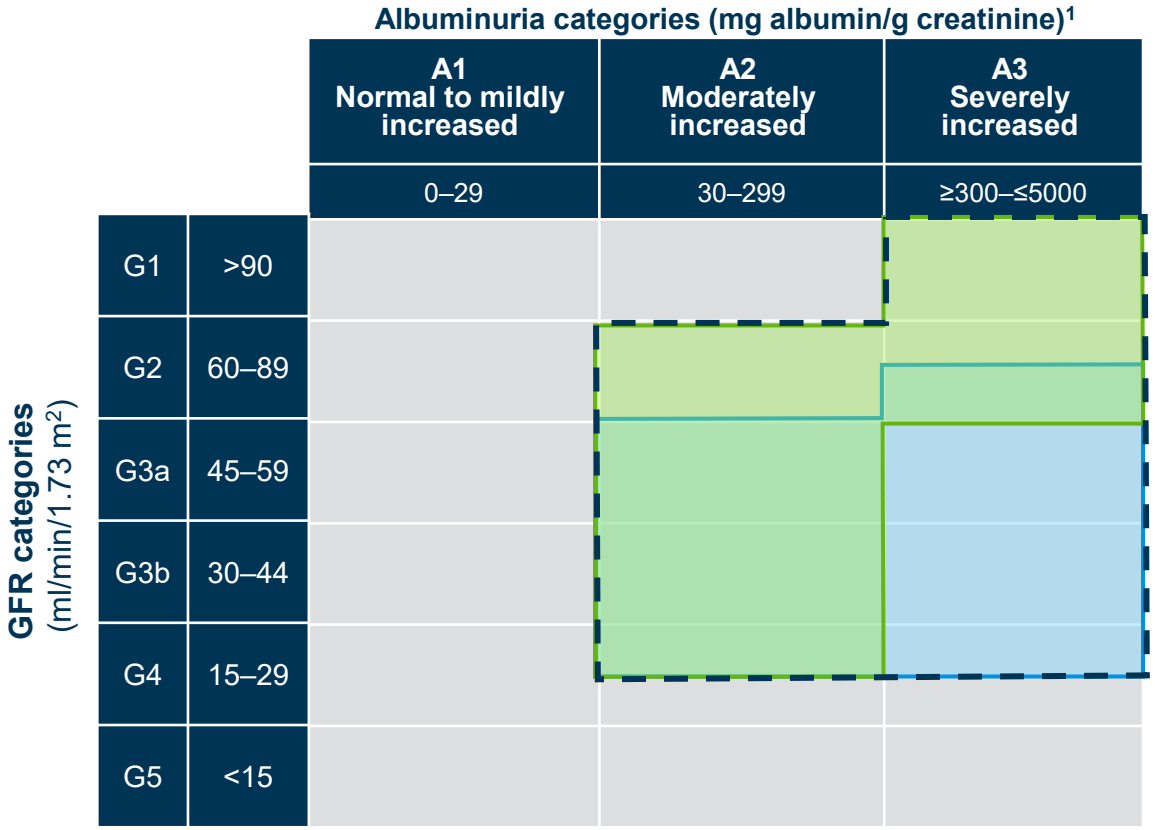
18.9% (n=128) = potential treatment side-effects

*Spironolactone on top of usual care compared with usual care alone.
ACR, albumin creatinine ratio; CI, confidence interval; CV, cardiovascular; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; PAD, peripheral arterial disease; T2D, type 2 diabetes.

1. Hobbs FDR, et al. *Nat Med.* 2024. doi: 10.1038/s41591-024-03263-5; 2. Tofte N, et al. *Lancet Diabetes Endocrinol.* 2020;8:301–312.

Finerenone for patients with T2D and CKD

Finerenone was Investigated in the Largest Phase III Clinical Trial Programme in Patients with Early CKD (Stage 1–2) and More Advanced CKD (Stage 3–4) and T2D



FIGARO-DKD[3]

Finerenone in reducing **CV mortality and morbidity** (N=7437)

FIDELIO-DKD[2]

Finerenone in reducing **kidney failure and disease progression** (N=5734)

FIDELITY[4]

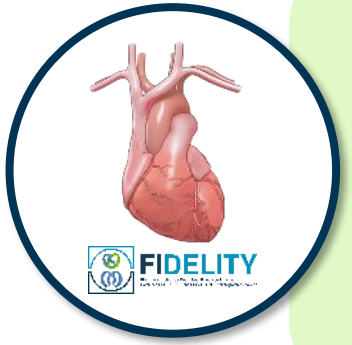
Prespecified pooled analysis (N=13,171)

G1: high and optimal; G2: mild; G3a: mild-to-moderate; G3b: moderate-to-severe; G4: severe; G5: kidney failure
CKD, chronic kidney disease; GFR, glomerular filtration rate; T2D, type 2 diabetes

1. KDIGO. Kidney Int Suppl 2013;3:1–150; 2. Bakris GL, et al. N Engl J Med 2020;383:2219–2229; 3. Pitt B, et al. N Engl J Med 2021;2021:385-2252; 4. Agarwal R, et al. Eur Heart J 2022;43:474–484

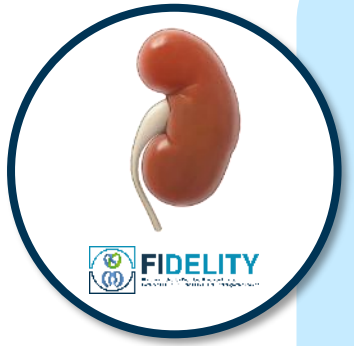
Finerenone demonstrated efficacy in heart and kidney disease outcomes, in early- and late-stage CKD [1–3]

Relative risk reductions for composite outcomes vs placebo in FIDELITY



14% relative risk reduction vs placebo for the CV composite*

CV death	Non-fatal MI	Non-fatal stroke	HHF
–12%	–9%	–1%	–22%



23% relative risk reductions were also seen in the kidney composite* outcomes compared with placebo

Kidney failure	ESKD#	eGFR decrease to/by: <15 ml/min/1.73 m²#	eGFR decrease to/by: ≥57%	Kidney-related death
–16%	–20%	–19%	–30%	N/A‡

*CV outcome: CV death, non-fatal MI, non-fatal stroke, HHF; 57% kidney composite: kidney failure, sustained ≥57% decrease in eGFR from baseline, or kidney-related death; #components of kidney failure; ‡kidney-related death (number of events): FIDELITY, n=2 in finerenone arm and n=4 in placebo arm; FIDELIO-DKD, n=2 in each arm; FIGARO-DKD: n=0 in finerenone arm and n=2 in placebo arm

1. Agarwal R, *et al. Eur Heart J* 2022;43:474–484 2. Bakris GL, *et al. N Engl J Med* 2020;383:2219–2229; 3. Pitt B, *et al. N Engl J Med* 2021;385:2252–2263

FIDELITY

Finerenone Demonstrates Greater Renal Benefits with Consistent CV Protection in the Asian Population

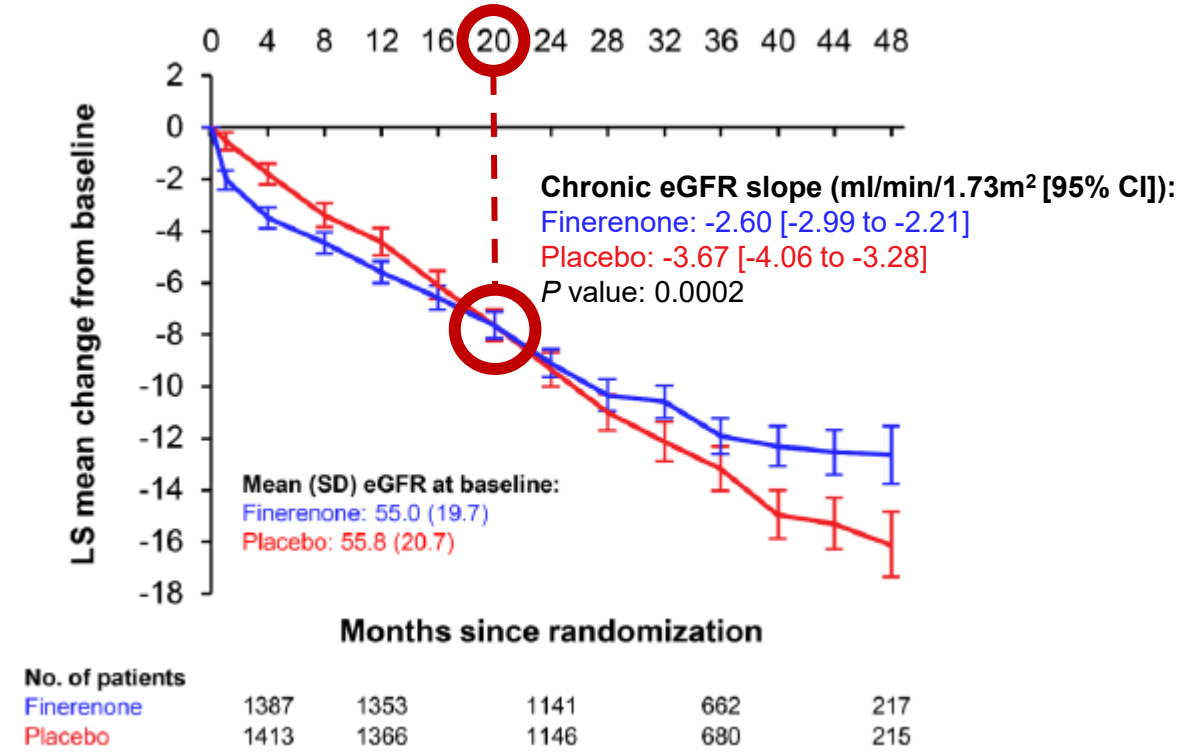
	Asian (n=2858)	Non-Asian (n=10132)	*P*-value for interaction
Age (years)	62.3	65.5	
HbA1c (%)	7.6	7.7	
eGFR (ml/min/1.73m^2)	55.4	58.2	
UACR (mg/g)	629.1	491.7	
≥40% Kidney Composite Outcome	↓ 36%	↓ 7%	0.0493
≥57% Kidney Composite Outcome	↓ 33%	↓ 15%	0.0009
CV Composite Outcome	↓ 10%	↓ 15%	0.8454

