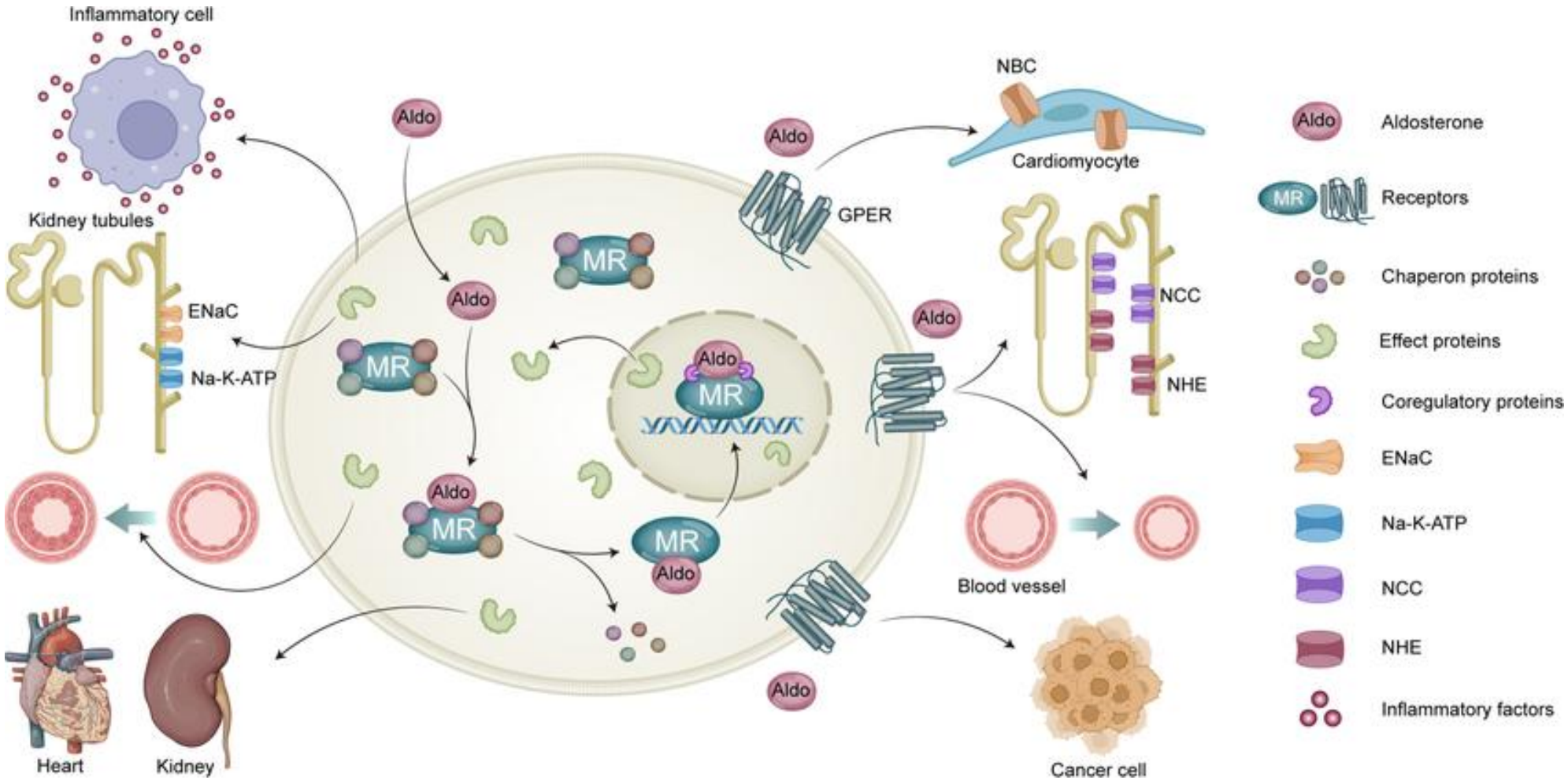
Νέες θεραπευτικές λύσεις για την Υπέρταση

Φωτεινή Ιατρίδη, MD, MSc, PhD
Εκλ. Επικ. Καθηγήτρια Νεφρολογίας,
Α' Νεφρολογική Κλινική Α.Π.Θ., Γ.Ν.Θ. «Ιπποκράτειο»

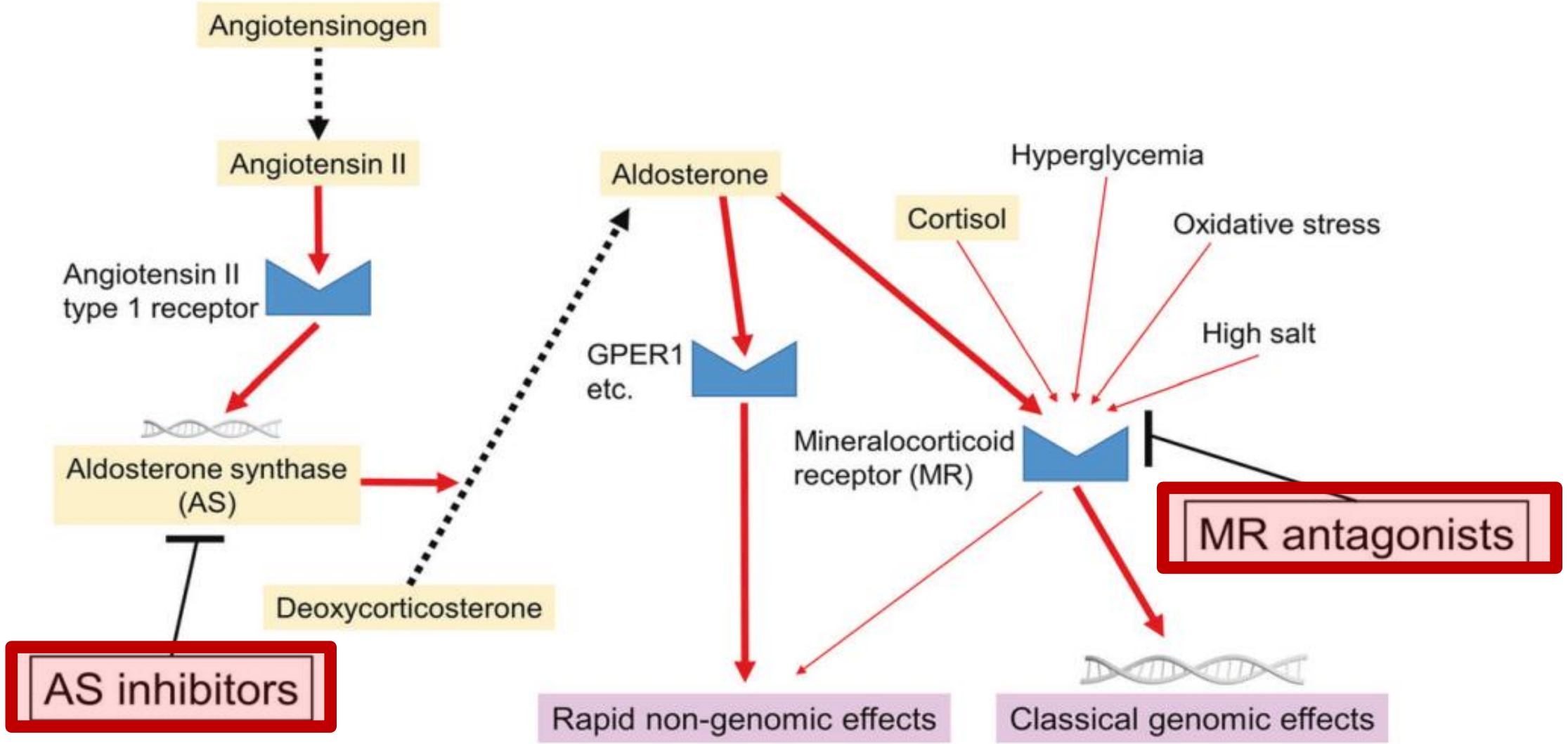
Αναστολείς συνθάσης αλδοστερόνης

Genomic and non-genomic aldosterone actions



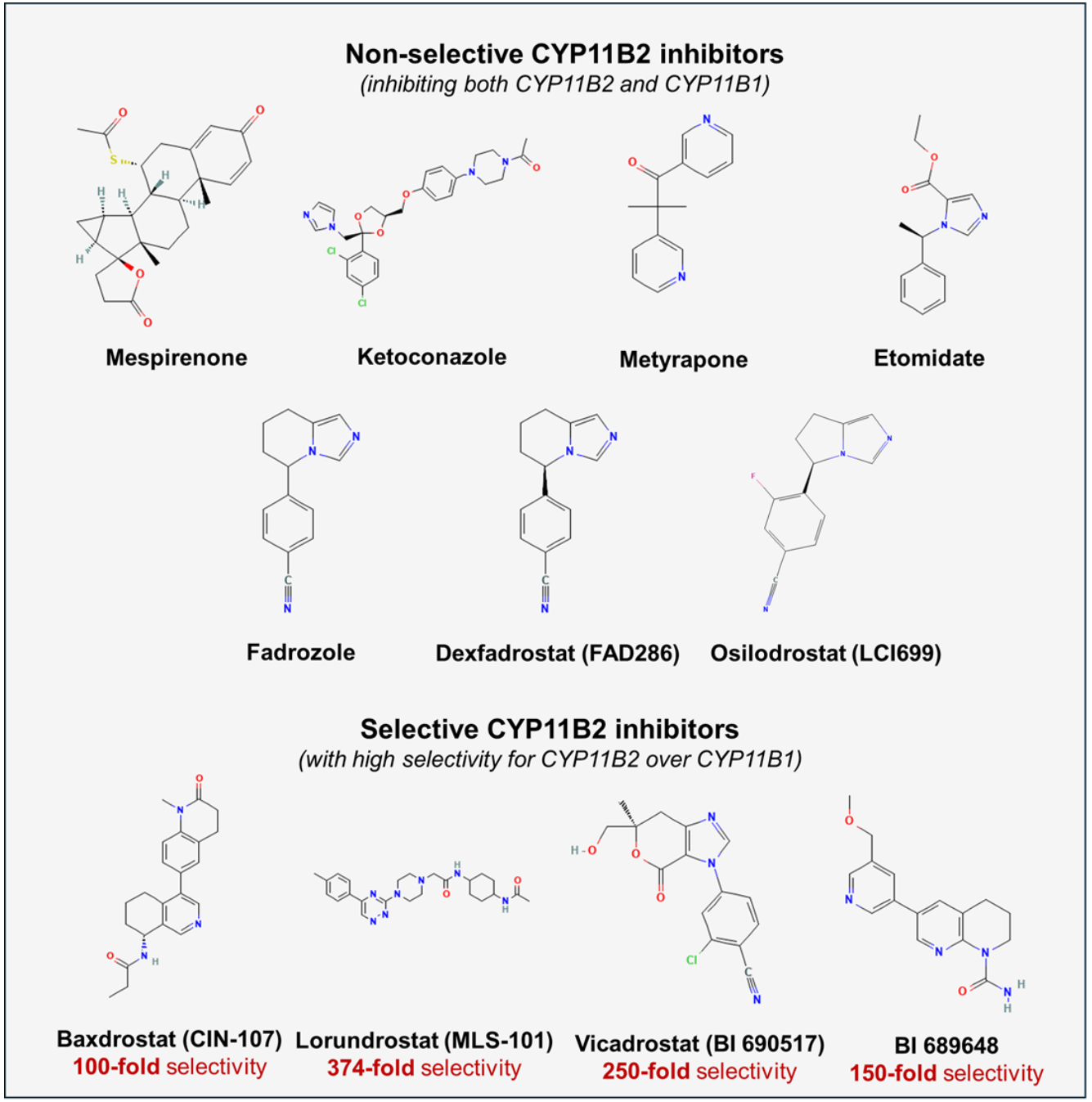
Li et al. Front Endocrinol 2023

Αναστολή δράσης της αλδοστερόνης



Hypertens Res 2023;46:1056-7

Αναστολείς συνθάσης αλδοστερόνης (ASIs)



Theodorakopoulou et al.
Nephrol Dial Transplant 2026

Αναστολείς συνθάσης αλδοστερόνης

Δεδομένα από κλινικές μελέτες

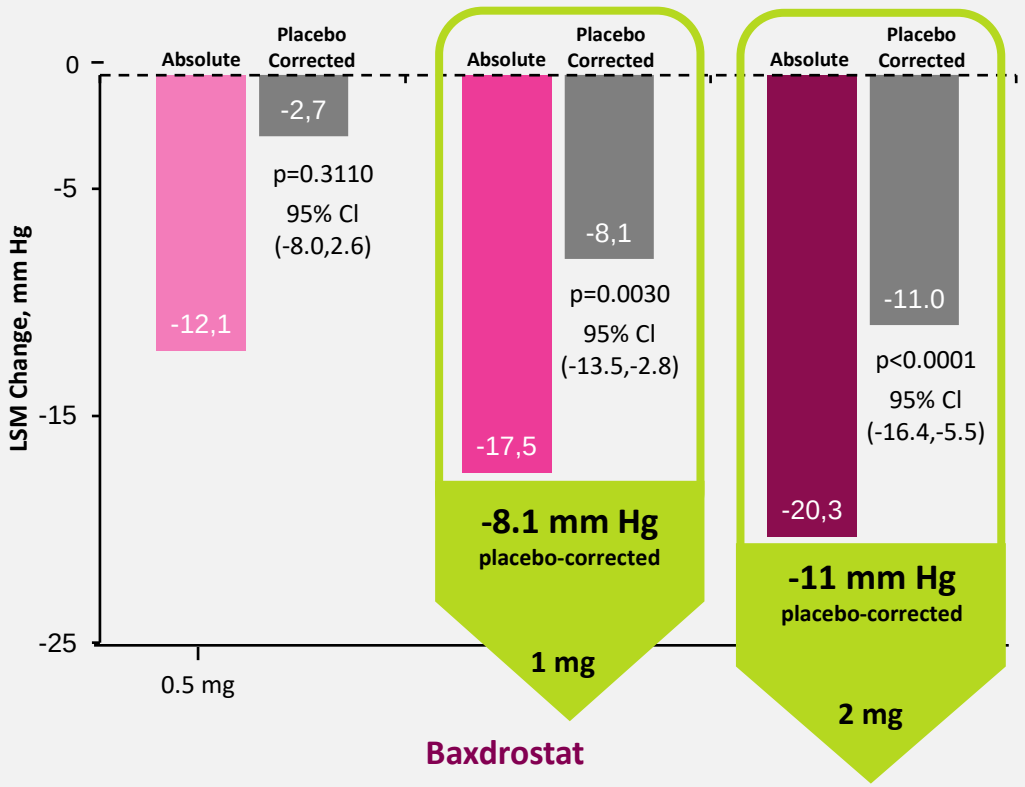
BrigHTN Ph2 study: δράση σε ΑΠ και αλβουμινουρία

248 patients on stable doses of at least three antihypertensive agents, including a diuretic with BP > 130/80 mm Hg

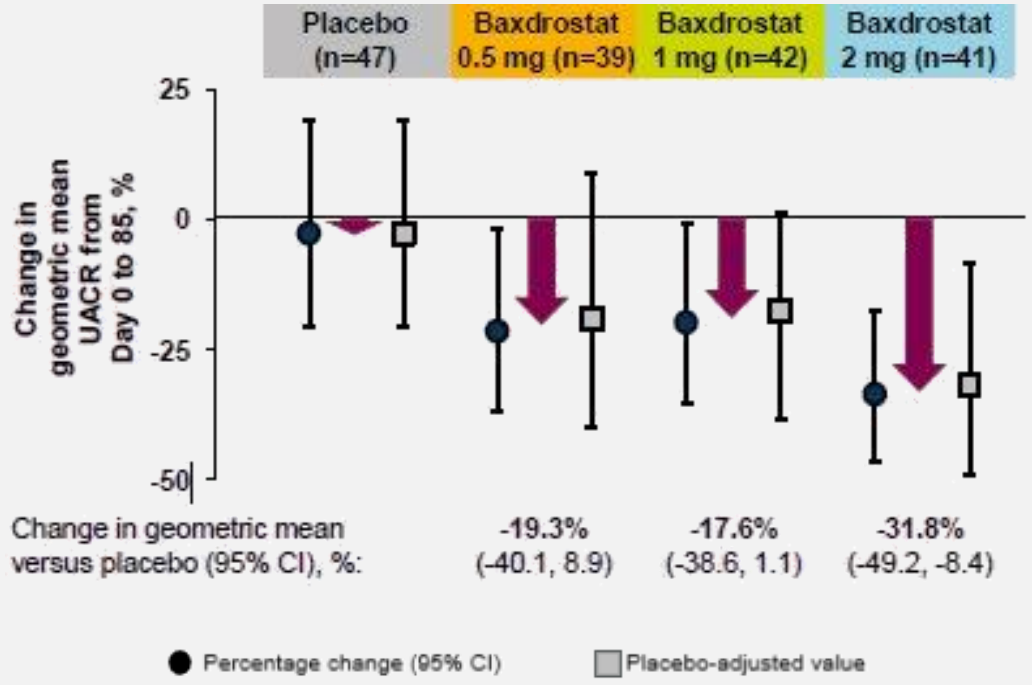
Dose-dependent decreases in BP were observed with baxdrostat in patients with treatment-resistant HTN[a]

Reduction in UACR was noted on a *post hoc* analysis[b]

Primary Endpoint: Change in Seated SBP (mm Hg)[a]



Percentage change in geometric mean UACR[b]



[a]Analyzed using linear regression, assuming missing BP values were missing at random. Analysis was in the modified ITT population; [b] Change in log-transformed UACR analyzed using analysis of covariance adjusting for baseline and stratification factors; Least-squares mean estimates were back-transformed to geometric mean ratios

CI, confidence interval; HTN, hypertension; ITT, intention-to-treat; LSM, least-squares mean; SBP, systolic blood pressure; UACR, urine albumin-to-ceatinine ratio; rHTN, resistant hypertension.

1. Freeman MW, et al. N Engl J Med. 2023;388(5):395–405. 2. UACR data Presented at the American Society of Nephrology (ASN) Kidney Week 2024, San Diego, CA, USA , October 23–27, 2024.

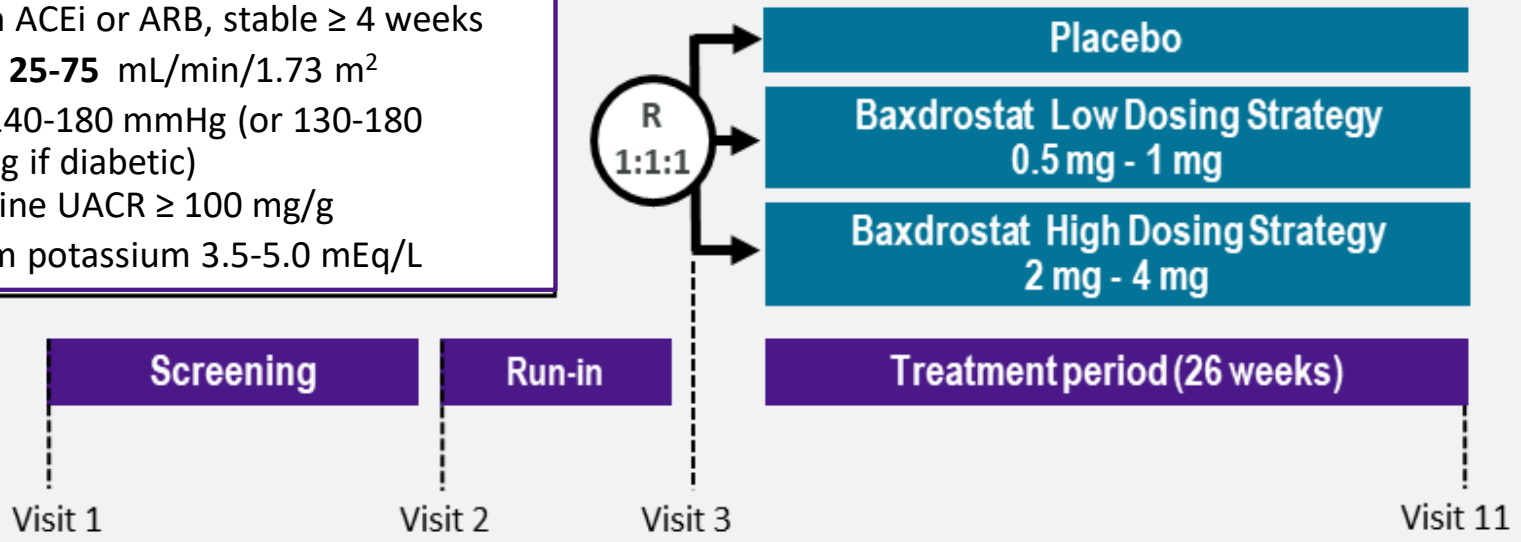
Freeman et al. N Engl J Med 2023
Heerspink H. ASN Kidney Week 2024

FigHTN Ph2 –baxdrostat σε XNN

A Phase II, randomized, double-blind, placebo-controlled, multicenter, parallel-group, dose-ranging study to evaluate the efficacy and safety of CIN-107 (baxdrostat) as compared to placebo after 26 weeks for the treatment of hypertension in adult participants with uHTN and CKD

Key eligibility criteria

- All on ACEi or ARB, stable ≥ 4 weeks
- **eGFR 25-75** mL/min/1.73 m^2
- SBP 140-180 mmHg (or 130-180 mmHg if diabetic)
- Baseline UACR ≥ 100 mg/g
- Serum potassium 3.5-5.0 mEq/L



Primary endpoint

- Change from **baseline in SBP** at week 26 for baxdrostat (pooled doses) vs placebo

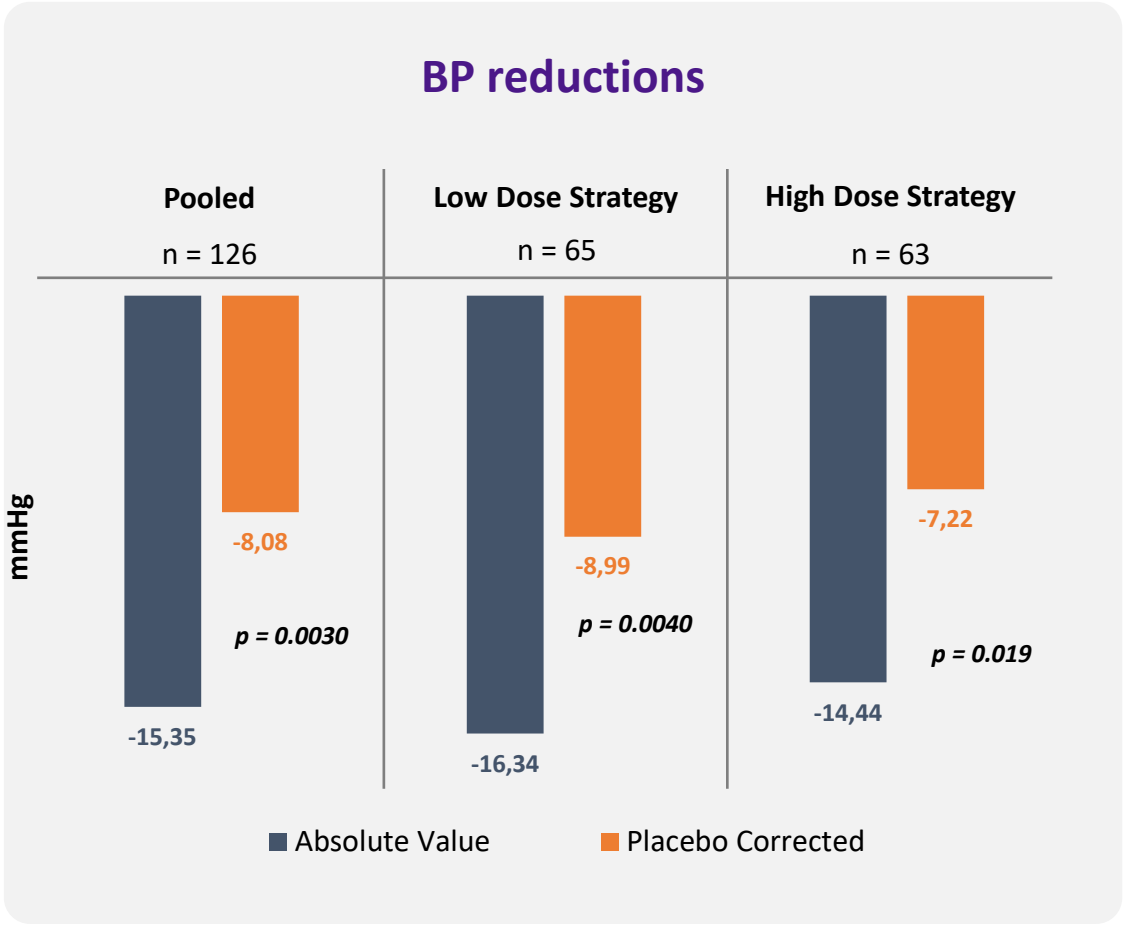
Exploratory endpoint

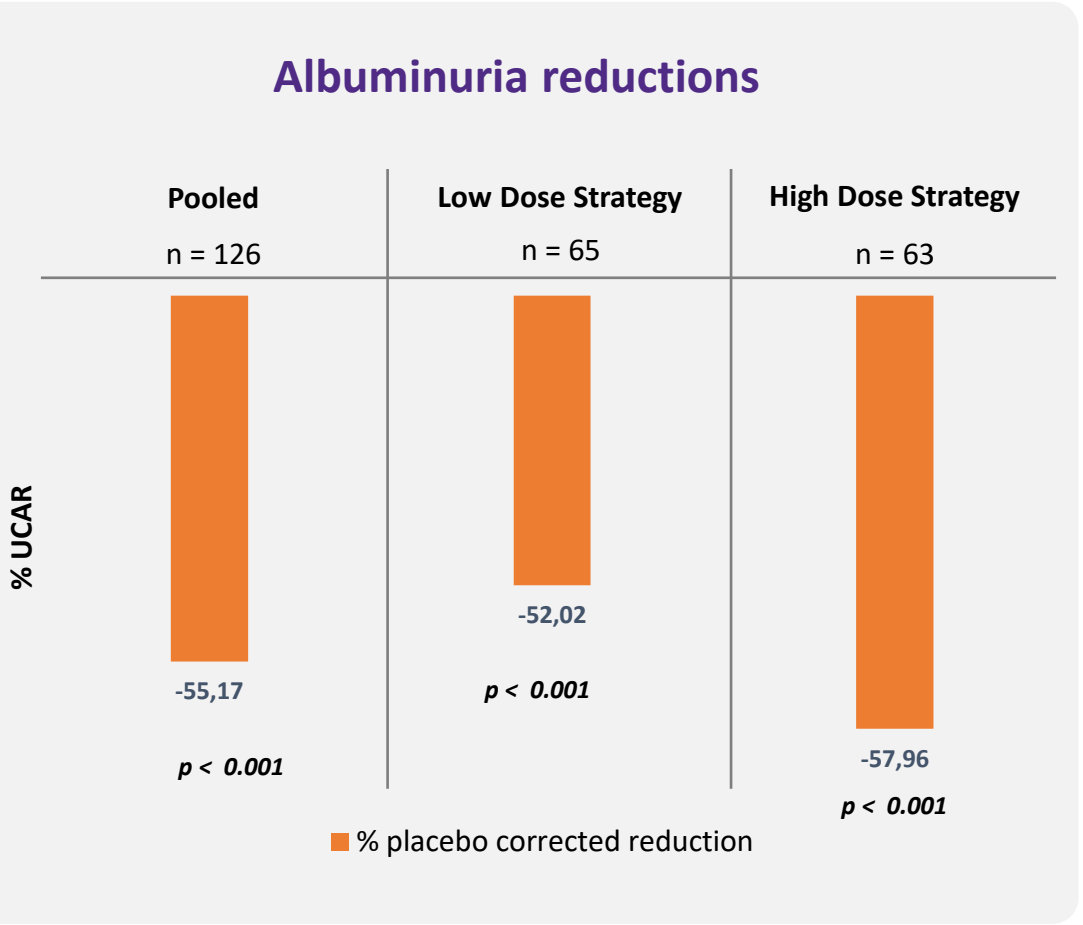
- Percentage change from **baseline in UACR** by dosing strategy of baxdrostat vs placebo at Week 26

195 participants randomized, FSI April 2022

Dwyer J et al. J Am Soc Nephrol 2025

FigHTN Ph2 μείωση ΑΠ και αλβουμινουρίας

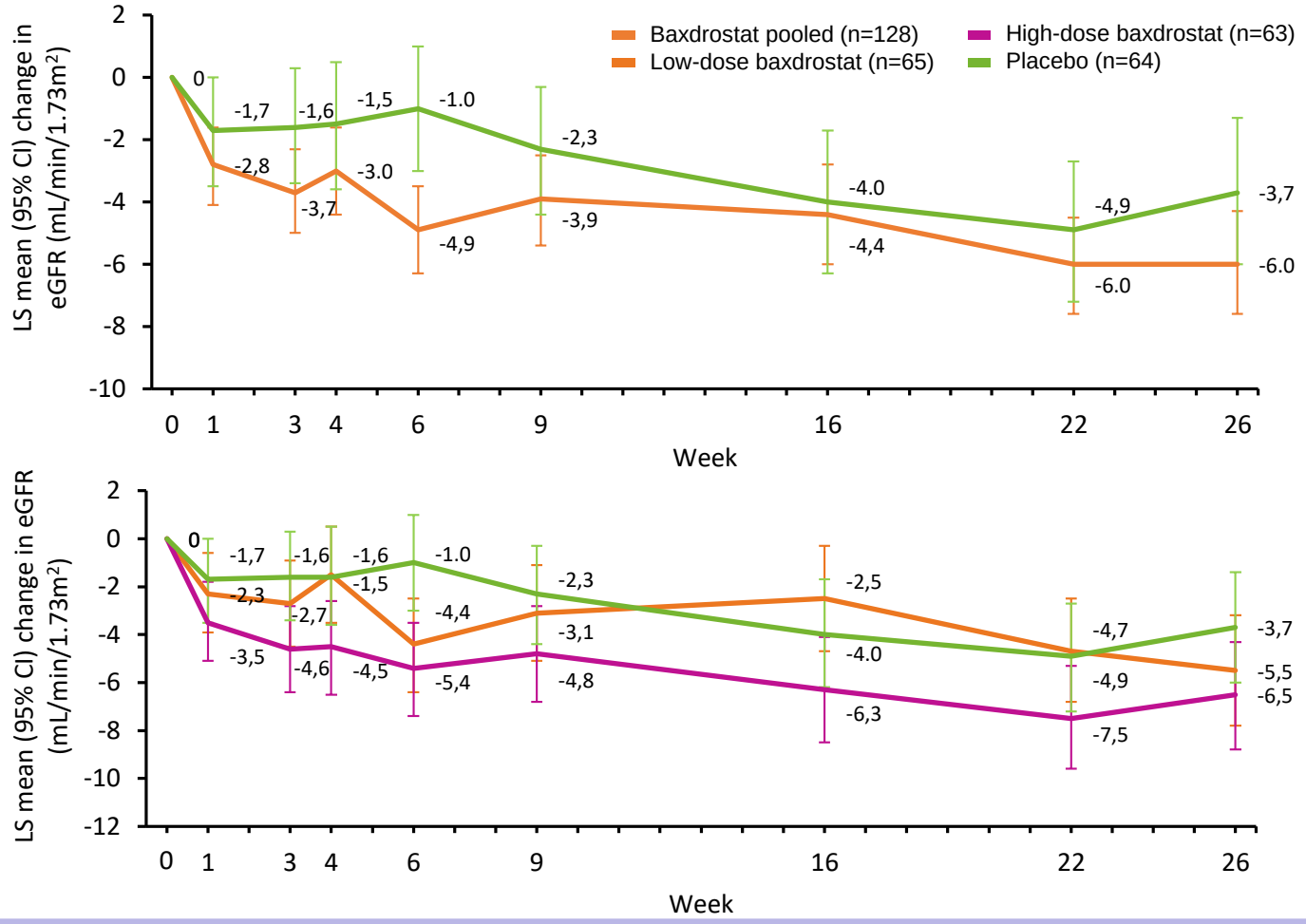




Dwyer J et al. J Am Soc Nephrol 2025

Μεταβολές του eGFR

eGFR



Reductions in eGFR
from one visit to the next:

>30%

Pooled baxdrostat: 19 (15%)
Placebo: 11 (17%)

>50%

Pooled baxdrostat: 0
Placebo: 1 (2%)

Mean eGFR changes from baseline were expected. The acute change in eGFR likely reflects an early response to baxdrostat, which may have a favorable long-term implication

CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least squares.