Kidney Dis 2025. DOI: 10.1159/000545415

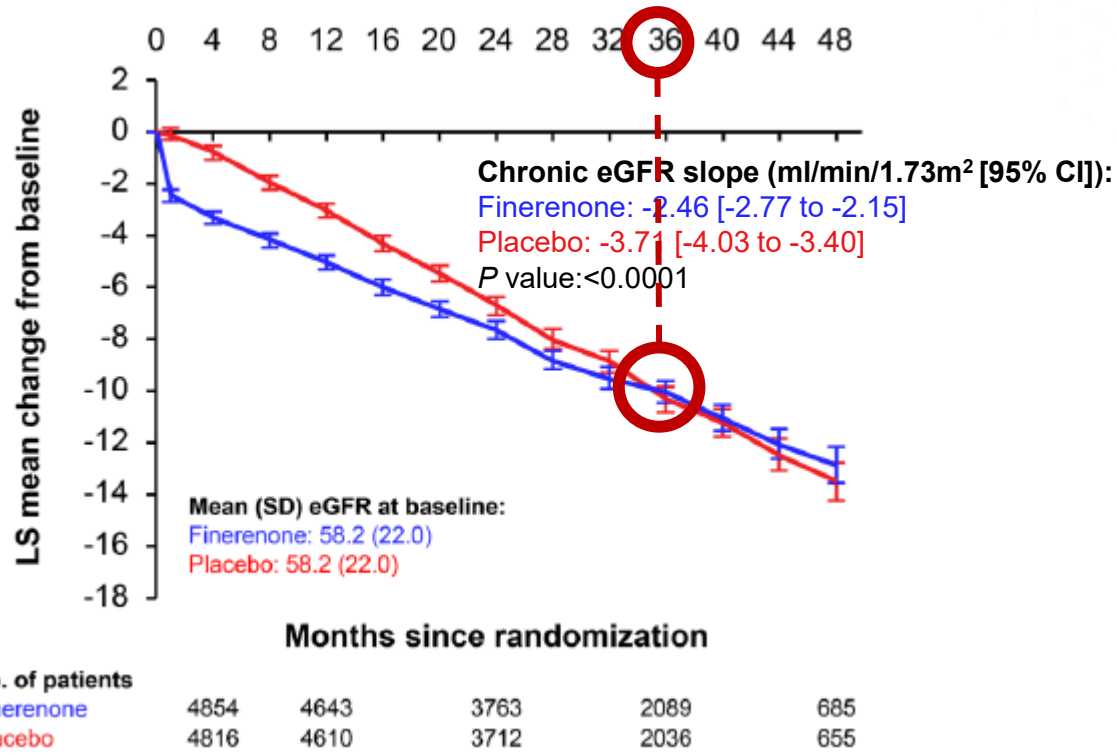
Compared to the non-Asian population, the Asian subpopulation showed an earlier eGFR crossover time between finerenone vs. placebo

Change in eGFR from baseline with finerenone vs placebo

Asian



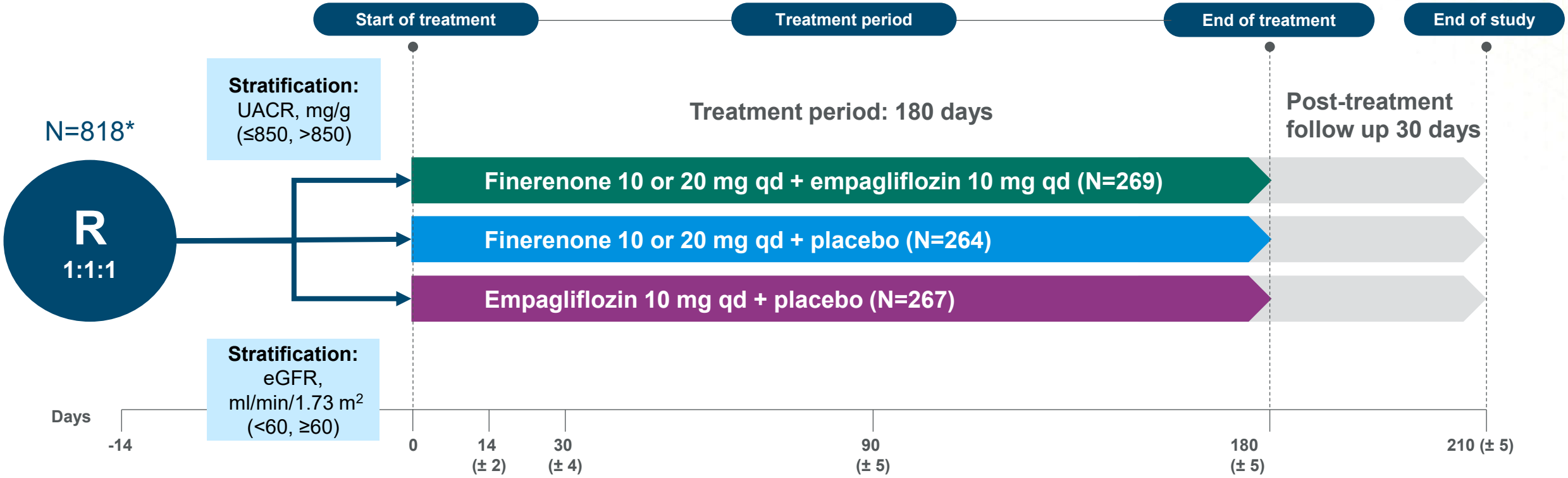
Non-Asian



Kidney Dis (Basel). 2025 May 22;11(1):402-415.

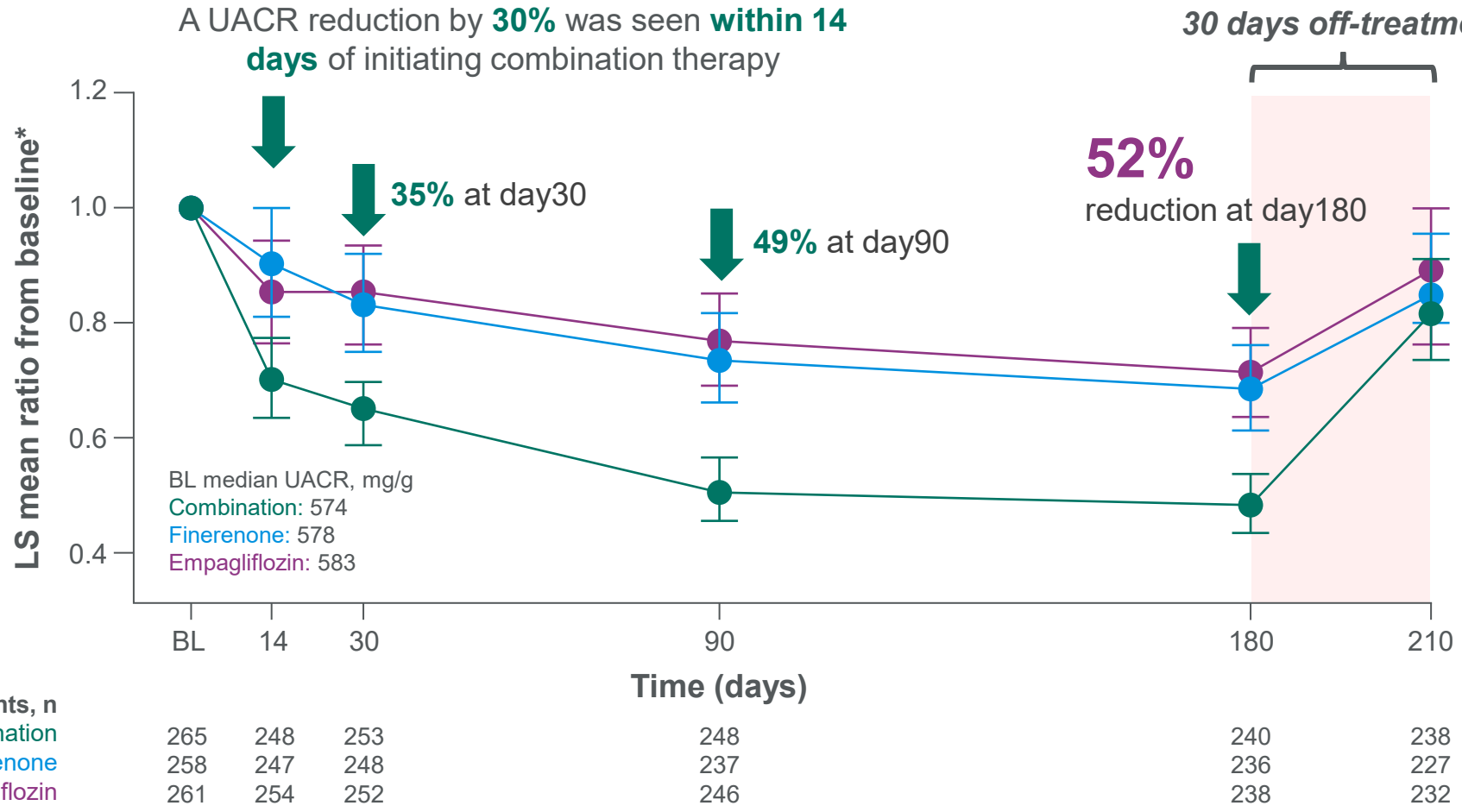
CONFIDENCE was a randomized, double-blind, double-dummy, multicenter, three-armed, parallel-group, phase II study

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



Agarwal R, et al. N Engl J Med. 2025

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



Primary efficacy endpoints met for combination at day180:

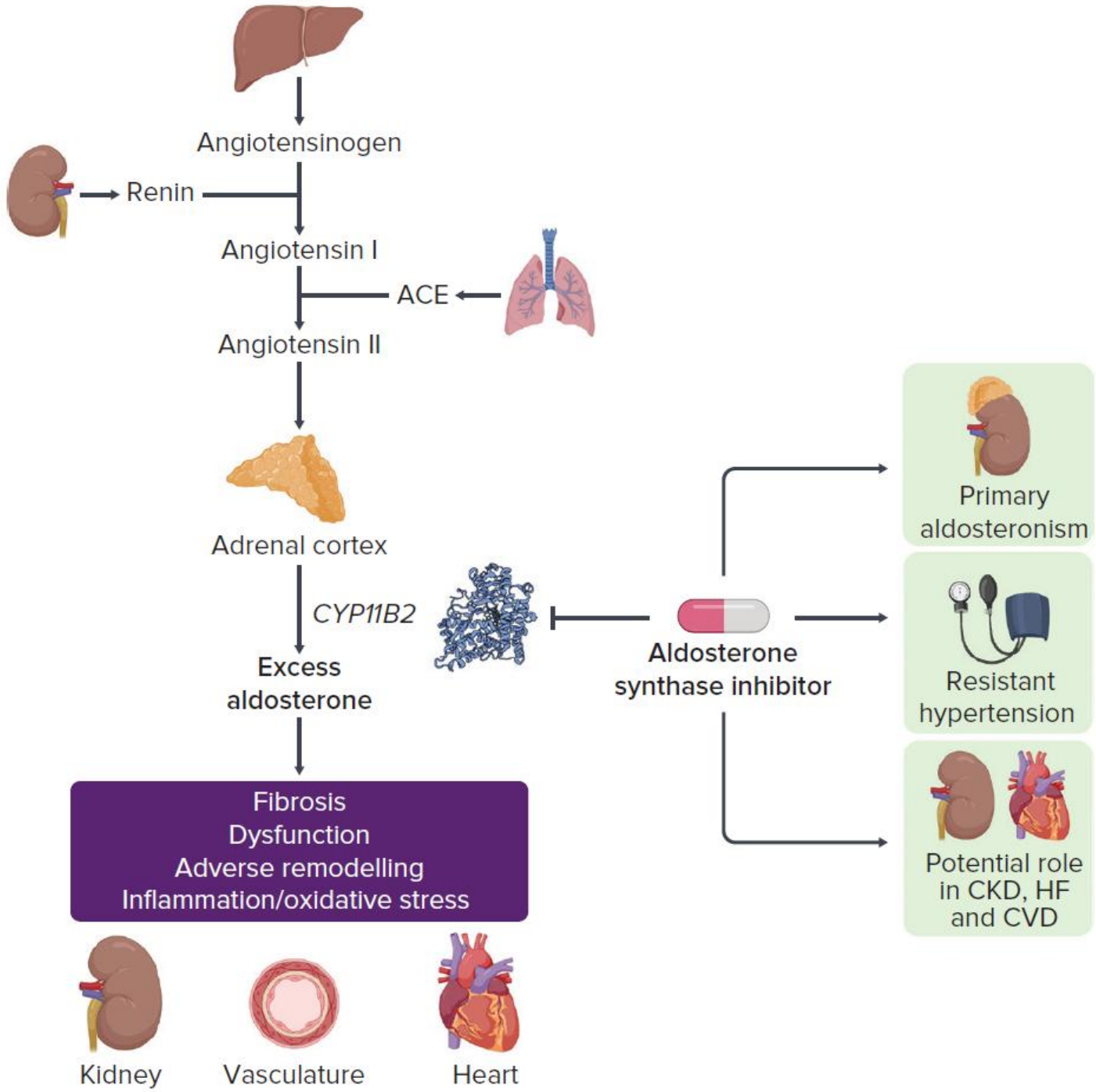
- 32% greater reduction vs empagliflozin
- 29% greater reduction vs finerenone

*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.

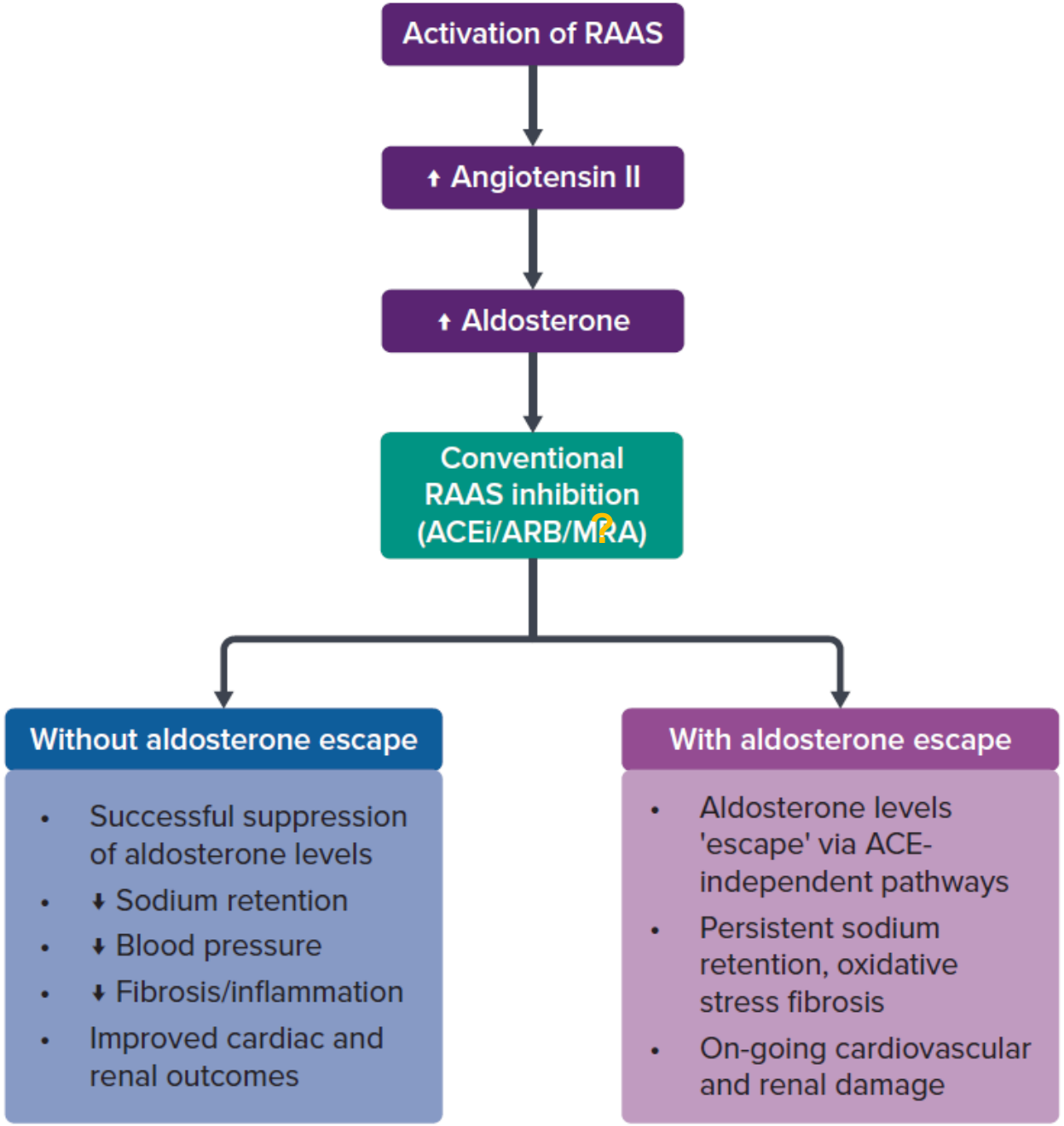
CONFIDENCE

Aldosterone Synthase Inhibitors (ASI), a new weapon for Aldosterone Inhibition?

The Pathological Consequences of Excess Aldosterone and Potential Therapeutic Applications of Aldosterone Synthase Inhibitors



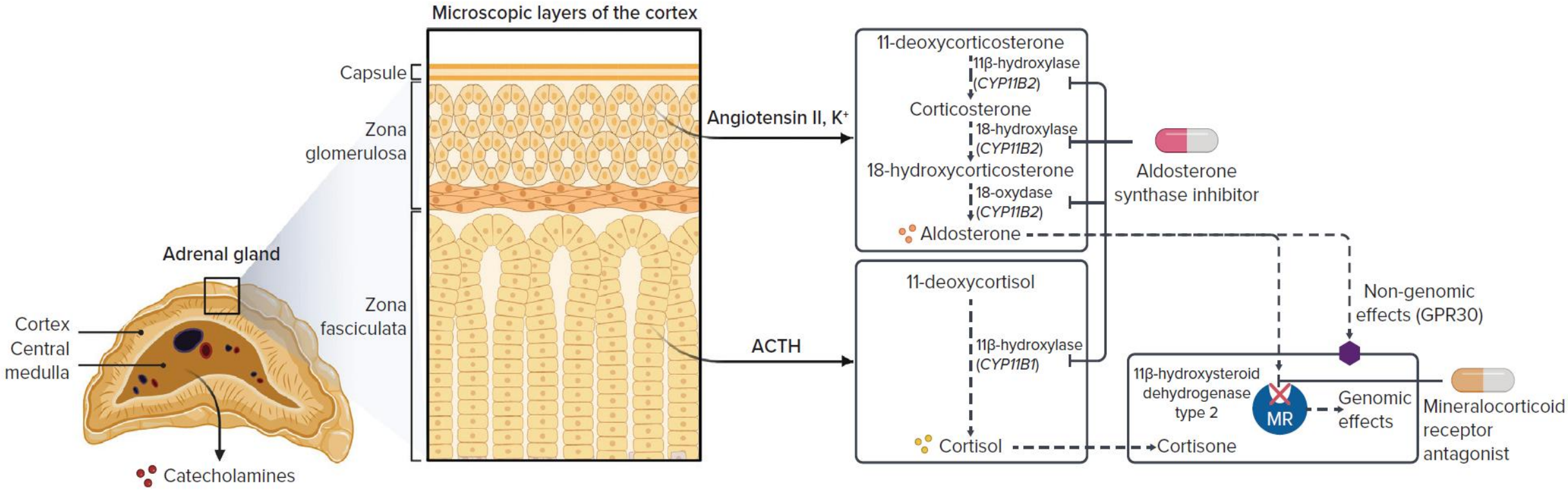
Aldosterone Escape



Aldosterone Synthase Inhibitors

- ASIs have been developed for more than a decade
- The target enzyme aldosterone synthase (CYP11B2) is >90% homologous with 11b-hydroxylase (CYP11B1), which is responsible for the final step in cortisol synthesis
- First generation ASIs (osilodrostat etc)
  - Due to shared affinity for CYP11B1, inhibited cortisol synthesis leading to clinically relevant adrenal insufficiency
    - Repurposed for Cushing's disease
  - Accumulation of precursor mineralocorticoids (e.g., 11-deoxycorticosterone) which offset the BP lowering effect of aldosterone synthase inhibition