FigHTN Ph2 - υπερκαλιαιμία

Table 2. Summary of adverse events on-study (safety outcomes)

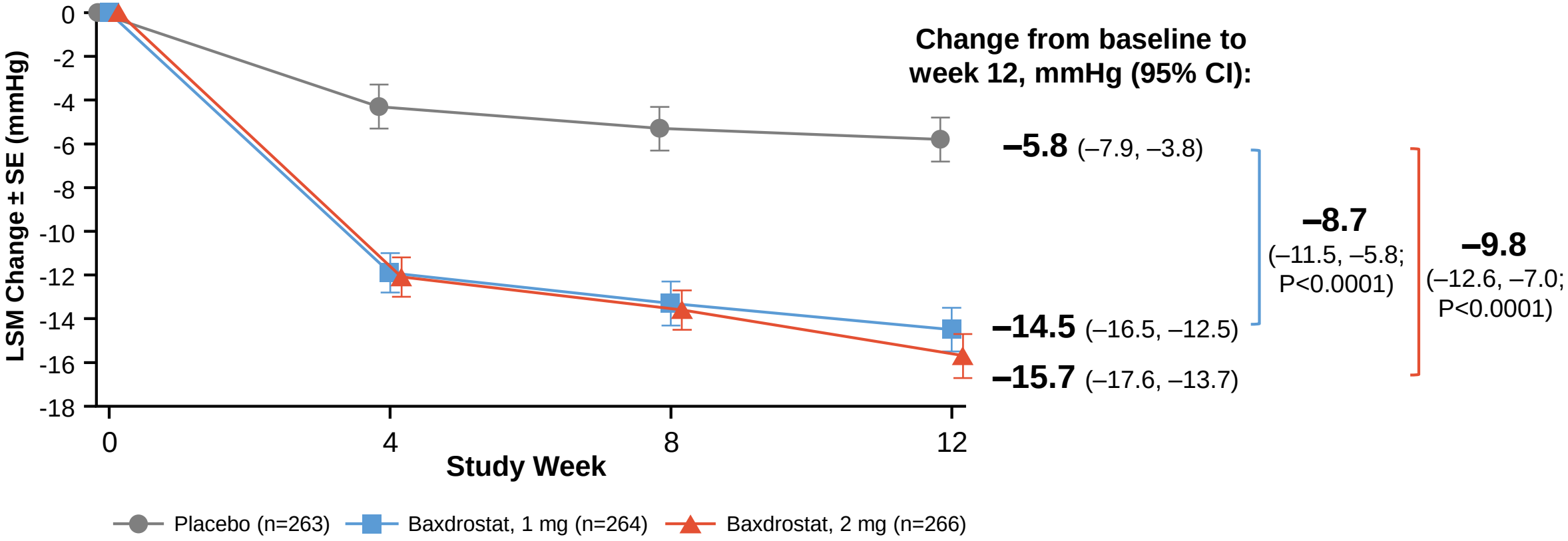
TEAE/TESAE Category,[a] *n* (%; No. of Occurrences)[b]	Baxdrostat Low-Dose *n*=65	Baxdrostat High-Dose *n*=63	Baxdrostat Treatment Groups Pooled *n*=128	Placebo *n*=64	Total *N*=192
Any TEAE	48 (74; 165)	52 (83; 171)	100 (78; 336)	35 (55; 119)	135 (70; 455)
Treatment-related[c]	23 (35; 55)	31 (49; 69)	54 (42; 124)	14 (22; 20)	68 (35; 144)
Any TESAEs	7 (11; 14)	5 (8; 11)	12 (9; 25)	2 (3; 3)	14 (7; 28)
Treatment-related[c]	2 (3; 4)	1 (2; 1)	3 (2; 5)	1 (2; 2)	4 (2; 7)
Any TEAE or TESAE leading to death	0	0	0	0	0
Any TEAE leading to treatment discontinuation	10 (15; 13)	11 (17; 20)	21 (16; 33)	5 (8; 8)	26 (14; 41)
Any TESAE leading to treatment discontinuation	2 (3; 5)	2 (3; 3)	4 (3; 8)	1 (2; 1)	5 (3; 9)
Treatment-emergent AESIs[d]	11 (17; 16)	12 (19; 16)	23 (18; 32)	4 (6; 4)	27 (14; 36)
Most common TEAEs (reported in ≥15% of patients)					
Hyperkalemia	21 (32; 32)	32 (51; 53)	53 (41; 85)	3 (5; 4)	56 (29; 89)
Blood creatinine increased	11 (17; 14)	15 (24; 20)	26 (20; 34)	5 (8; 7)	31 (16; 41)

Dwyer et al. J Am Soc Nephrol 2025

BaxHTN Ph3

796 patients with uHTN or rHTN were randomised to a 1:1:1 ratio to receive baxdrostat 1 mg (264), baxdrostat 2 mg (266), or placebo (264) once daily for 12 weeks

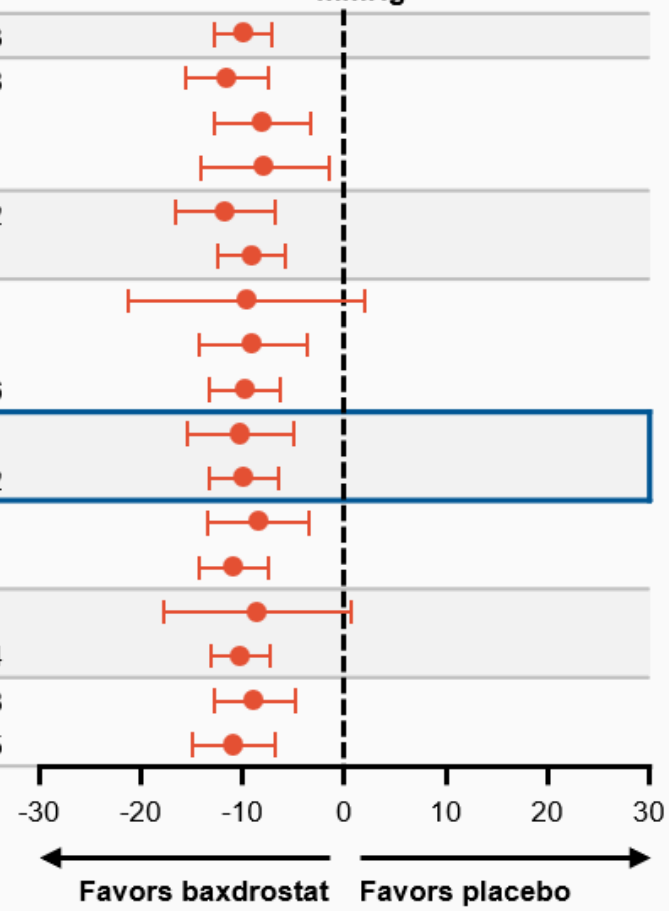
Change in seated-SBP: baxdrostat versus placebo; baseline to week 12



CI, confidence interval; LSM, least-squares mean; SBP, systolic blood pressure; SE, standard error.

Changes in seated SBP at week 12 were consistent across all pre-specified subgroups with baxdrostat 2 mg

Subgroup		Baxdrostat 2 mg n	Placebo n
Overall		266	263
Age – years	<65	145	138
	≥65 to <75	88	91
	≥75	33	34
Sex	Female	103	102
	Male	163	161
Race	Black or African American	21	15
	Asian	72	72
	White	168	166
Baseline hypertension	Uncontrolled hypertension	67	71
	Resistant hypertension	199	192
Baseline SBP – mmHg	<145	92	92
	≥145	174	171
Baseline eGFR – mL/min/1.73m²	<60	30	29
	≥60	236	234
Baseline body mass index – kg/m²	<30	126	128
	≥30	140	135



CI, confidence interval, eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure.

BaxHTN Ph3

- AEs were mostly mild
- One death in the placebo group
- No reports of adrenal insufficiency
- Most common AEs – numerically higher for baxdrostat versus placebo:
  - Hyperkalemia
  - Hyponatremia
  - Hypotension
  - Muscle spasms
  - Dizziness
- There were low rates of:
  - Confirmed serum potassium >6.0 mmol/L
  - Hyperkalemia leading to discontinuation

Event, n (%)	Placebo (N=264)	Baxdrostat, 1 mg (N=264)	Baxdrostat, 2 mg (N=266)
Any adverse event	109 (41.3)	125 (47.3)	119 (44.7)
Moderate/severe	23 (8.7)	27 (10.2)	37 (13.9)
Severe	5 (1.9)	3 (1.1)	7 (2.6)
Any adverse event leading to discontinuation	5 (1.9)	7 (2.7)	12 (4.5)
Hyperkalemia leading to discontinuation	0 (0.0)	2 (0.8)	4 (1.5)
Any serious adverse event*	7 (2.7)	5 (1.9)	9 (3.4)
Death	1 (0.4)	0 (0.0)	0 (0.0)
Adverse event of special interest†			
Hyperkalemia	0 (0.0)	7 (2.7)	21 (7.9)
Hyponatremia	1 (0.4)	2 (0.8)	6 (2.3)
Hypotension	2 (0.8)	5 (1.9)	6 (2.3)
Serum potassium – mmol/L			
>5.5 mmol/L	1/260 (0.4)	16/262 (6.1)	29/261 (11.1)
>6.0 mmol/L	1/262 (0.4)	6/262 (2.3)	8/263 (3.0)
Confirmed >6.0 mmol/L‡	0/262 (0.0)	3/262 (1.1)	3/263 (1.1)

*One case of hyperkalaemia (baxdrostat, 1 mg) and two cases of hyponatremia (baxdrostat, 1 mg and 2 mg) were deemed by investigators to be possibly related to study drug. †Elevated potassium levels, low sodium levels, and low blood pressure were adverse events of special interest if they required clinical intervention. ‡Central laboratory measurement >6.0 mmol/L confirmed with a local laboratory potassium measurement from the same day. AE, adverse event.

Bax24 trial - Phase 3 Trial of Baxdrostat on Ambulatory BP in rHTN

Multicenter, multinational, double-blind, randomized, placebo-controlled, parallel-group study[1]

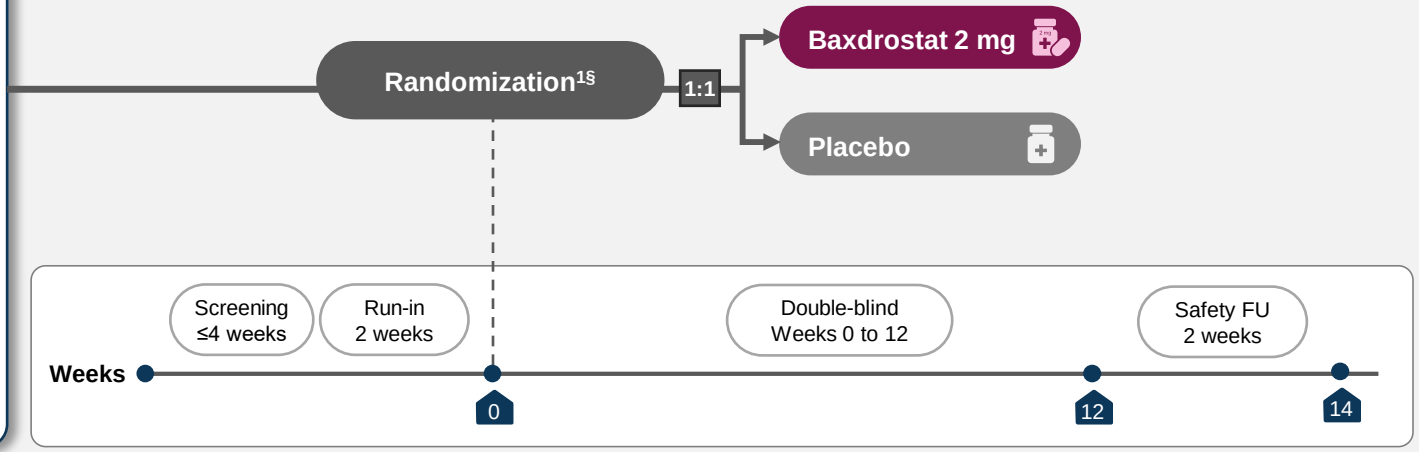
Key Inclusion Criteria[1,2]

- ≥18 years of age
- Mean seated SBP* ≥140 and <170 mmHg
- 24-hour SBP >130 mmHg
- rHTN - Stable regimen of ≥3 antihypertensives† from different classes‡
- eGFR ≥45 mL/min/1.73 m^2
- Serum K^+ ≥3.5 & <5.0 mmol/L

218 Patients[d]

Key Exclusion Criteria[1,2]

- Mean seated SBP* ≥170 mmHg or DBP* ≥110 mmHg
- Renal artery stenosis, uncontrolled/untreated hypo- or hyperthyroidism, pheochromocytoma, Cushing's syndrome, aortic coarctation
- Persistent AF
- NYHA Class IV HF at screening



Primary Endpoint[1,2]

- Change in ambulatory 24-hour average SBP from baseline[¶]

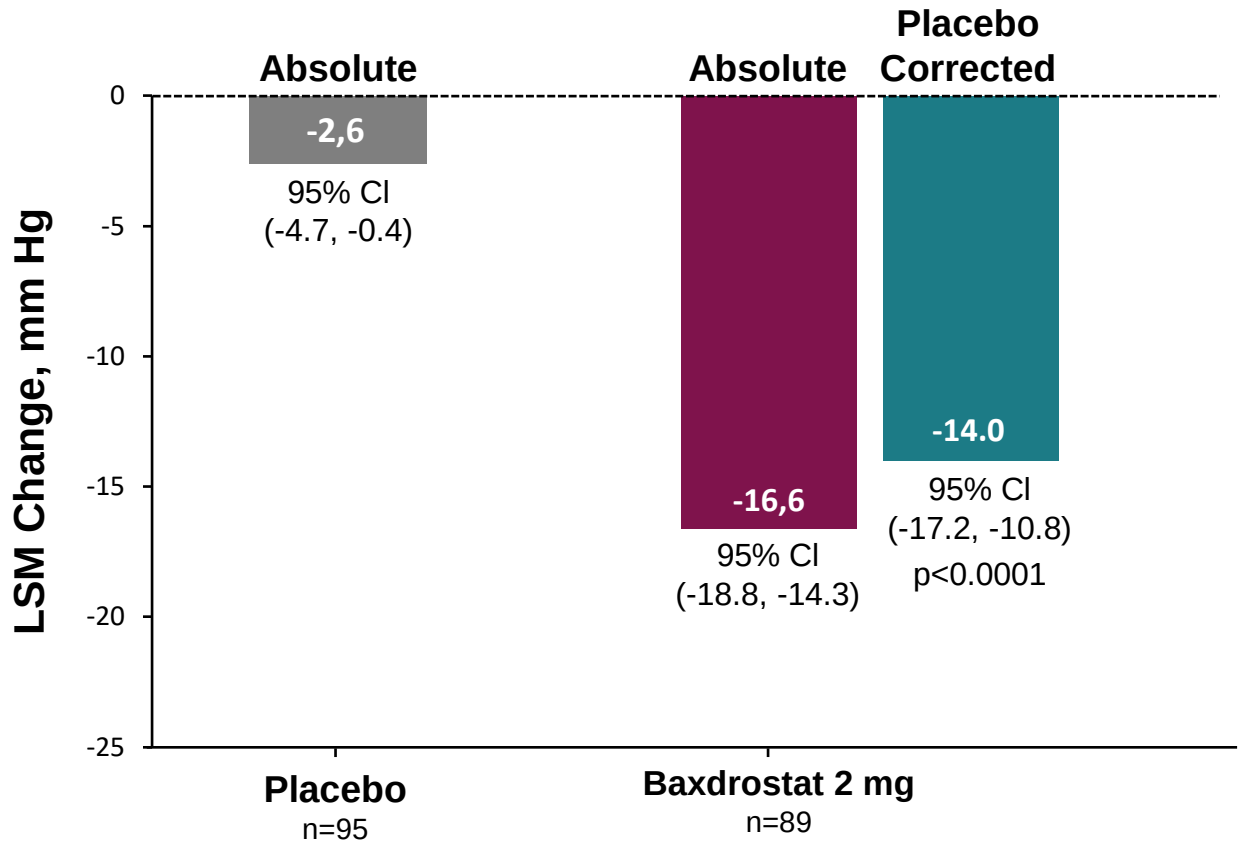
Secondary Endpoints[1]

- Change in ambulatory night-time and daytime average SBP and DBP from baseline
- Percentage achieving ambulatory 24-hour average SBP <130 mmHg
- Change in seated SBP and DBP from baseline
- Change in ambulatory 24-hour DBP from baseline
- Percentage achieving nocturnal SBP dipping of ≥10%[‖]

Note: All endpoints measured at Week 12.[2]
*By automated office blood pressure measurement.[2] †At max tolerated dose based on investigator judgement for ≥4 weeks prior to screening.[2] ‡Included a diruretic.[1,2] §A total of 218 patients were randomized and 217 received treatment.[1] ¶Analyzed only with patients with complete ABPM data at baseline and at 12-weeks.[1] ‖Defined as ≥10% reduction in night-time SBP compared to day-time SBP.
ABPM=ambulatory blood pressure monitoring; AF=atrial fibrillation; BP=blood pressure; DBP=diastolic blood pressure; eGFR=estimated glomerular filtration rate; HF=heart failure; ITT=intention-to-treat; K^+=potassium; NYHA=New York Heart Association; rHTN=resistant hypertension; SBP=systolic blood pressure.
1. Willams B et al. Abstract presented at AHA Scientific Sessions 2025. 2. ClinicalTrials.gov. NCT06168409. https://clinicaltrials.gov/study/NCT06168409. Updated October 3, 2025.

Baxdrostat Demonstrated Significant Placebo-Corrected Reductions in 24-Hour Ambulatory SBP in Patients With rHTN

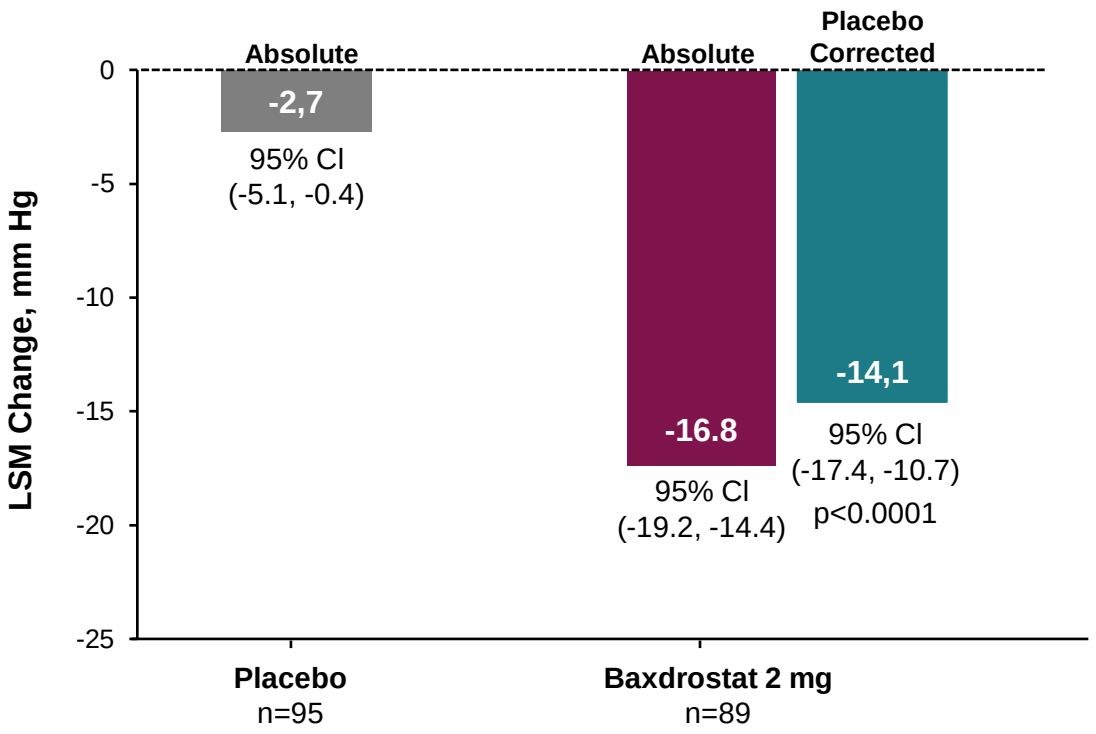
Primary Endpoint – Change in 24-Hour Ambulatory SBP from Baseline to Week 12[a]



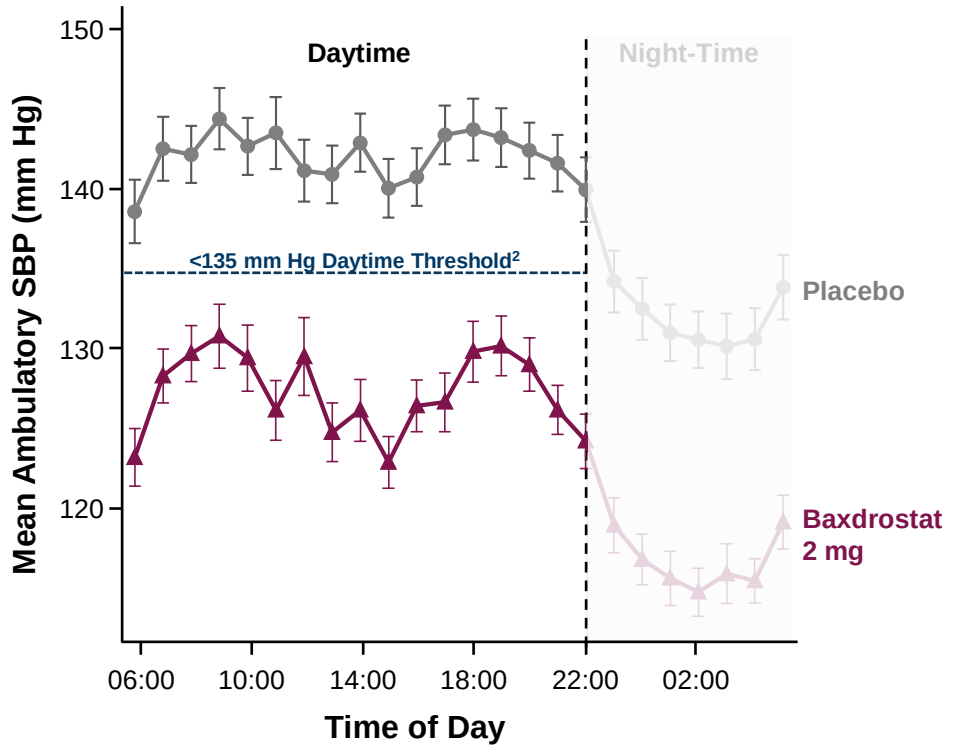
[a]Analyzed using ANCOVA model with treatment as a factor and 24-hour baseline ambulatory SBP as the covariate for patients with valid ABPM at both baseline and week 12.
ABPM = ambulatory blood pressure monitoring; ANCOVA = analysis of covariance; CI = confidence interval; LSM = least-squares mean; SBP = systolic blood pressure.
Willams B et al. Presented at: American Heart Association (AHA) Scientific Sessions; November 8-10, 2025; New Orleans, LA

Baxdrostat Demonstrated Significant Placebo-Corrected Reductions in Daytime Ambulatory SBP in Patients with rHTN[1]

Secondary Endpoint – Change in Daytime Ambulatory SBP from Baseline to Week 12[1,a]



Hourly Mean Daytime Ambulatory SBP Profile at Week 12[1,b,c]



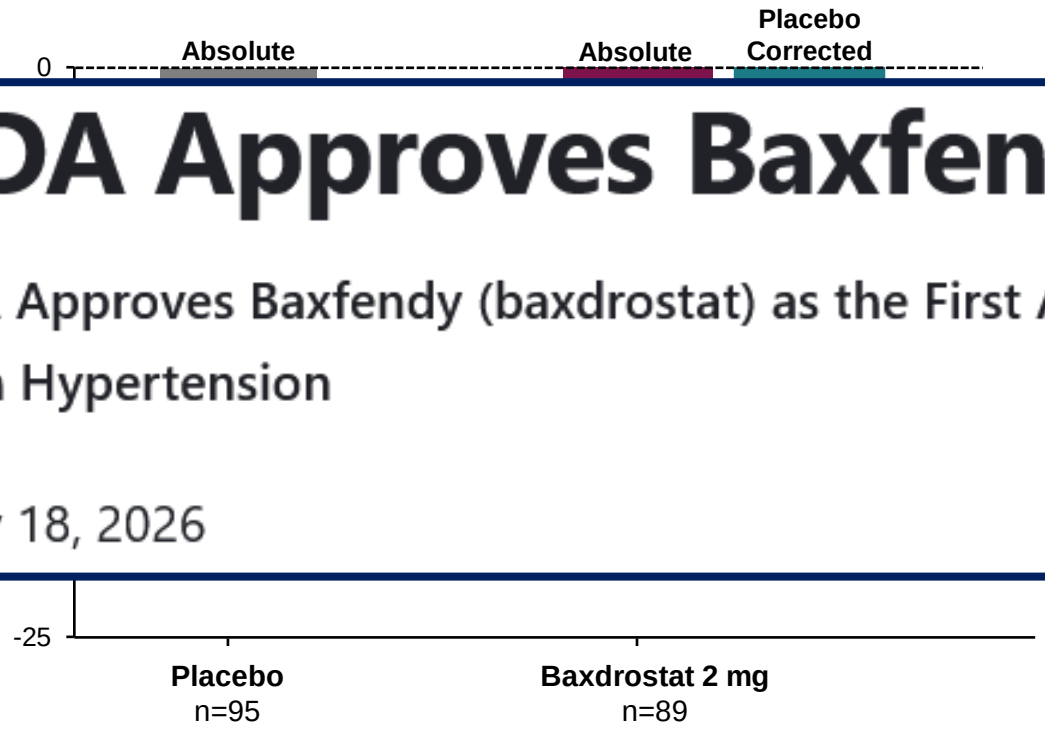
[a]Endpoint analyzed for patients with valid ABPM at both baseline and week 12 using an ANCOVA model with treatment as a factor; the covariate was ambulatory daytime SBP; [b]Daytime was defined from 06:00-21:59 while night-time was 22:00-05:59; [c]Bars on the line graphs indicate SE.

ABPM = ambualtory blood pressure monitoring; ANCOVA = analysis of covariance; CI = confidence interval; LSM = least-squares mean; rHTN = resistant hypertension; SBP = systolic blood pressure; SE = standard error.

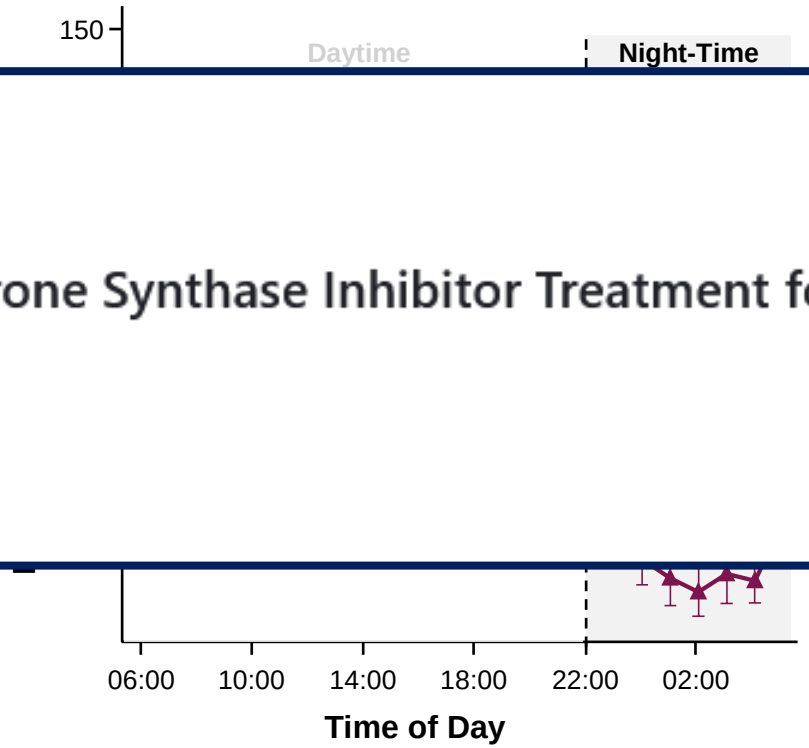
1. Willams B et al. Presented at: American Heart Association (AHA) Scientific Sessions; November 8-10, 2025; 2. Williams B, et al. *Eur Heart J*. 2018.