Overview of the Adrenal Gland Structure, Steroidogenesis Pathways and the Role of Aldosterone Synthase Inhibition



Genomic pathway: (slow, MR-dependent)
Non-genomic (rapid, MR-independent)

Patel SK, Cardiac Fail Rev 2025

The NEW ENGLAND JOURNAL of MEDICINE

Lorundrostat Efficacy and Safety in Patients with Uncontrolled Hypertension

A Research Summary based on Laffin LJ et al. | 10.1056/NEJMoa2501440 | Published on April 23, 2025

WHY WAS THE TRIAL DONE?

Among patients with uncontrolled, treatment-resistant hypertension, aldosterone dysregulation is increasingly recognized as a driver of persistent blood-pressure elevation. The aldosterone synthase inhibitor lorundrostat may be an effective therapy through direct targeting of aldosterone biosynthesis, but data on its efficacy and safety in patients with uncontrolled hypertension are limited.

HOW WAS THE TRIAL CONDUCTED?

Adults with an average 24-hour ambulatory blood pressure of 130/80 mm Hg or higher after 3 weeks of standardized treatment were assigned to receive placebo, lorundrostat at a dose of 50 mg daily (stable-dose group), or lorundrostat at a starting dose of 50 mg daily, with an increase to 100 mg daily if systolic blood pressure was 130 mm Hg or higher after 4 weeks (dose-adjustment group). The primary efficacy end point was the change in 24-hour average systolic blood pressure from baseline to week 12.

TRIAL DESIGN

- Phase 2b
- Prospective
- Double-blind
- Placebo-controlled
- Location: 103 U.S. sites

RESULTS

At 12 weeks, 24-hour average systolic blood pressure had decreased significantly more in each lorundrostat group than in the placebo group. A potassium level above 6.0 mmol per liter was more common with lorundrostat than with placebo.

LIMITATIONS AND REMAINING QUESTIONS

- The trial was relatively short, at 12 weeks. An assessment of the effects of lorundrostat use over a longer period is ongoing in an open-label extension of the present trial.
- The trial lacked a direct comparison of lorundrostat with other antihypertensive medications, including mineralocorticoid receptor antagonists.

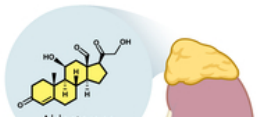
CONCLUSIONS

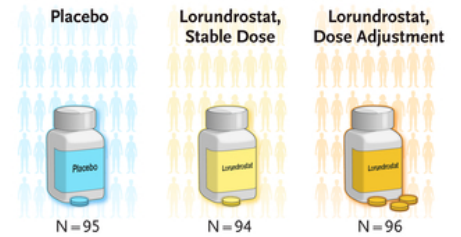
In adults with uncontrolled hypertension after 3 weeks of standardized antihypertensive treatment, use of lorundrostat was associated with greater reductions in 24-hour average blood pressure than placebo.

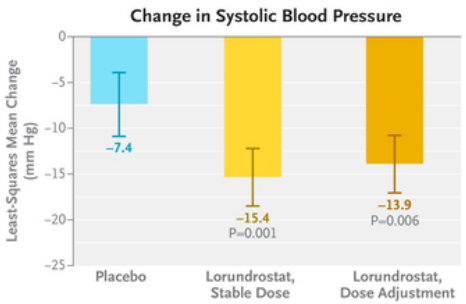
NEJM QUICK TAKE

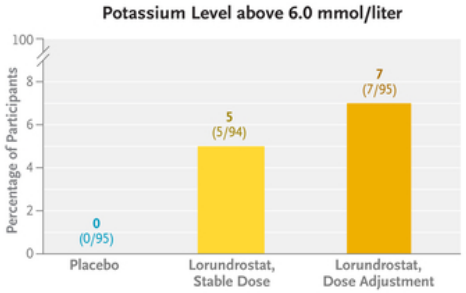
Participants

- 285 adults
- Mean age, 60 years
- Men: 60%; Women: 40%









The NEW ENGLAND JOURNAL of MEDICINE

Efficacy and Safety of Baxdrostat in Uncontrolled and Resistant Hypertension

A Research Summary based on Flack JM et al. | DOI: 10.1056/NEJMoa2507109 | Published on August 30, 2025

WHY WAS THE TRIAL DONE?

Hard-to-control hypertension is often driven by aldosterone dysregulation. Baxdrostat is a highly selective, potent aldosterone synthase inhibitor that has been associated with mixed results in trials involving patients with uncontrolled or resistant hypertension. Additional data are needed.

HOW WAS THE TRIAL CONDUCTED?

Adults with hard-to-control hypertension despite treatment with maximally tolerated doses of either two antihypertensive medications (uncontrolled hypertension) or three or more such medications (resistant hypertension) were enrolled. After a 2-week placebo run-in period, patients who had a seated systolic blood pressure of 135 mm Hg or more were assigned to receive baxdrostat (1 mg or 2 mg) or placebo once daily for 12 weeks. The primary efficacy end point was the change in seated systolic blood pressure from baseline to week 12.

TRIAL DESIGN

- Phase 3
- Multinational
- Double-blind
- Randomized
- Placebo-controlled

RESULTS

At 12 weeks, seated systolic blood pressure had decreased significantly more with each dose of baxdrostat than with placebo. A potassium level of more than 6.0 mmol per liter was reported more often with baxdrostat than with placebo.

LIMITATIONS AND REMAINING QUESTIONS

- Ambulatory blood pressure was measured in only a small number of patients.
- The percentages of women and Black patients were smaller than those in the general population with hypertension, which limits the generalizability.
- Medication adherence was not measured directly by objective methods throughout the trial.

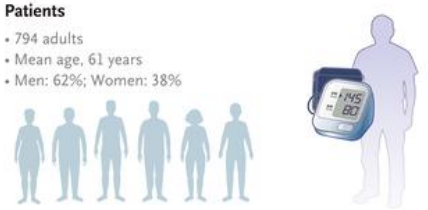
CONCLUSIONS

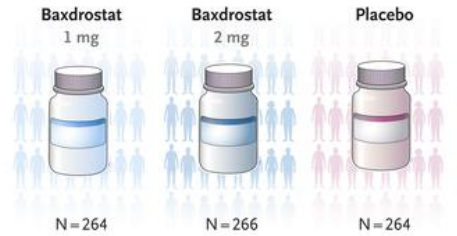
In adults with uncontrolled or resistant hypertension, the addition of once-daily baxdrostat to background antihypertensive therapy resulted in significantly greater reductions in seated systolic blood pressure at 12 weeks than placebo.