Baxdrostat Demonstrated Significant Placebo-Corrected Reductions in Night-Time Ambulatory SBP in Patients with rHTN[1]

Secondary Endpoint – Change in Night-Time Ambulatory SBP from Baseline to Week 12[1,a]



Hourly Mean Night-Time Ambulatory SBP Profile at Week 12[1,b,c]



FDA Approves Baxfendy

FDA Approves Baxfendy (baxdrostat) as the First Aldosterone Synthase Inhibitor Treatment for Adults with Hypertension

May 18, 2026

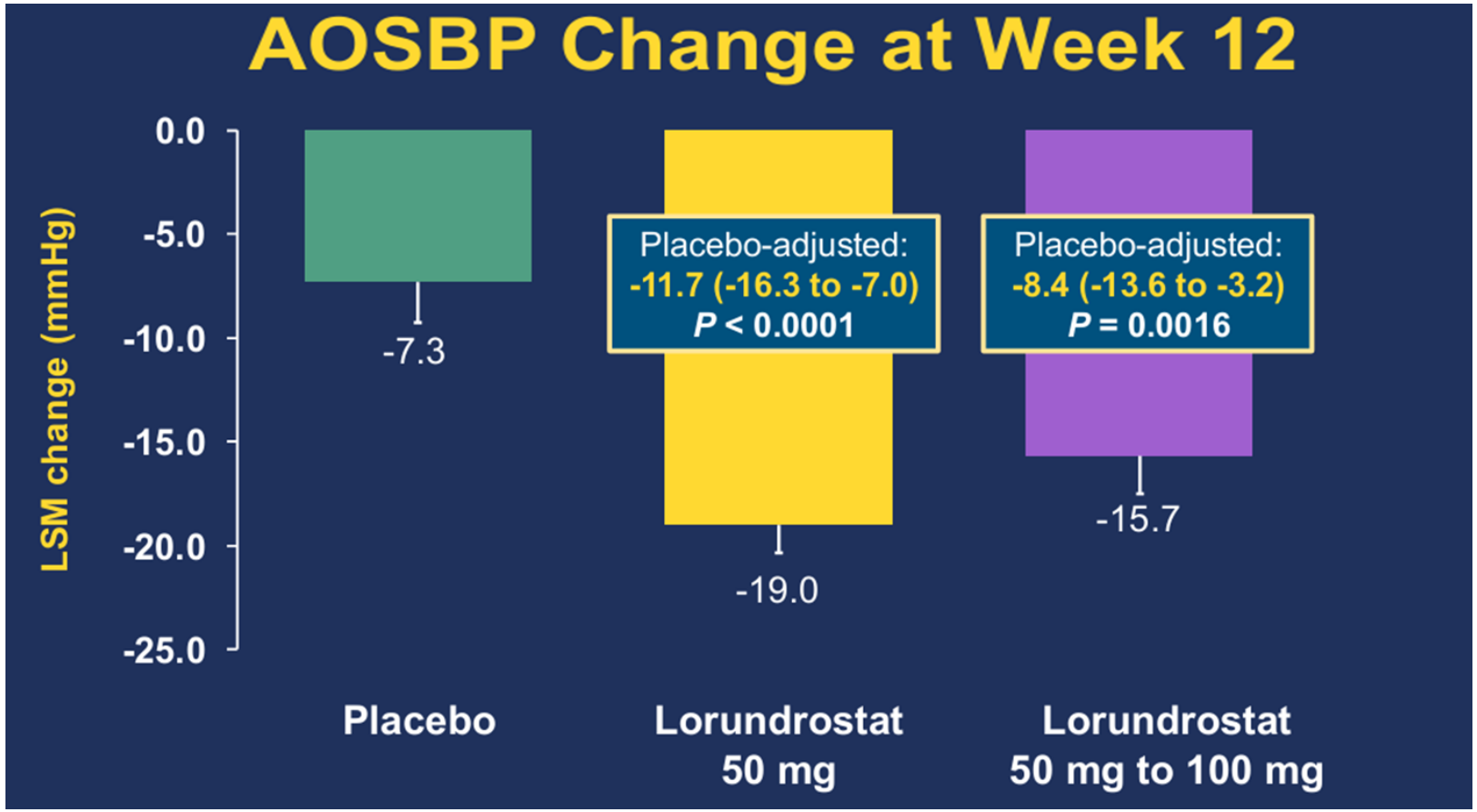
[a]Endpoint analyzed for patients with valid ABPM at both baseline and week 12 using an ANCOVA model with treatment as a factor; the covariate was ambulatory night-time SBP; [b]Daytime was defined from 06:00-21:59 while night-time was 22:00-05:59; [c]Bars on the line graphs indicate SE.

ABPM = ambualtory blood pressure monitoring; ANCOVA = analysis of covariance; CI = confidence interval; LSM = least-squares mean; rHTN = resistant hypertension; SBP = systolic blood pressure; SE = standard error.

1. Willams B et al. Presented at: American Heart Association (AHA) Scientific Sessions; November 8-10, 2025; 2. Williams B, et al. *Eur Heart J*. 2018.

Launch-HTN Phase 3 – lorundrostat σε uHTN και rHTN

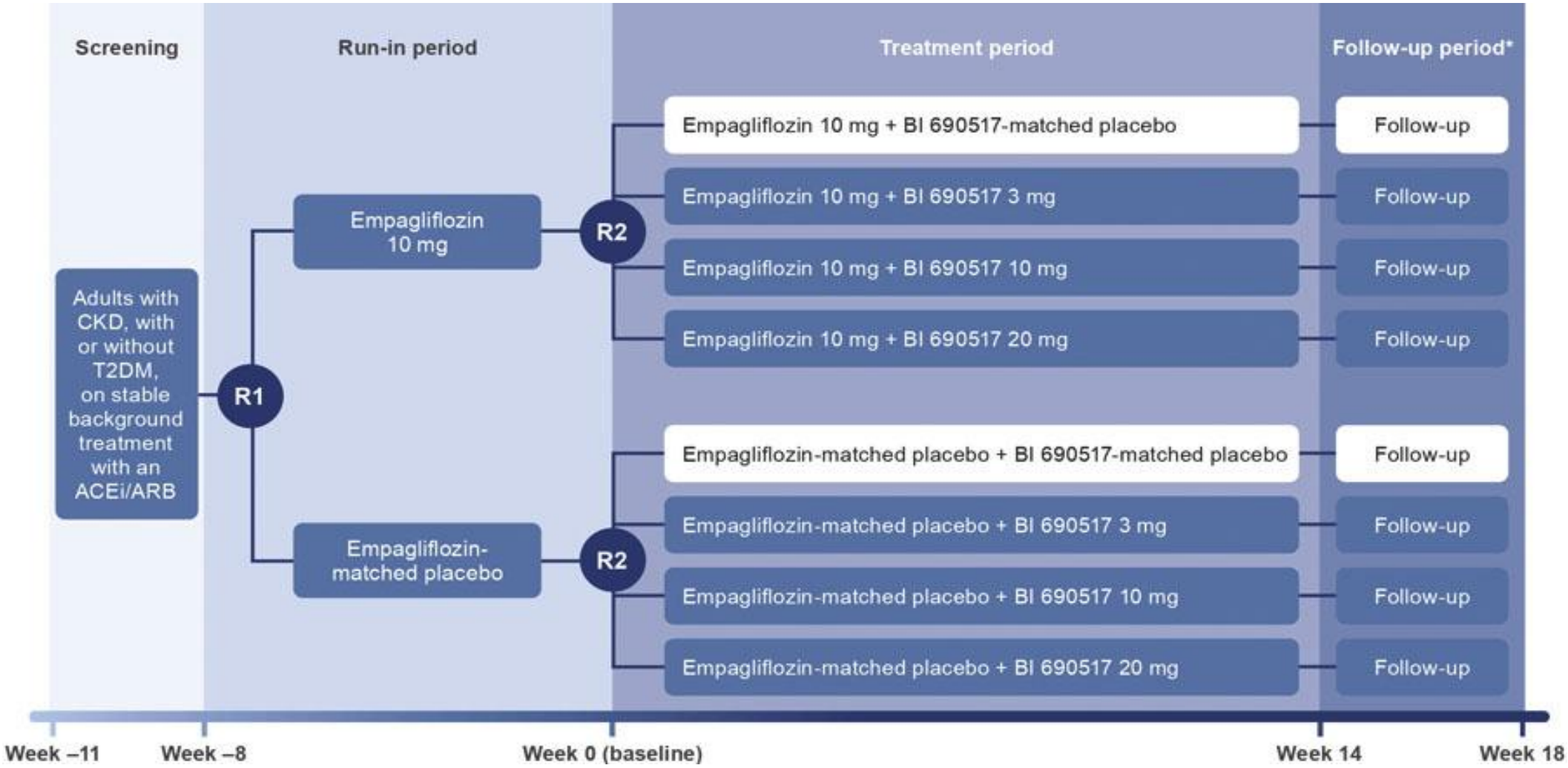
1083 participants with uHTN were randomized with a 1:2:1 ratio to 50 mg/d of lorundrostat for 6 weeks followed by 100 mg/d of lorundrostat for 6 weeks (n = 270) if they met prespecified criteria, 50 mg/d of lorundrostat for 12 weeks (n = 541), or daily placebo for 12 weeks (n = 272)



Saxena M. et al. JAMA 2025

Efficacy and safety of aldosterone synthase inhibition with and without empagliflozin for chronic kidney disease: a randomised, controlled, phase 2 trial

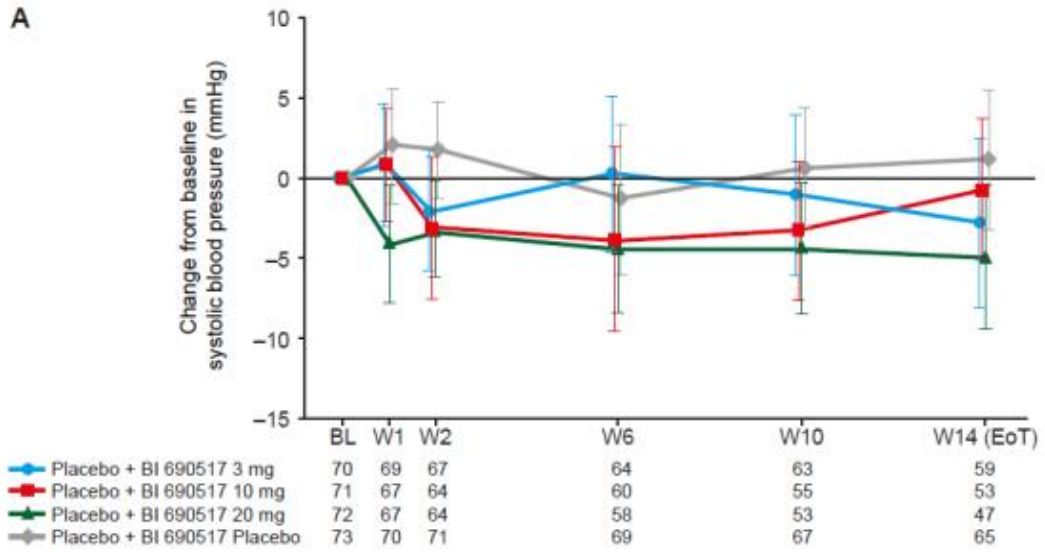
Lancet 2024; 403: 379–90



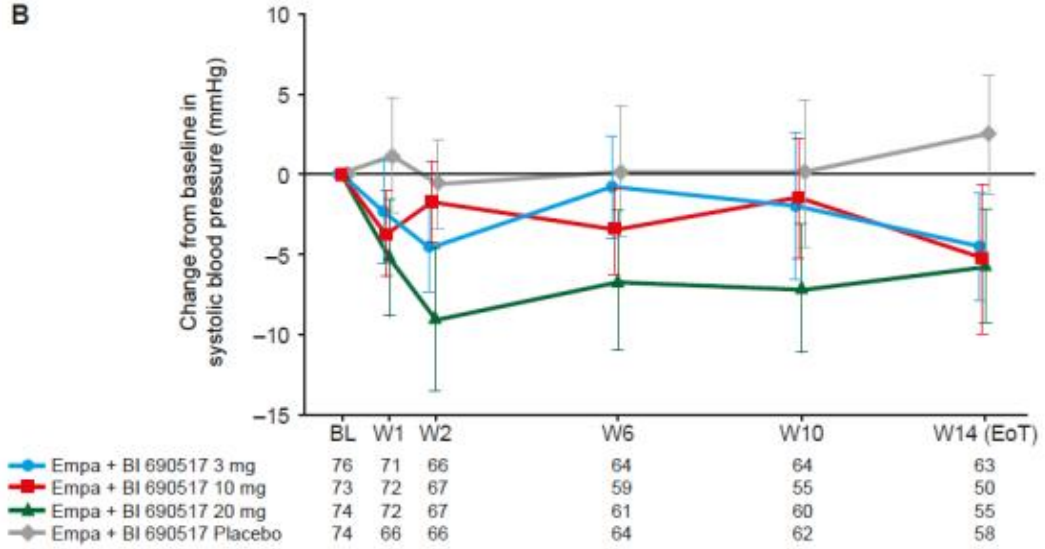
N=586

Tuttle KR et al. Lancet 2024

Change in office SBP



	Change, mean (95% CI)	Placebo-corrected change, mean (95% CI)
BI 690517 placebo	1·09 (–3·35, 5·53)	..
BI 690517 3 mg	–2·80 (–8·15, 2·56)	–3·89 (–10·73, 2·95)
BI 690517 10 mg	–0·72 (–5·18, 3·74)	–1·81 (–8·10, 4·48)
BI 690517 20 mg	–4·94 (–9·44, –0·43)	–6·03 (–12·44, 0·38)

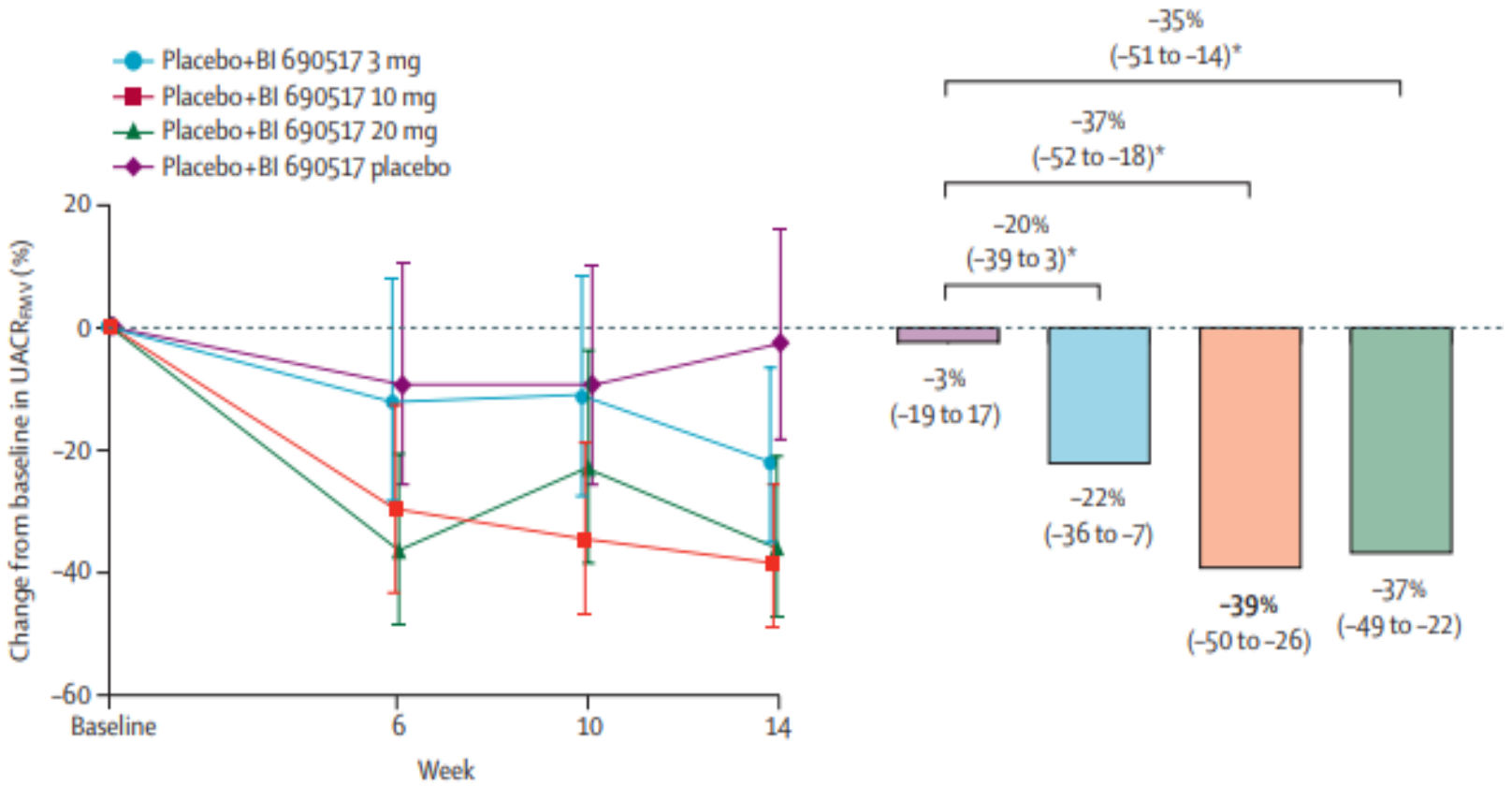


	Change, mean (95% CI)	Placebo-corrected change, mean (95% CI)
BI 690517 placebo	2·47 (–1·30, 6·23)	..
BI 690517 3 mg	–4·56 (–7·94, –1·17)	–7·02 (–12·02, –2·02)
BI 690517 10 mg	–5·34 (–10·04, –0·64)	–7·81 (–13·69, –1·92)
BI 690517 20 mg	–5·78 (–9·37, –2·19)	–8·25 (–13·40, –3·09)

Tuttle KR et al. Lancet 2024

Change in UACR with vicadrostat

N=586

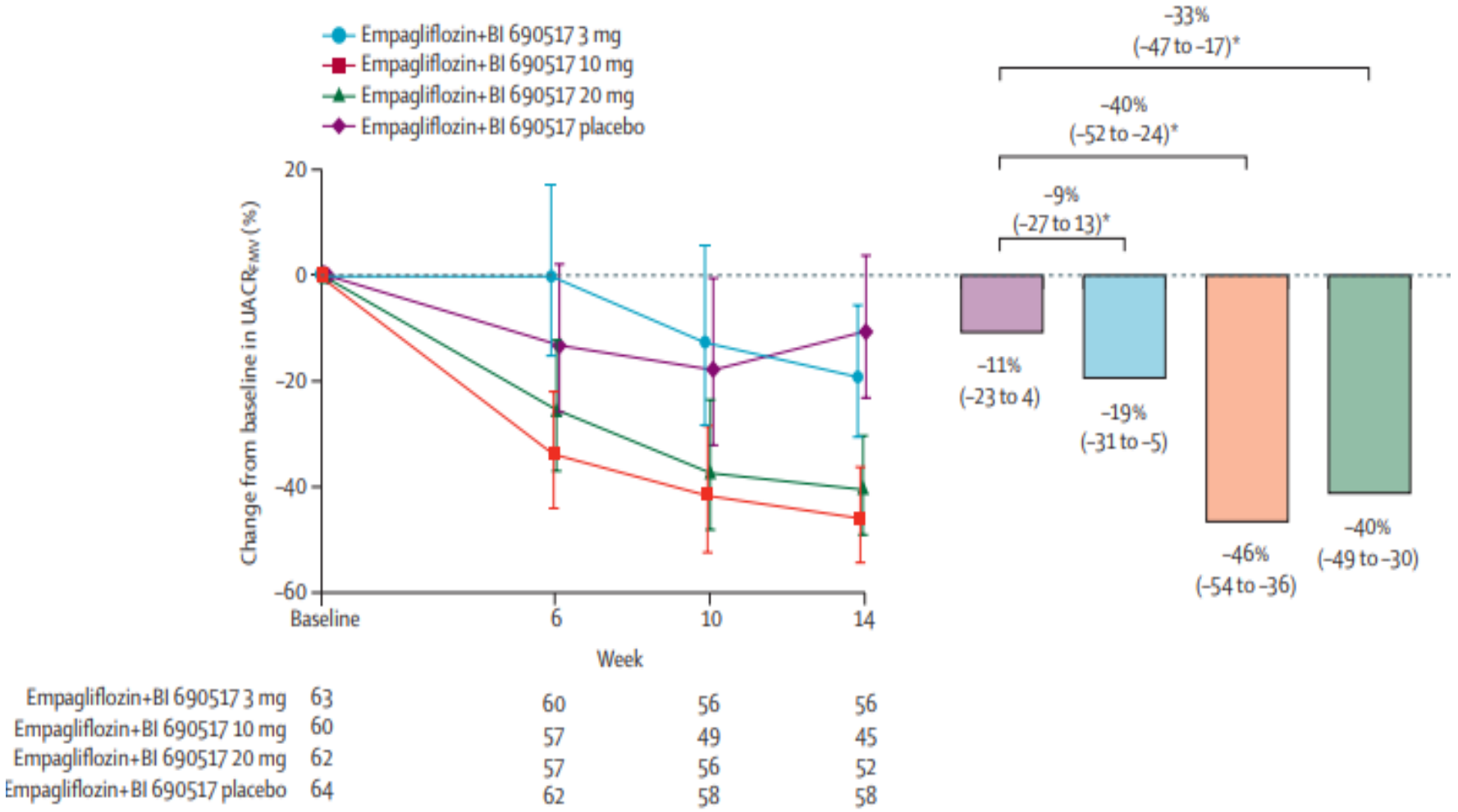


Placebo+BI 690517 3 mg	65	62	61	59
Placebo+BI 690517 10 mg	61	58	51	53
Placebo+BI 690517 20 mg	59	54	48	43
Placebo+BI 690517 placebo	69	67	63	62

Tuttle KR et al. Lancet 2024

Change in UACR with BI 690517 (vicadrostat) + empagliflozin

N=586

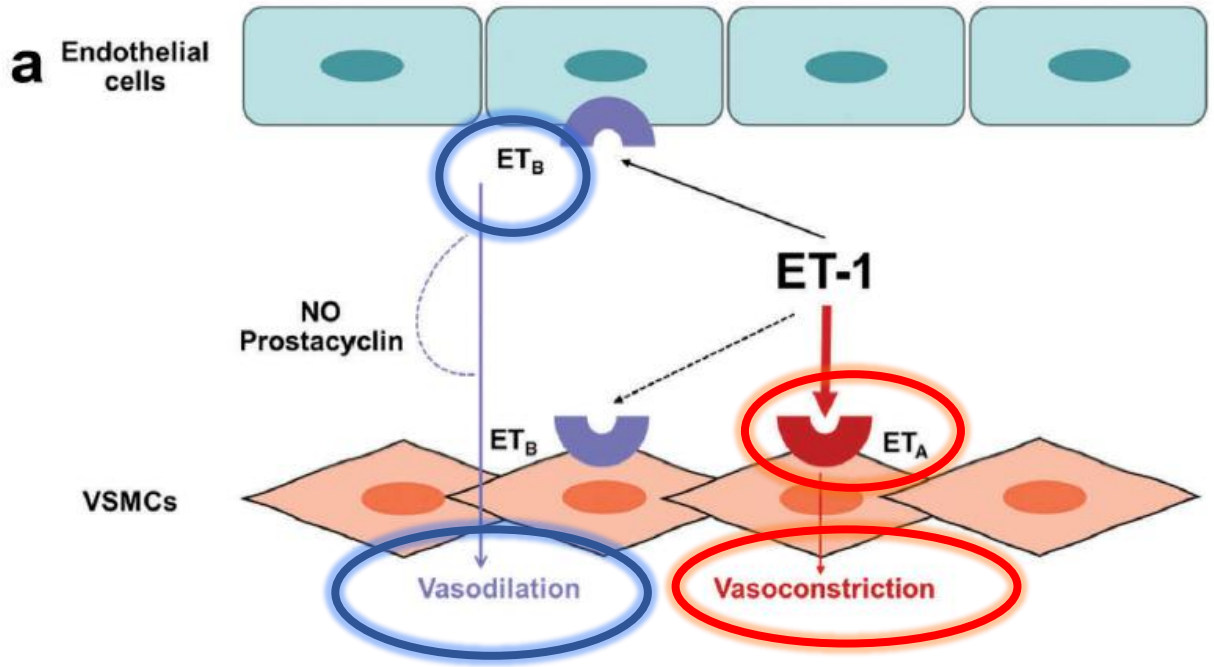


Tuttle KR et al. Lancet 2024

Ανταγωνιστές υποδοχέων ενδοθηλίνης

Δράση σε ενδοθηλιακά και λεία μυικά κύτταρα

Δύο κατηγορίες υποδοχέων ενδοθηλίνης (ET_AR & ET_BR)
→ Διττός τρόπος δράσης



Ενεργοποίηση ET_AR → Αγγειοσύσπαση

vs.

Ενεργοποίηση ET_BR → Αγγειοδιαστολή

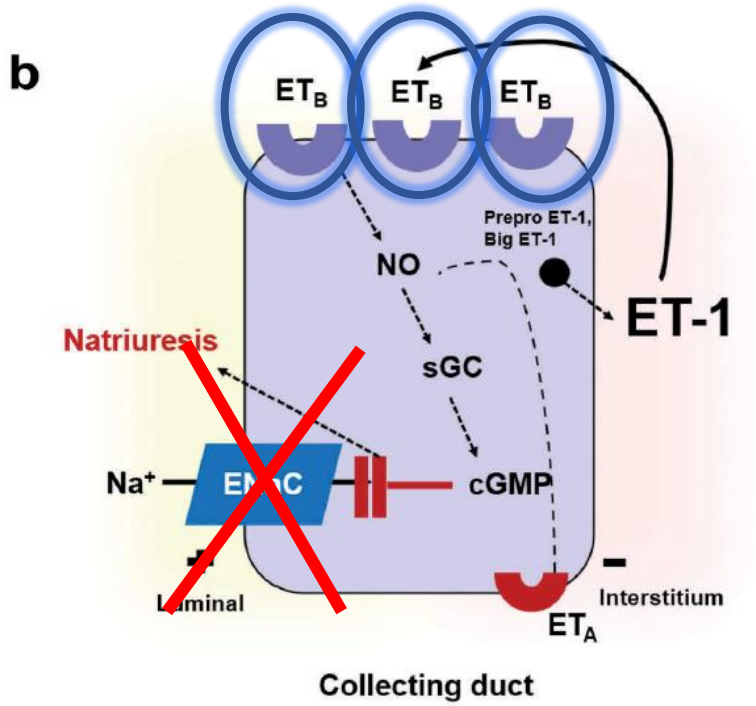
- Τρεις ισομορφές του πεπτιδίου: **ET-1 (κυριότερη)**, ET-2, ET-3
- Ερεθίσματα μεταξύ των οποίων η **υπεργλυκαιμία** προάγουν την παραγωγή της
- Αυτοκρινής και παρακρινής δράση με τη συστηματική κυκλοφορία

Anyfanti P, Theodorakopoulou M, Iatridi F, Sarafidis P. Exp Opin Invest Drugs 2025

Δράση στο νεφρό

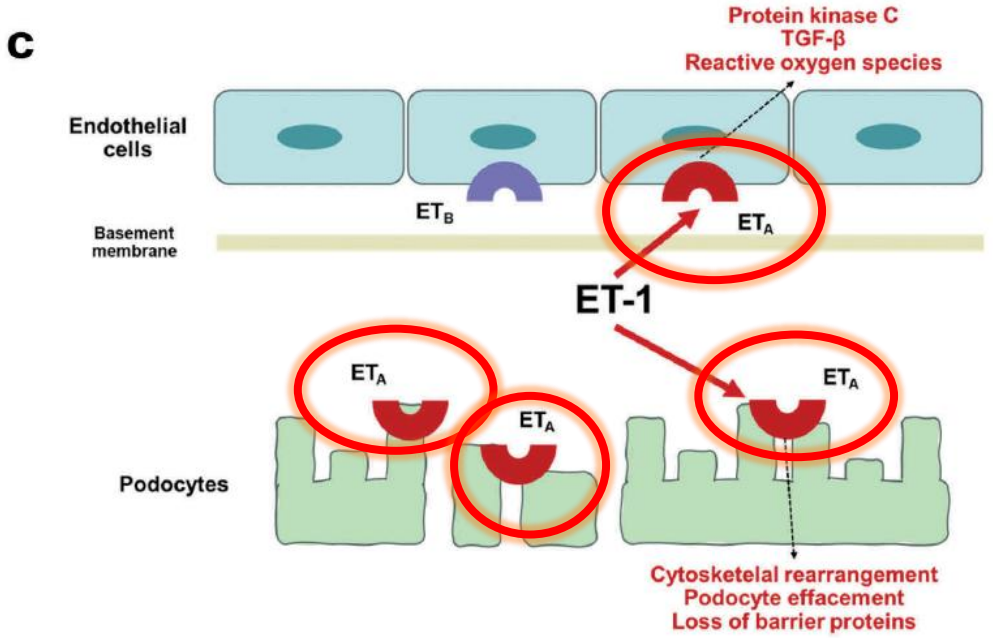
Αθροιστικά σωληνάρια

νατριούρηση μέσω ενεργοποίησης ET_BR



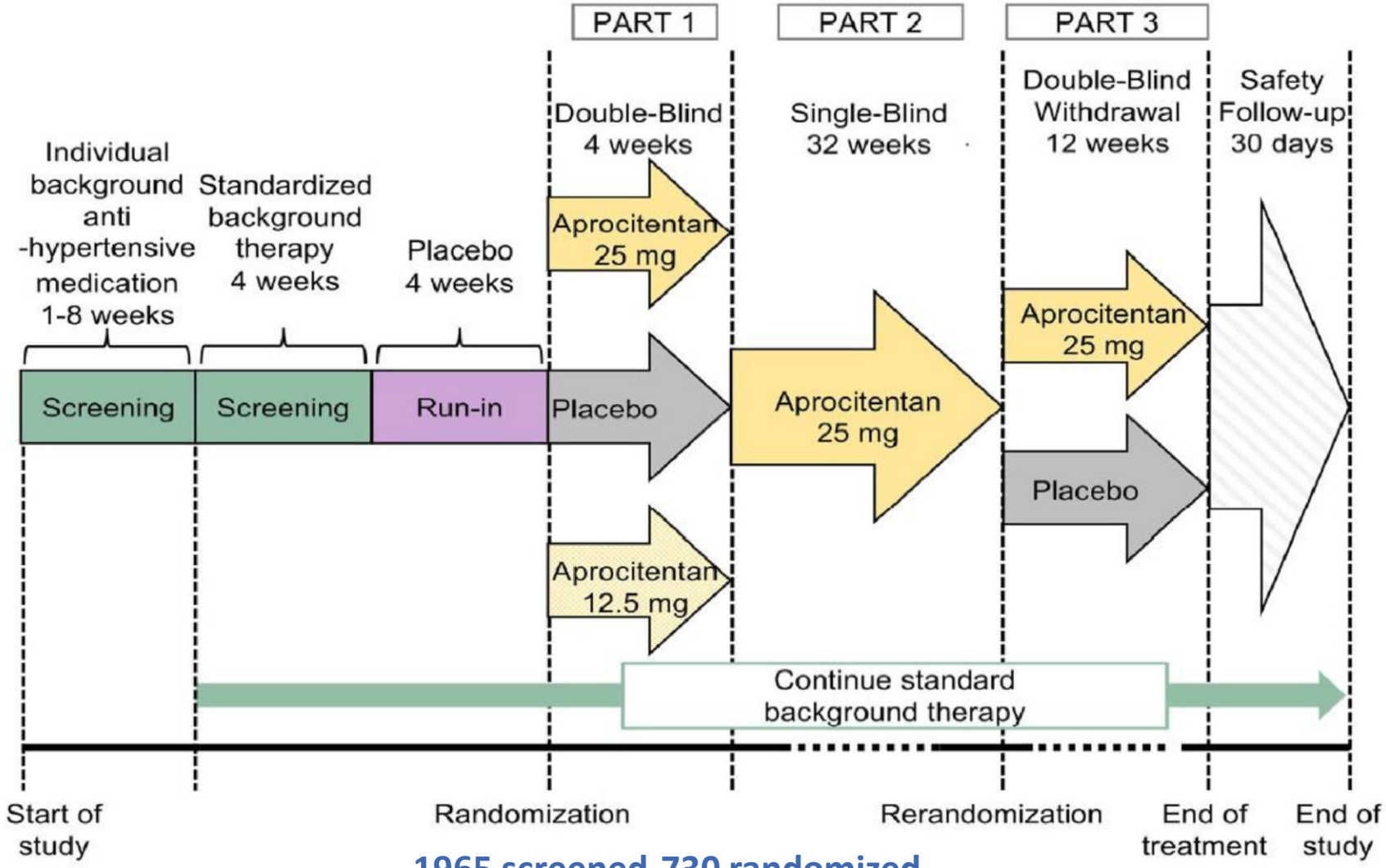
Σπείραμα

ίνωση και την πρωτεϊνουρία μέσω ενεργοποίησης ET_AR



Anyfanti P, Theodorakopoulou M, Iatridi F, Sarafidis P. Exp Opin Invest Drugs 2025