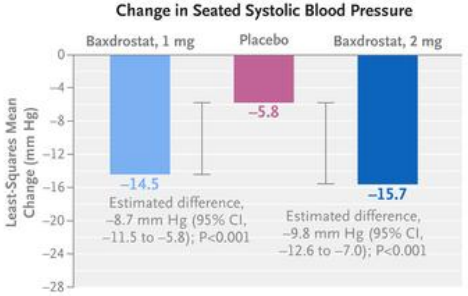
NEJM QUICK TAKE | EDITORIAL

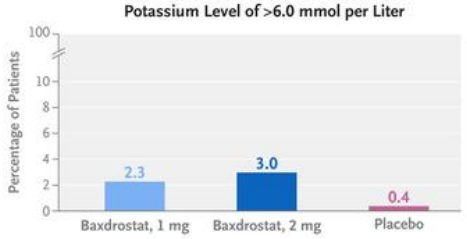
Patients

- 794 adults
- Mean age, 61 years
- Men: 62%; Women: 38%

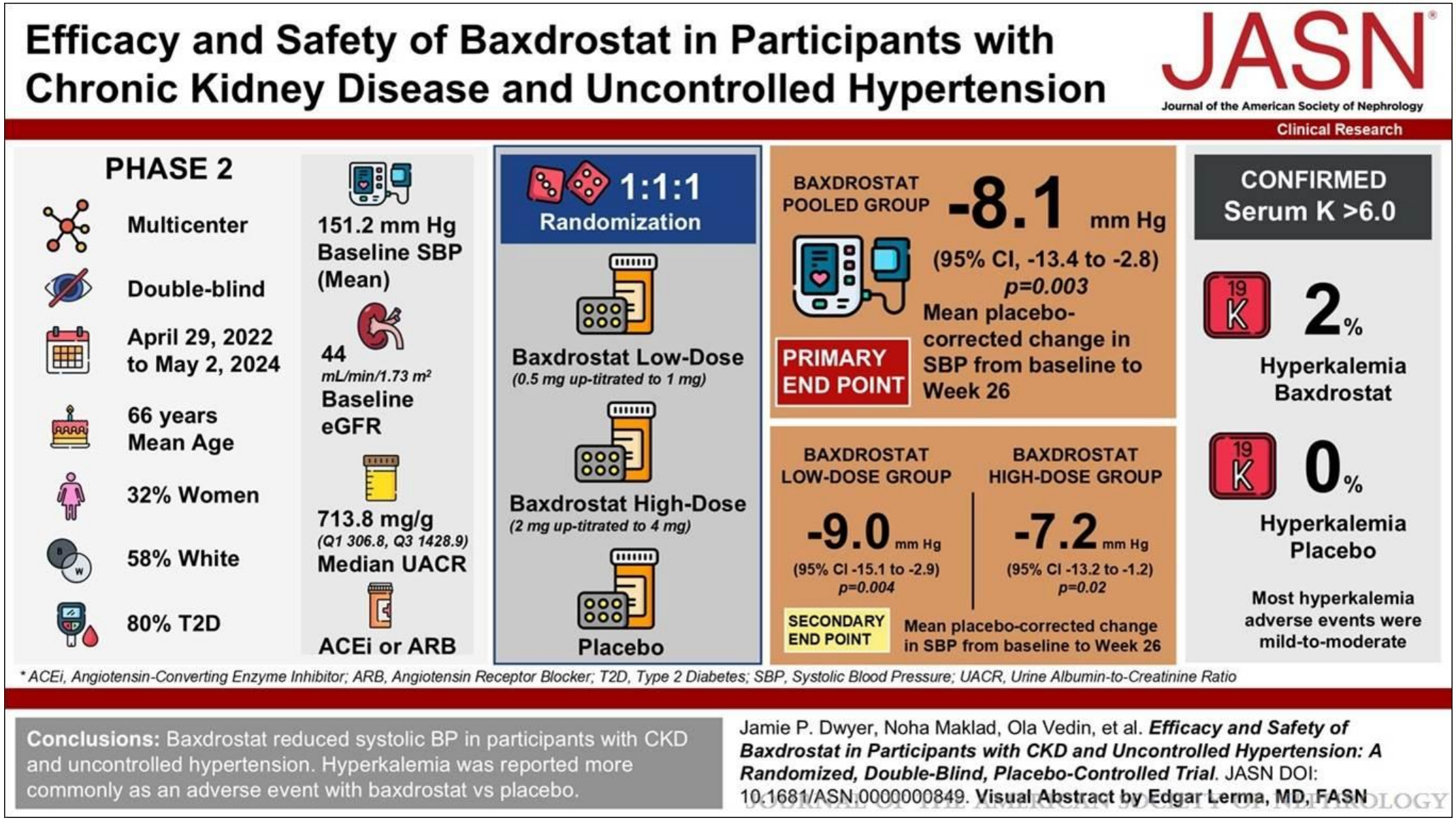




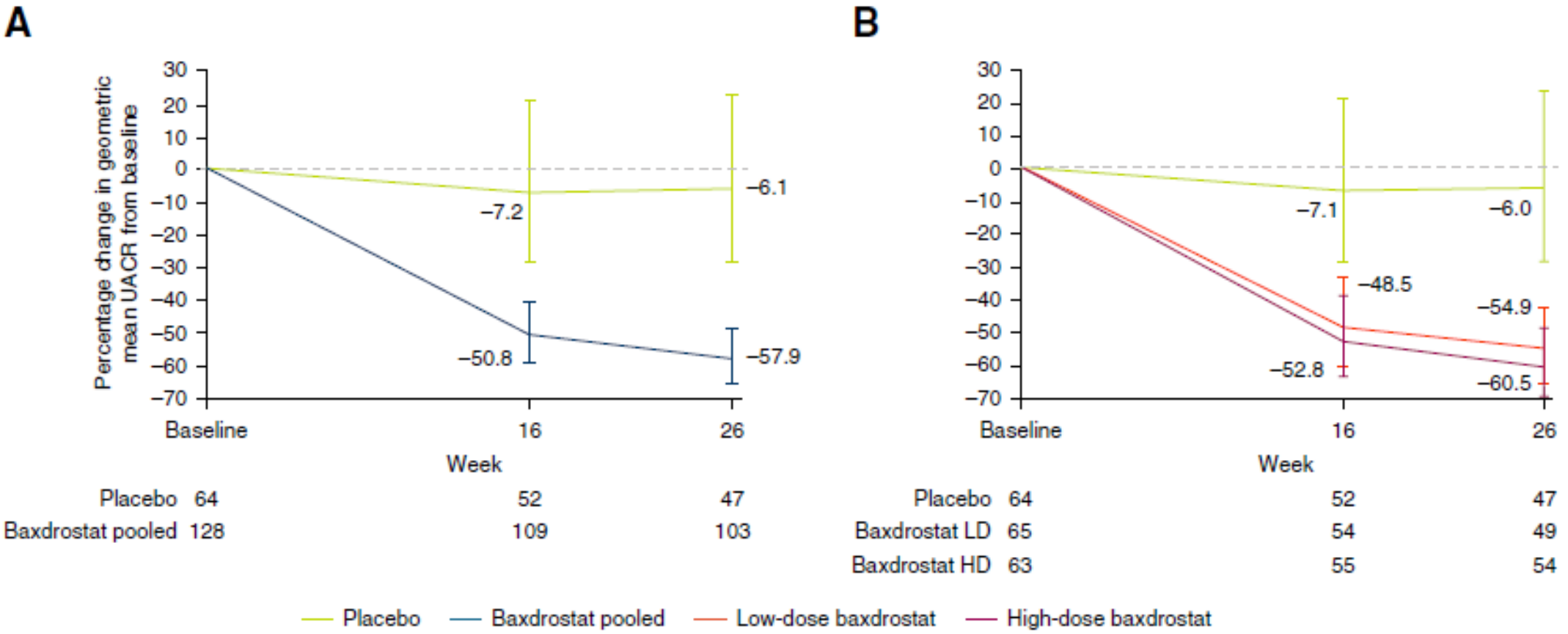




FigHTN-CKD phase II study



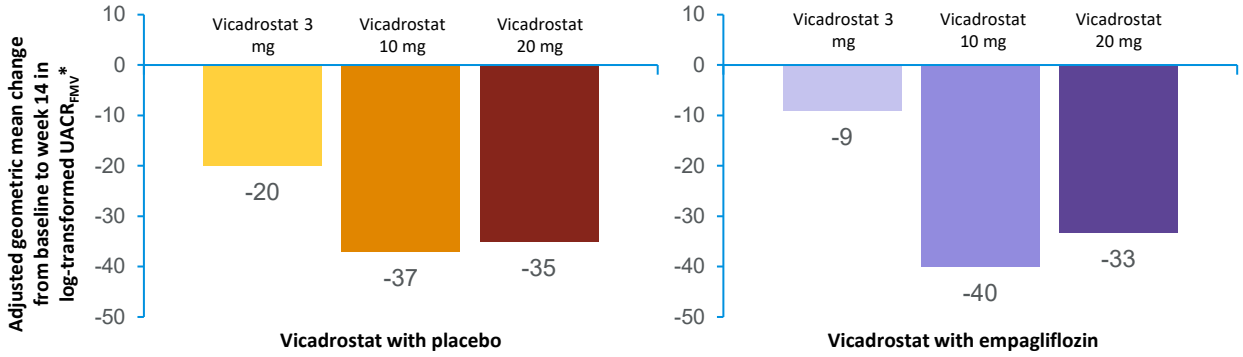
Baxdrostat may reduce albuminuria though no dosing dependent



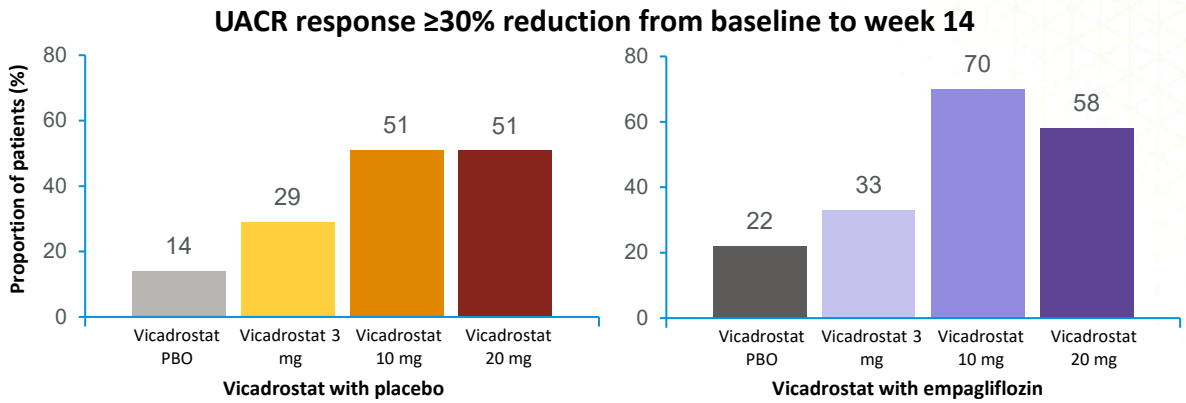
Dwyer JP, J Am Soc Nephrol 2025

Phase II study of BI 690517(vicadrostat) combined with empagliflozin in patients with CKD

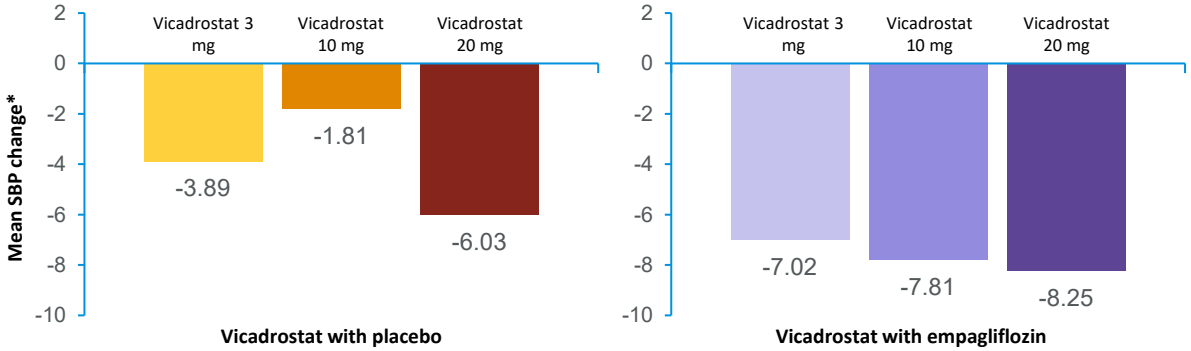
Vicadrostat showed **additive effects† on top of empagliflozin** for change from baseline in **UACR**