PRECISION study - Dual ET_A/ET_B antagonist aprocitentan



1965 screened-730 randomized

- 4 εβδομάδες τυφλή run-in φάση με σταθερή θεραπεία και placebo
- Ένα χάπι/τριπλός συνδυασμός (αμιλοδιπίνη, βαλσαρτάνη, υδροχλωροθειαζίδη) 5/160/25 mg ή 10/160/25 mg
- ΑΠ ιατρείου (unattented) >140 mmHg
- Στο screening, 63% ασθενών 4 ή > φάρμακα (βητα-αναστολεας)

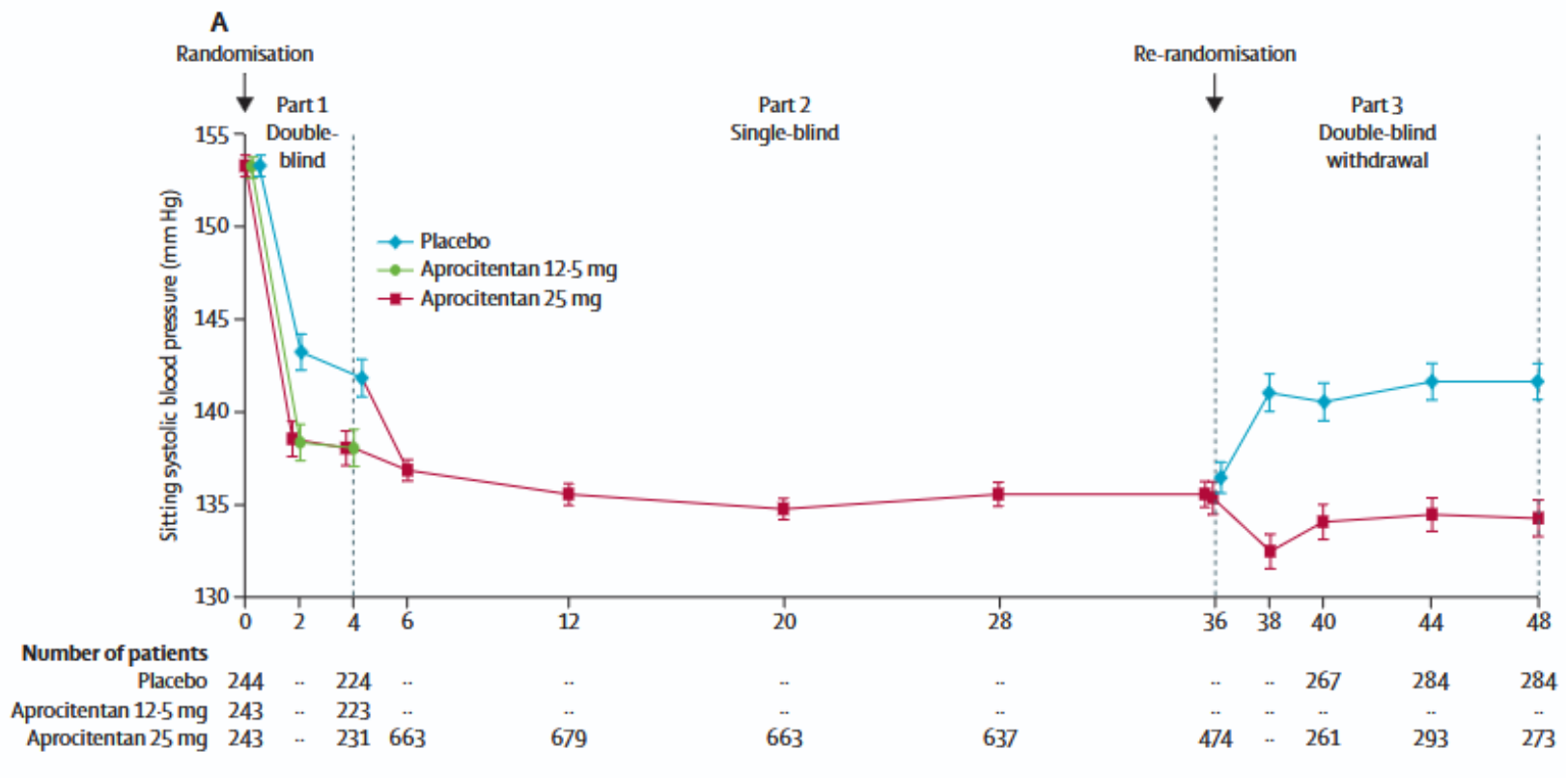
Schlaich MP et al. Lancet, 2022

Μεταβολές της συστολικής ΑΠ ιατρείου

Placebo-corrected change in unattended automated SBP/DBP:

Week 4: -3.8mmHg and -3.7mmHg compared to placebo for aprocitentan 12.5 and 25mg respectively

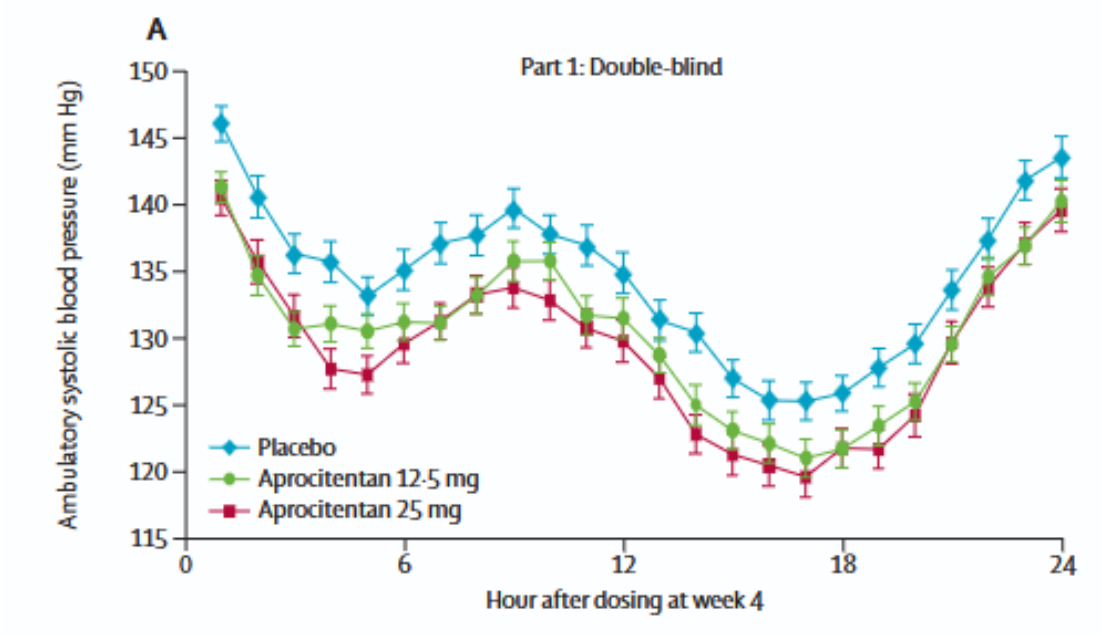
Week 40: - 5.8mmHg compared to placebo (aprocitentan 25mg)

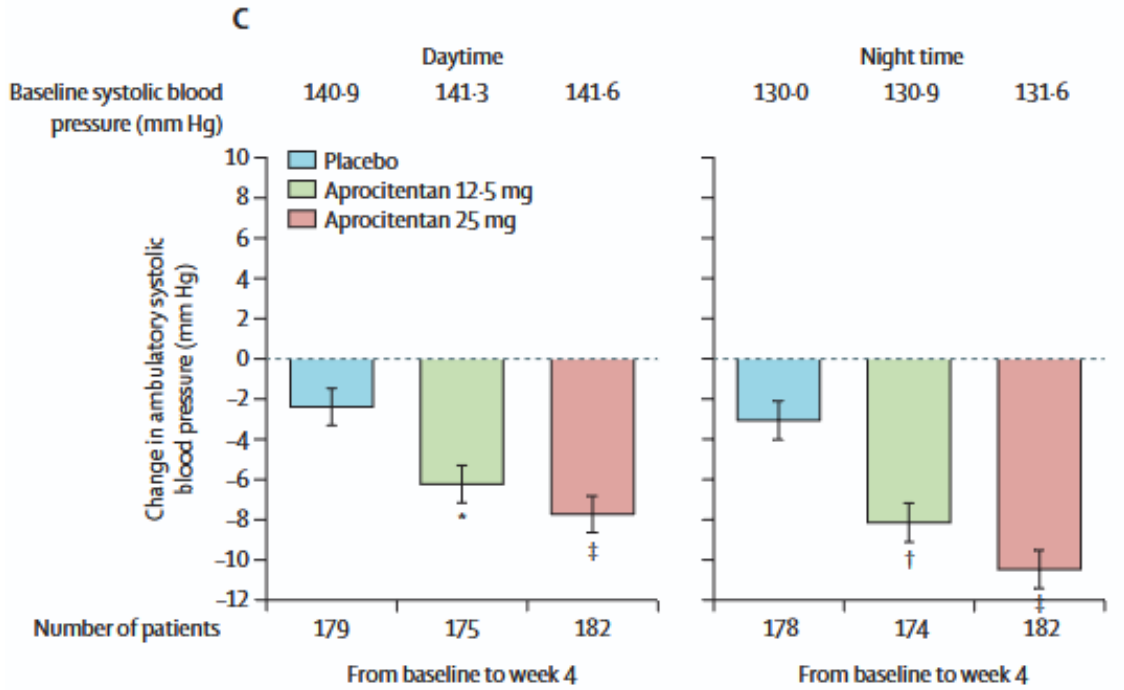


Schlaich MP et al. Lancet, 2022

PRECISION study: ABPM

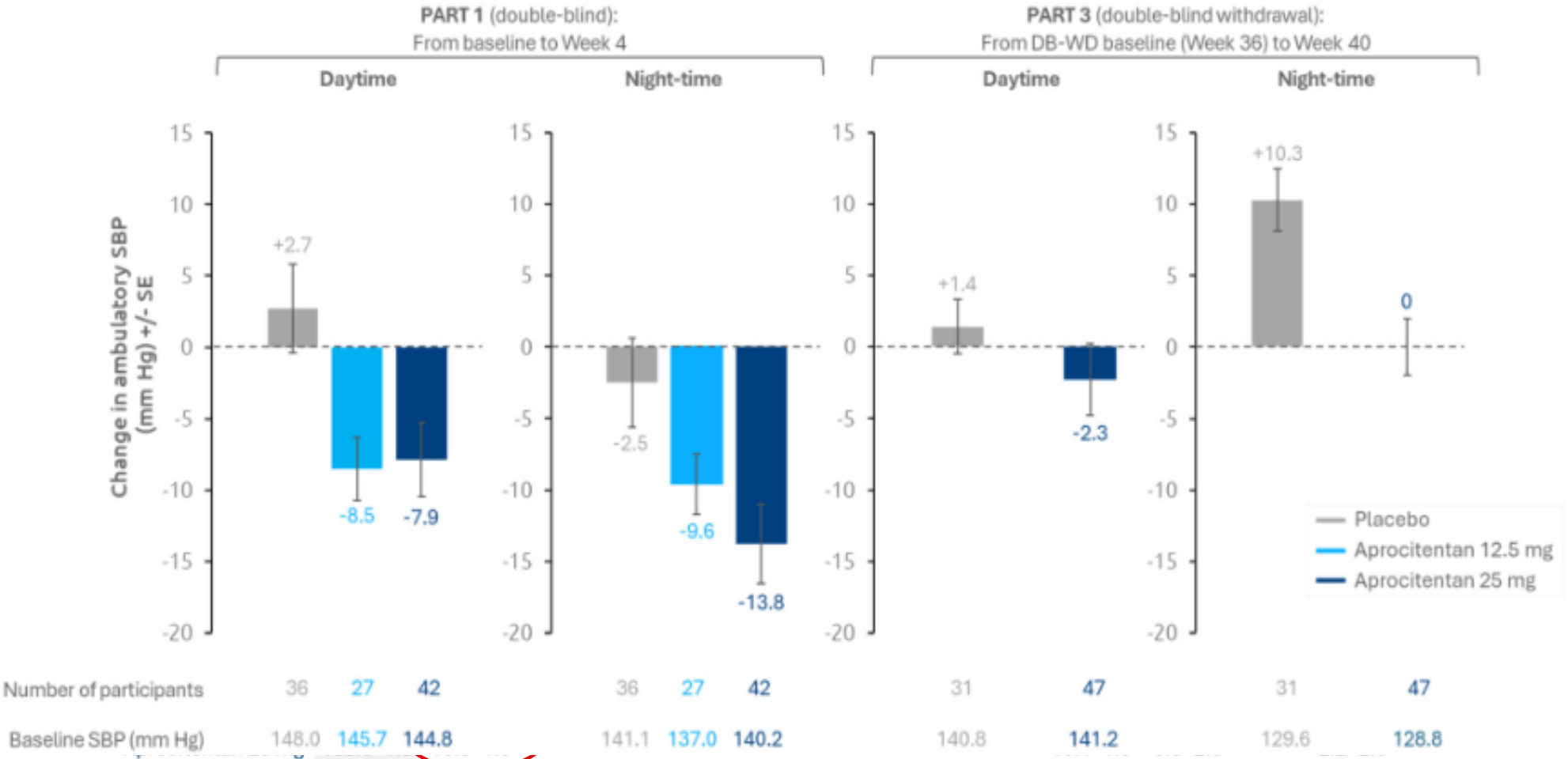
- 24h SBP: **-4.2 and -5.9 mmHg** compared to placebo
- Daytime SBP: **-3.8 and -5.3 mmHg** compared to placebo
- Nighttime SBP: **-5.1 and -7.4 mmHg** compared to placebo for aprocitentan 12.5 and 25mg respectively





Schlaich MP et al. Lancet, 2022

PRECISION study: post-hoc ανάλυση ασθενών με CKD ≥ high risk



Rossignol P et al. Hypertension, 2025

Ανεπιθύμητες εκβάσεις

	Aprocitentan 12·5 mg	Aprocitentan 25 mg	Placebo
Part 1: Double-blind	243	245	242
Patients with at least one event	30 (12·3%)	47 (19·2%)	7 (2·9%)
Oedema or fluid retention	22 (9·1%)	45 (18·4%)	5 (2·1%)
Anaemia or haemodilution	9 (3·7%)	3 (1·2%)	0
Hepatic disorder	0	1 (0·4%)	2 (0·8%)
Part 2: Single-blind	--	704	--
Patients with at least one event	--	185 (26·3%)	--
Oedema or fluid retention	--	128 (18·2%)	--
Anaemia or haemodilution	--	63 (8·9%)	--
Hepatic disorder	--	16 (2·3%)	--
Part 3: Double-blind withdrawal	--	310	303
Patients with at least one event	--	18 (5·8%)	15 (5·0%)
Oedema or fluid retention	--	8 (2·6%)	4 (1·3%)
Anaemia or haemodilution	--	6 (1·9%)	4 (1·3%)
Hepatic disorder	--	4 (1·3%)	7 (2·3%)