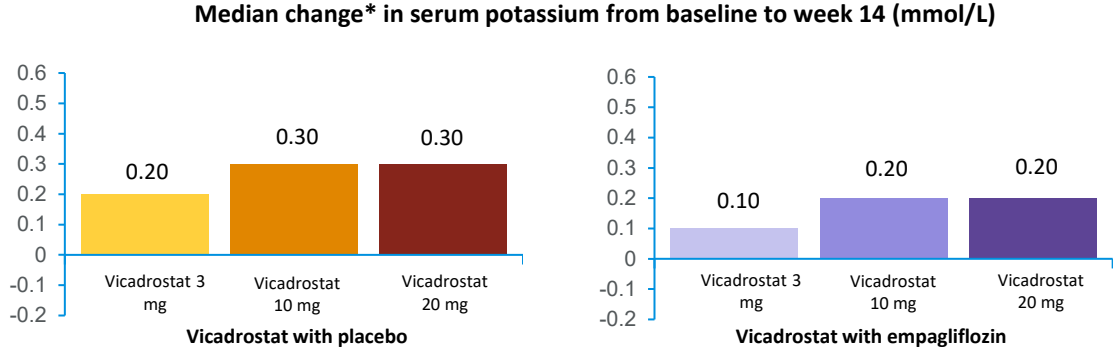
Vicadrostat showed **more pronounced efficacy results for response rates** when given in **combination with empagliflozin**



Vicadrostat showed **more pronounced SBP reduction** when given in **combination with empagliflozin**



Combination with empagliflozin across all doses **mitigated the potassium increase** associated with vicadrostat



Tuttle KR, et al. *Lancet.* 2024

Adverse Events

Finereone, Fidelity analysis

Treatment-emergent AEs[a]	Number of patients with event (%)	
	Finerenone (*n* = 6510)	Placebo (*n* = 6489)
Any AE	5602 (86.1)	5607 (86.4)
AE related to study drug	1206 (18.5)	862 (13.3)
AE leading to treatment discontinuation	414 (6.4)	351 (5.4)
Any serious AE[b]	2060 (31.6)	2186 (33.7)
Serious AE[b] related to study drug	83 (1.3)	61 (0.9)
Serious AE[b] leading to treatment discontinuation	145 (2.2)	154 (2.4)
Investigator-reported hyperkalaemia[c]	912 (14.0)	448 (6.9)
Hyperkalaemia related to study drug	573 (8.8)	249 (3.8)
Permanent discontinuation due to hyperkalaemia	110 (1.7)	38 (0.6)
Serious hyperkalaemia[b]	69 (1.1)	16 (0.2)
Hospitalization due to serious hyperkalaemia	61 (0.9)	10 (0.2)
Fatal hyperkalaemia	0 (0.0)	0 (0.0)

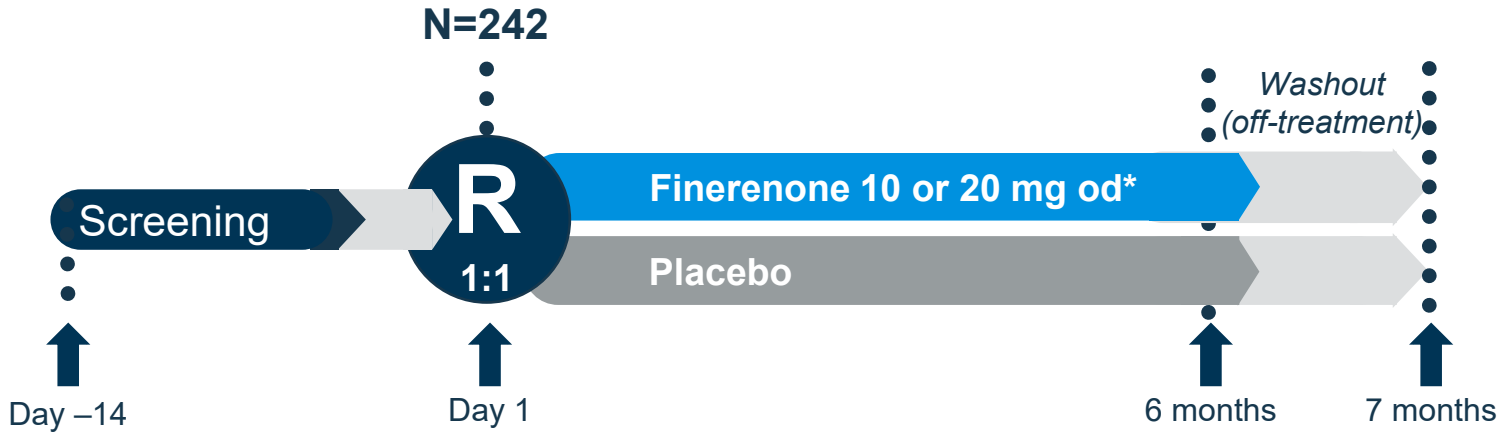
Vicadrostat + Empa, phase II

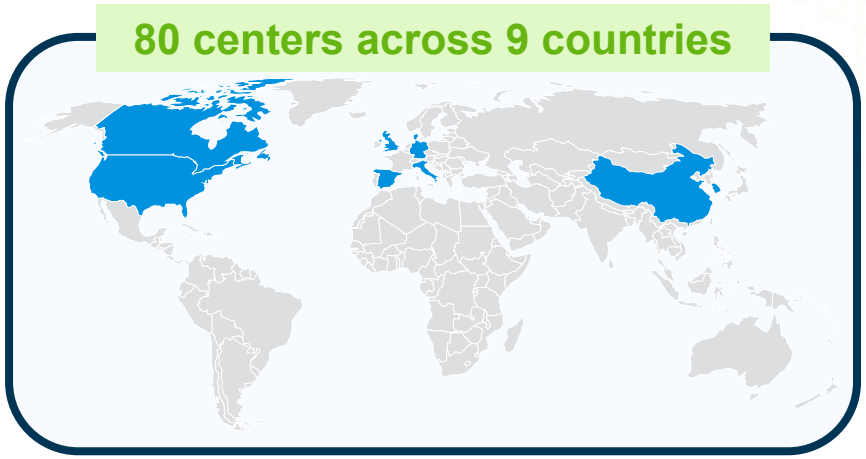
	Pooled BI 690517, placebo (N=147)	Pooled BI 690517, 3 mg (N=146)	Pooled BI 690517, 10 mg (N=144)	Pooled BI 690517, 20 mg (N=146)
Any adverse event	79 (54%)	80 (55%)	88 (61%)	91 (62%)
Any serious adverse event	10 (7%)	7 (5%)	11 (8%)	11 (8%)
Adverse event of special interest	1 (1%)	1 (1%)	4 (3%)	4 (3%)
Adrenal insufficiency	1 (1%)	1 (1%)	3 (2%)	3 (2%)
Cushing's syndrome	0	0	0	0
Ketoacidosis	0	0	1 (1%)	0
Events leading to lower limb amputation	0	0	0	1 (1%)
Other important adverse events				
Investigator-reported hyperkalaemia	9 (6%)	14 (10%)	22 (15%)	26 (18%)
Hypotension	1 (1%)	1 (1%)	4 (3%)	2 (1%)
Orthostatic hypotension	1 (1%)	0	0	0
Acute kidney injury	1 (1%)	0	2 (1%)	4 (3%)

Ongoing clinical trials of nsMRAs and ASIs in CKD management

FINE-ONE is a global, randomized, phase III clinical trial evaluating UACR reduction in people with T1D and CKD[1,2]

To investigate the efficacy (reducing UACR) and safety of finerenone versus placebo, when given on top of SoC, in adult people with T1D and CKD





Key dates

Actual study start:
February 2024

Study completion:
September 2025

*For participants with an eGFR ≥25 to <60 mL/min/1.73 m2, starting dose is 10 mg od. For participants with an eGFR ≥60 mL/min/1.73 m^2, starting dose is 20 mg od. Up-titration and down-titration of study intervention will be based on local serum [K^+] and kidney function (eGFR) values.

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; [K^+], potassium concentration; od, once daily; R, randomized; SoC, standard of care; T1D, type 1 diabetes; UACR, urine albumin-to-creatinine ratio.

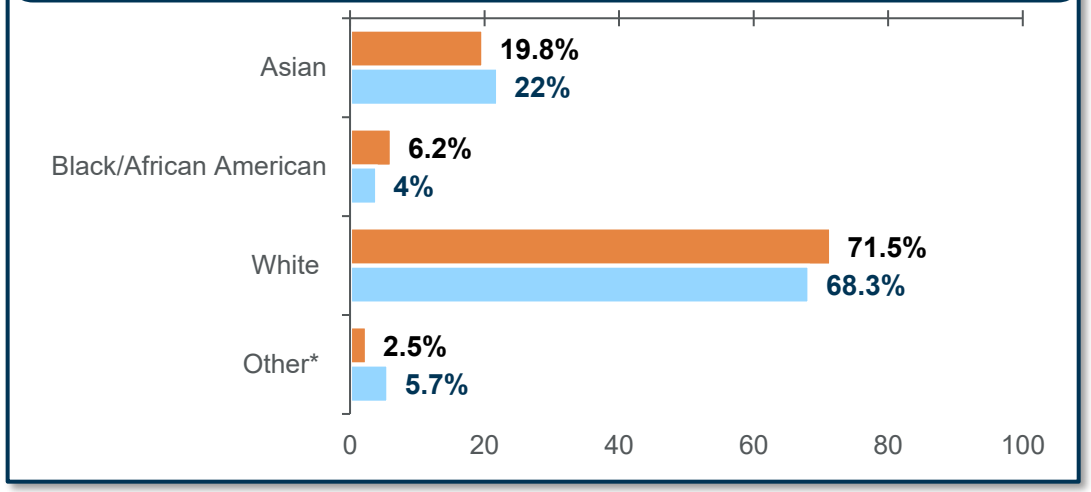
1. ClinicalTrials.gov. NCT05901831 (accessed November 2025); 2. Heerspink HJL, et al. *Diabetes Res Clin Pract*. 2023;204:110908.

FINE-ONE

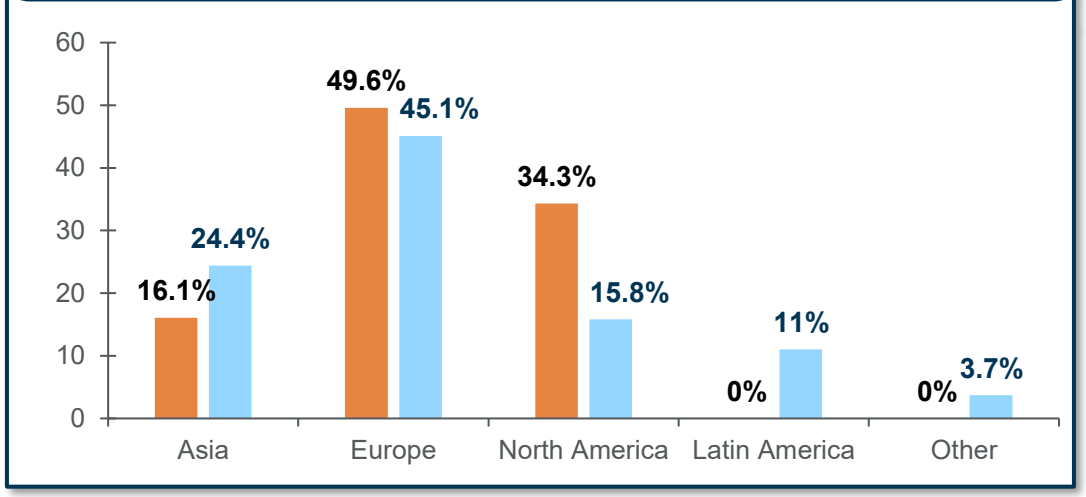
Key baseline characteristics were similar in FINE-ONE and the FIDELITY pooled analysis[1]

	Sex	Mean age	Mean BMI	Mean blood pressure: Systolic	Mean blood pressure: Diastolic
FINE-ONE	65% ♀ 35% ♂	51.6 years	27.6 kg/m²	135.2 mmHg	77.5 mmHg
FIDELITY	70% ♀ 30% ♂	64.8 years	31.3 kg/m²	136.8 mmHg	76.4 mmHg

Race



Region



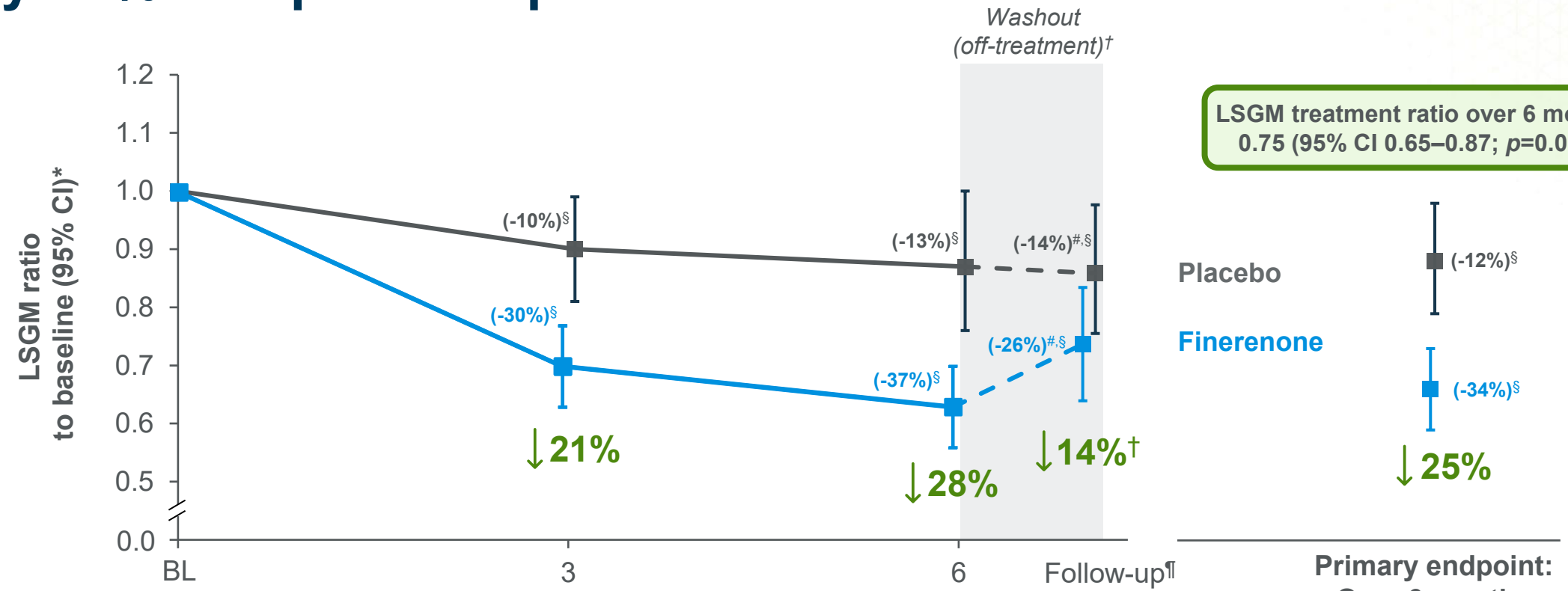
Will UACR reduction in a T1D population comparable to FIDELITY lead to similar associated benefits?

*American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or not reported.

1. Heerspink HJL, et al. *Nephrol Dial Transplant.* 2025; doi: 10.1093/ndt/gfaf183.

FINE-ONE FIDELITY

Finerenone significantly reduced UACR over 6 months by 25% compared to placebo



No. of patients					
Finerenone	120	120	120	114	120
Placebo	122	122	122	106	122

*Up to 3 daily UACR measures were combined into a geometric mean UACR prior to the analysis of the ratio to baseline of geometric mean UACR; †Assessment of data for the washout period was conducted using an ANCOVA model for the ratio to baseline in UACR at follow-up with the model including log baseline UACR; ‡Geometric mean ratio of treatment group ratios to baseline over the study period (i.e. average of geometric mean of treatment effect at month 3 and month 6 visits); §LSGM difference from baseline; ¶30 days after last dose of study intervention.

ANCOVA, analysis of covariance; BL, baseline; CI, confidence interval; LSGM, least-squares geometric mean; UACR, urinary albumin-to-creatinine ratio.

Heerspink HL, et al. *ASN* 2025; Oral presentation (TH-OR082).

FINE-ONE

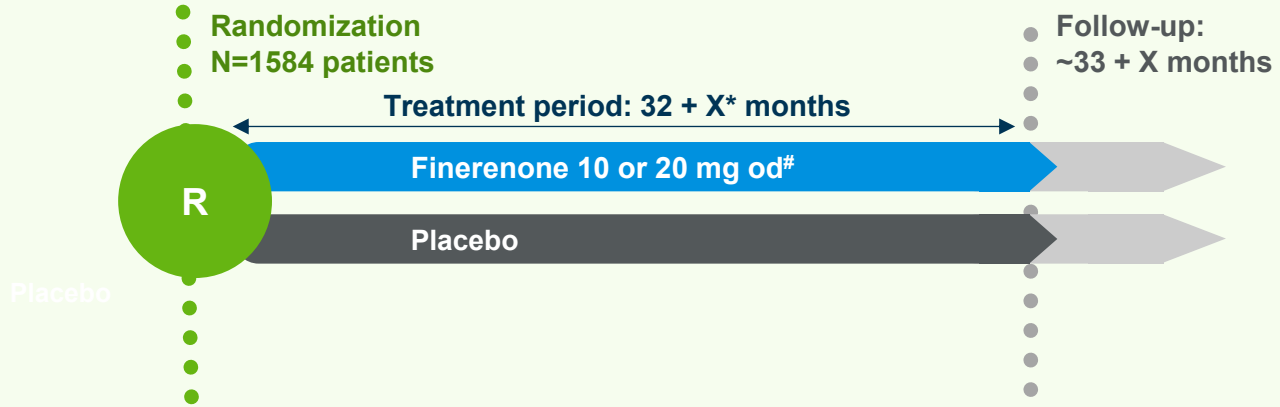
FIND-CKD is investigating finerenone in patients with non-diabetic CKD[1,2] (1/2)

Objective

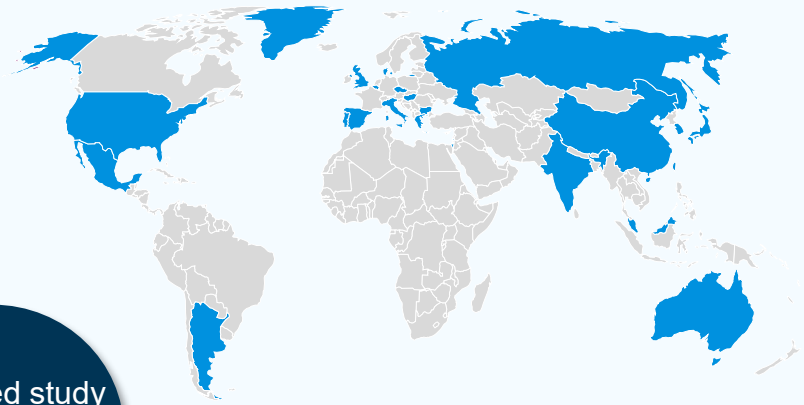
To investigate whether finerenone can provide kidney protection to patients with **CKD without diabetes** who are on optimal medical therapies

Design

Multicentre, randomised, double-blind, parallel-group, placebo-controlled phase III study



24 countries



Estimated study completion date: **February 2026**

Study duration and the number of study visits will depend on the time of enrolment of the patient
*Participants will stay in the study until the last randomised participant has reached 32 months of treatment; #starting dose of finerenone is based on the patient's eGFR level at the screening visit. Finerenone will be up- or down-titrated based on potassium and eGFR levels

1. Bayer. https://clinicaltrials.gov/study/NCT05047263 [accessed 20 March 2025]; 2. Heerspink HJL, *et al*. *Nephrol Dial Transplant* 2024: doi: 10.1093/ndt/gfae132

FIND-CKD

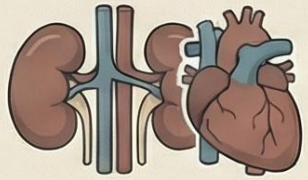
Drug	Key Trials	Population / Phase	Primary Endpoint
Baxdrostat (CIN-107)	BrigHTN	Resistant hypertension (Phase II)	Change in seated systolic BP
	HALO	Uncontrolled hypertension (Phase II)	Change in seated systolic BP
	FigHTN-CKD	CKD with uncontrolled hypertension (Phase II)	Change in seated systolic BP at 26 weeks
	Spark-PA	Primary aldosteronism (Phase II)	Long-term safety and tolerability
	Bax24	Resistant hypertension (Phase III)	Change in 24-hour ambulatory systolic BP
	BaxHTN	Uncontrolled or resistant hypertension (Phase III)	Change in seated systolic BP
	NCT06268873	CKD with hypertension on dapagliflozin (Phase III)	Change in eGFR slope
Lorundrostat (MLS-101)	Target-HTN	Uncontrolled hypertension (Phase II)	Change in automated office systolic BP
	Advance-HTN	Uncontrolled or resistant hypertension (Phase II)	Change in 24-hour ambulatory systolic BP
	Launch-HTN	Uncontrolled/resistant hypertension (Phase III)	Change in AOBP systolic BP at week 6
	NCT06150924	Hypertension with CKD and albuminuria (Phase II)	Change in systolic BP at 4 weeks; safety
Vicadrostat (BI690517)	NCT05182840	CKD with albuminuria (Phase II)	Percent change in UACR
	EASi-KIDNEY	~11,000 CKD patients (Phase III)	Kidney progression / HF hospitalization / CV death
	EASi-HF	HF with EF ≥40% (Phase III)	CV death or first HF hospitalization
Dexfadrostat (DP-13)	NCT04007406	Primary aldosteronism (Phase II)	Change in aldosterone-renin ratio and 24-hour BP

A Snapshot of the EASi-KIDNEY™ Phase III Trial Design

A high-level, academic summary of the EASi-KIDNEY™ clinical trial's objectives, population, and methodology.

The EASi-KIDNEY™ trial is a large-scale, Phase III study evaluating the effectiveness of vicadrostat, an aldosterone synthase inhibitor, when used with empagliflozin. The goal is to assess its potential for kidney and heart protection in a broad population of potential and the traditional for kidney and heart protection in a broad population of patients with chronic kidney disease (CKD).

Trial Population & Objectives



Dual Focus on Kidney & Heart Protection

Aims to protect against both kidney disease progression and cardiovascular events in CKD patients

~11,000 Participants with CKD

Enrolls patients both with and without type 2 diabetes (T2D) in separate strata

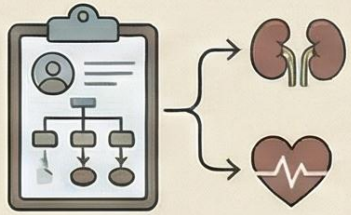
Key Inclusion Criteria

Adults (≥18) with specific eGFR and UACR levels indicating CKD at risk of progression

Intervention & Methodology

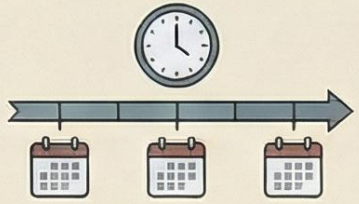
Combination Therapy Intervention

Patients receive vicadrostat 10mg or placebo, on top of empagliflozin and standard care



Composite Primary Outcome

Measures kidney failure/eGFR decline OR cardiovascular death/hospitalization for heart failure



3–4 Year Study Duration

Features a run-in period followed by semi-annual follow-up visits until the final assessment

Overview of the BaxDuo Phase III CKD Clinical Program

Therapy & Mechanism

Investigational Drug: Dapagliflozin + Baxdrostat

A combination of an SGLT2 inhibitor and an Aldosterone Synthase inhibitor (ASi+).

Expected Synergistic Benefits

Reduce albuminuria, inflammation, and fibrosis

Improving blood pressure control

Target Patient Profile

Designed for patients with Chronic Kidney Disease (CKD) and Hypertension (SBP >130mmHg).

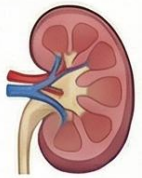
Pivotal Study Comparison

Directly compare the key design parameters and endpoints of the two main clinical trials.

Feature	eGFR Slope Study	Renal Outcome Study
Primary Endpoint	Change in eGFR over time	Renal composite (50% eGFR decline, kidney failure, CV death)
Patient Enrollment	2,500 total	5,000 total
Trial Duration	2 years	~5 years (event-driven)
Key Inclusion Criteria	eGFR: 30-90 / UACR: >200	eGFR: 30-75 / UACR: >30

The Evolution of Aldosterone Inhibition for Kidney Disease

Context: Overactivation of the Mineralocorticoid Receptor (MR) is a key driver of chronic kidney disease (CKD) progression.



MR Overactivation

CKD Progression

The Evolution of MRAs: Steroidal vs. Non-Steroidal

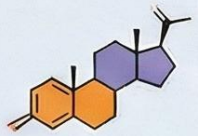
Steroidal MRAs (e.g., Spironolactone) Failed to Protect Kidneys in CKD Trials.

Showed **no reduction** in **adverse cardiovascular outcomes** and were often stopped due to **side effects**.

Non-Steroidal MRA Finerenone Reduced Kidney Disease Progression by 23%.

23%

Also demonstrated a **14% relative risk reduction** for **major cardiovascular events** in large clinical trials.

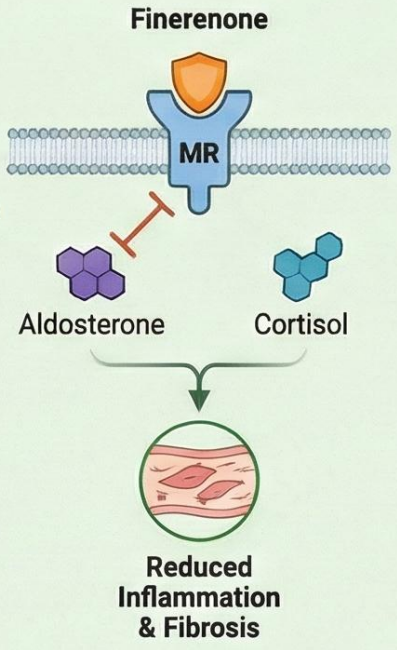


Finerenone offers **higher selectivity** for the MR with **fewer hormonal side effects.**

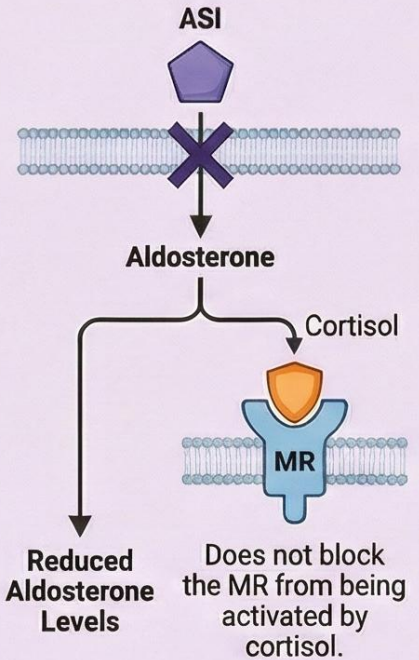
Unlike steroidal MRAs, finerenone **is not associated with sexual side effects.**

The Next Frontier: Non-Steroidal MRAs vs. Aldosterone Synthase Inhibitors (ASIs)

How Finerenone Works:
Directly blocks the Mineralocorticold Receptor (MR).

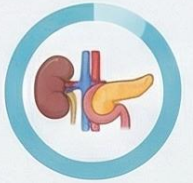


How ASIs Work:
Inhibit the synthesis of aldosterone upstream.



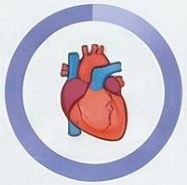
Future Outlook

Multiple large-scale clinical trials are underway for both drug classes.

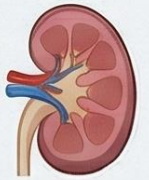


Non-Diabetic CKD

Heart Failure



Combination Therapies



Take Home Message

- MRAs (finerenone) have:
  - Well-characterized potassium effects
  - Proven long-term cardiovascular and renal benefit
  - Type 1 DM, non-DM CKD, HF
- ASI shows promising effects on BP and UACR, but comes with:
  - Unexpectedly hyperkalemia higher than finerenone
  - Early signals of adrenal insufficiency risk
- ASI versus MRA: Balancing: UACR & BP effects
  - Hyperkalemia-driven drug discontinuation
  - Long-term adrenal safety
  - Cardiorenal protection

Thank You Very Much for Your Attention !