Schlaich MP et al. Lancet, 2022

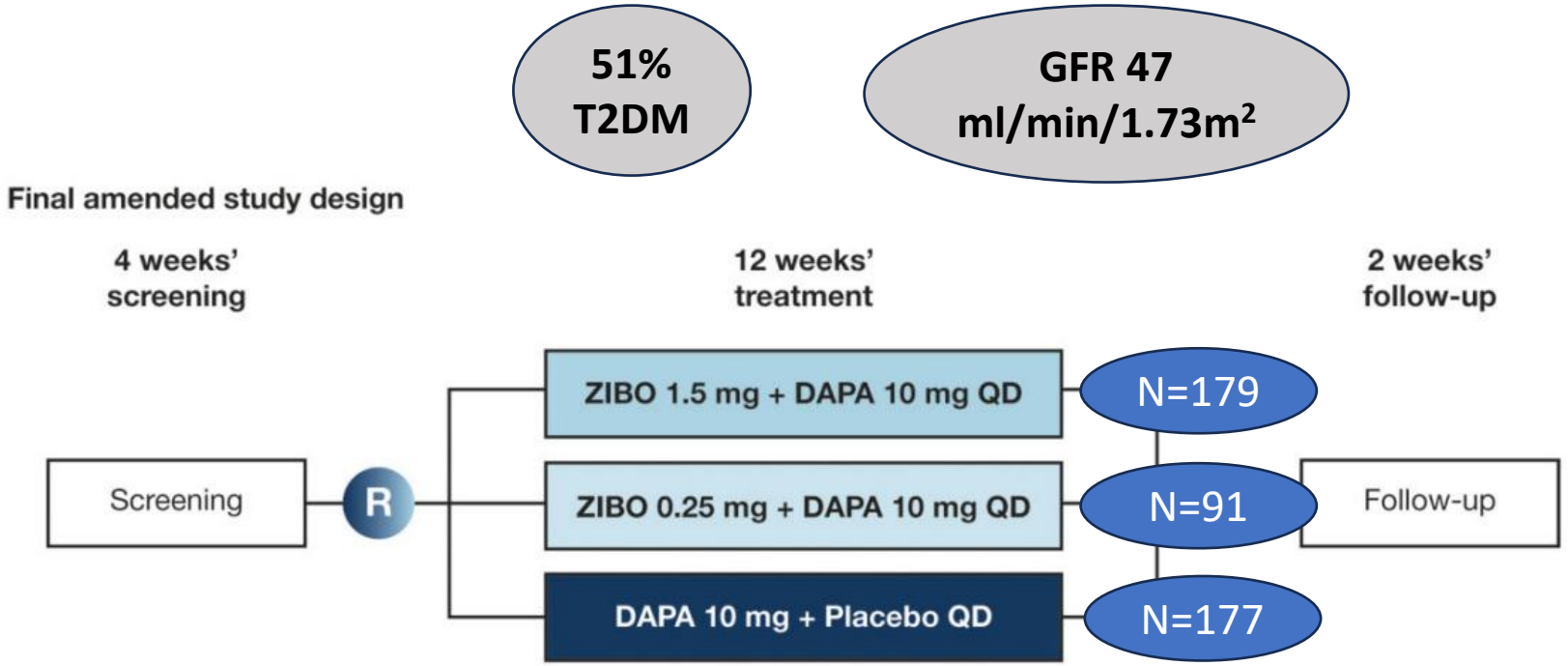
Αναστολείς υποδοχέων ενδοθηλίνης σε ασθενείς με ΧΝΝ

Trial	Population	Drug	Mechanism	Endpoints
ASCEND[58]	Diabetic nephropathy ACR ≥35 mg/mmol and serum creatinine between ≥115 and 265 mmol/L in men and ≥106 and 265 mmol/L in women	Avosentan 25 or 50 mg/day	Dual acting ET_A and ET_A blocker	Time to doubling of serum creatinine, ESRD, or death
SONAR[61]	Diabetic nephropathy eGFR 25–75 mL/min per 1·73 m2, and UACR 300–5000 mg/g	Atrasentan 0.75mg/day	ET_AR antagonist	Composite of doubling of serum creatinine (sustained for ≥30 days) or end-stage kidney disease (eGFR <15 mL/min per 1·73 m2 sustained for ≥90 days, chronic dialysis for ≥90 days, kidney transplantation, or death from kidney failure
ZENITH-CKD[64]	Diabetic patients eGFR ≥ 20 ml/min UACR ≥ 150 mg/g and ≤ 5000 mg/g	Zibotentan Dose A or dose B plus 10 mg of dapagliflozin, vs. placebo plus dapagliflozin	ET_AR antagonist + SGLT2 inhibitor vs. placebo	Change from baseline to Week 12 in Log-transformed UACR, BP, eGFR also to week 1 and 14 Number of participants experiencing adverse events
ZODIAC (NCT05570305)	Diabetic nephropathy eGFR ≥ 30 ml/min UACR ≥ 10 mg/g and ≤ 3500 mg/g	Cross-over study comparing zibotentan 1.5 mg vs zibotentan 1.5 mg + Dapagliflozin 10 mg vs. dapagliflozin vs. placebo	ET_AR antagonist + SGLT2 inhibitor vs. placebo	Change from baseline to Week 12 in Log-transformed UACR Change from baseline to week 4 in GFR, hematocrit, extracellular fluid by bioimpedance spectroscopy and iohexol clearance, bodyweight, NT-proBNP, BNP
PROTECT[66,67]	Biopsy proven IgA nephropathy eGFR>30 mL/min UACR > 1 g/g	Sparsentan 400mg/day	Dual acting ET_A and angiotensin receptor blocker	Change in UACR to week 36[66] and 110[67] Rate of change in eGFR over 58 and 110 weeks
ALIGN (NCT04573478)	Biopsy proven IgA nephropathy eGFR>30 mL/min UACR > 1 g/g.	Atrasentan 0.75mg/day	ET_AR antagonist	Change in UACR at week 24 Change in eGFR to 4 weeks after drug stopped (week 136)
DUPLEX[68,69]	Biopsy proven focal segmental glomerulosclerosis eGFR >30 mL/min UACR >1.5 g/g	Sparsentan 800mg/day	Dual acting ET_A and angiotensin receptor blocker	Proportion of patients achieving a UACR <1.5 g/g and > 40% reduction in UACR to week 36 and slope of eGFR between weeks 6 and 108

↓ αλβουμινουρία
↑Καρδιαγγειακά συμβάντα

↓ αλβουμινουρία και ΧΝΝ τελικού σταδίου

ZENITH-CKD study - selective ET_A antagonist zibotentan



Outcomes

Primary endpoint:
- Change in UACR from baseline to week 12

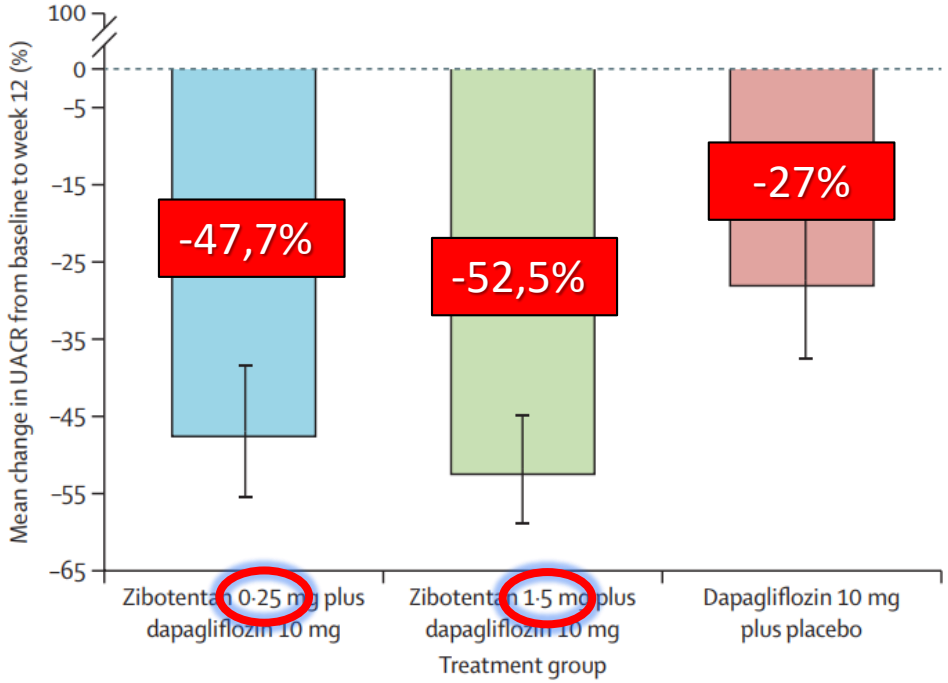
Secondary endpoints:
- Change in blood pressure at week 12
- Change in eGFR at week 12

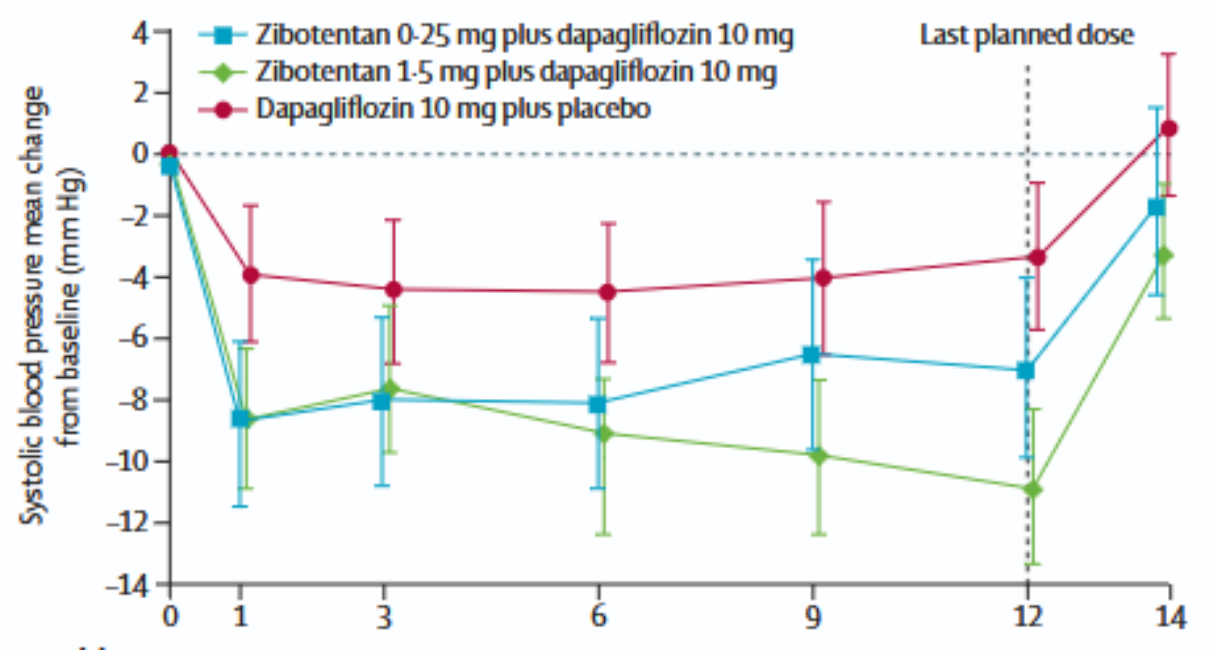
Fluid-related measures

Adverse events

Heerspink H et al. Lancet, 2023

ZENITH-CKD: επίδραση στην αλβουμινουρία και κατακράτηση υγρών





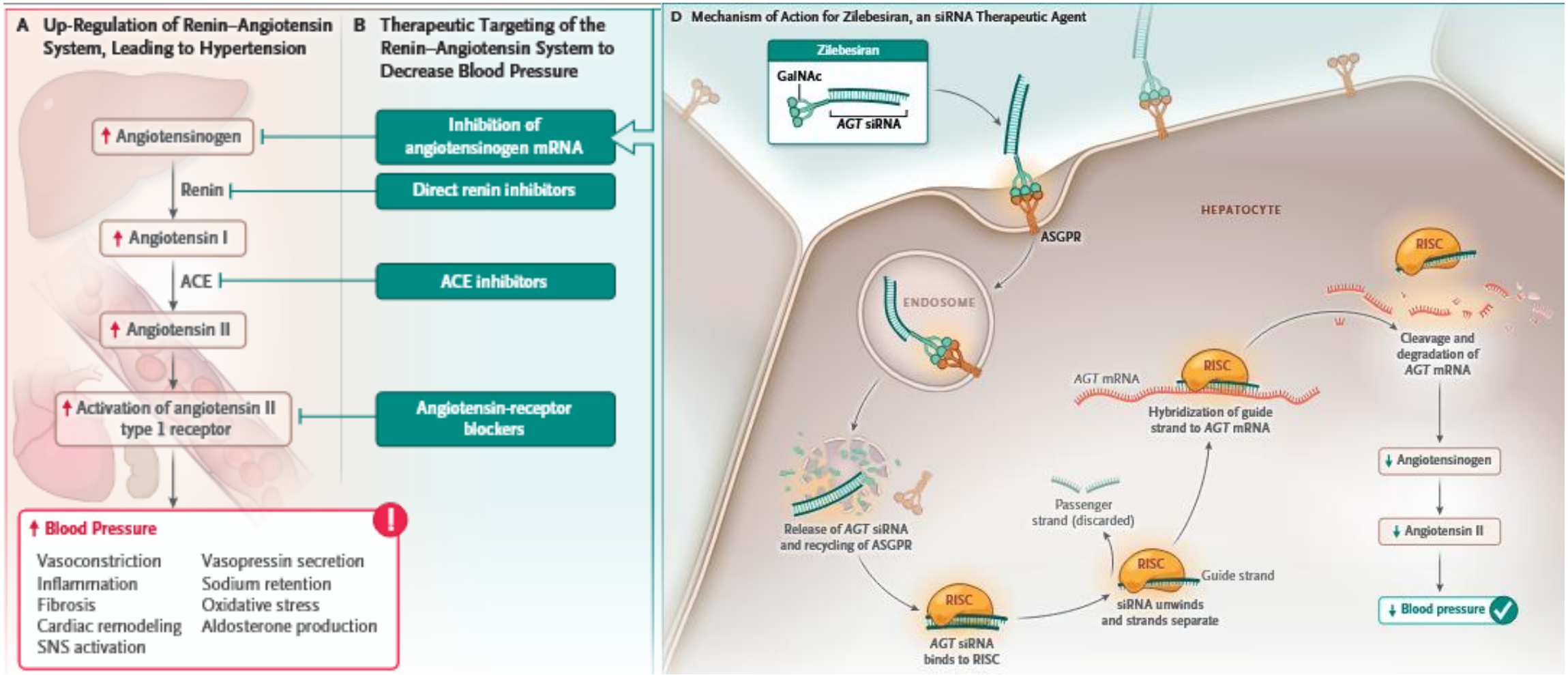
Fluid-retention events

ZIBO 1.5 mg + DAPA 10 mg QD	18%
ZIBO 0.25 mg + DAPA 10 mg QD	9%
DAPA 10 mg + Placebo QD	8%

Heerspink H et al. Lancet, 2023

RNA interference θεραπείες

siRNA therapies targeting the RAAS

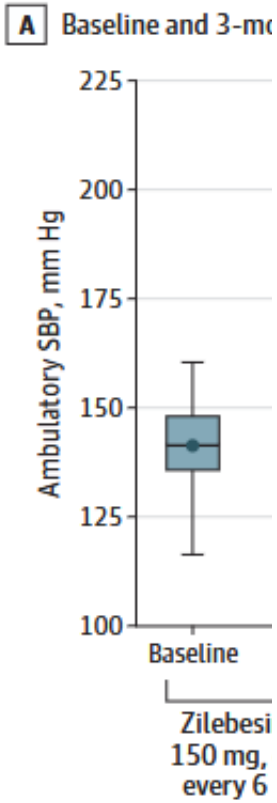


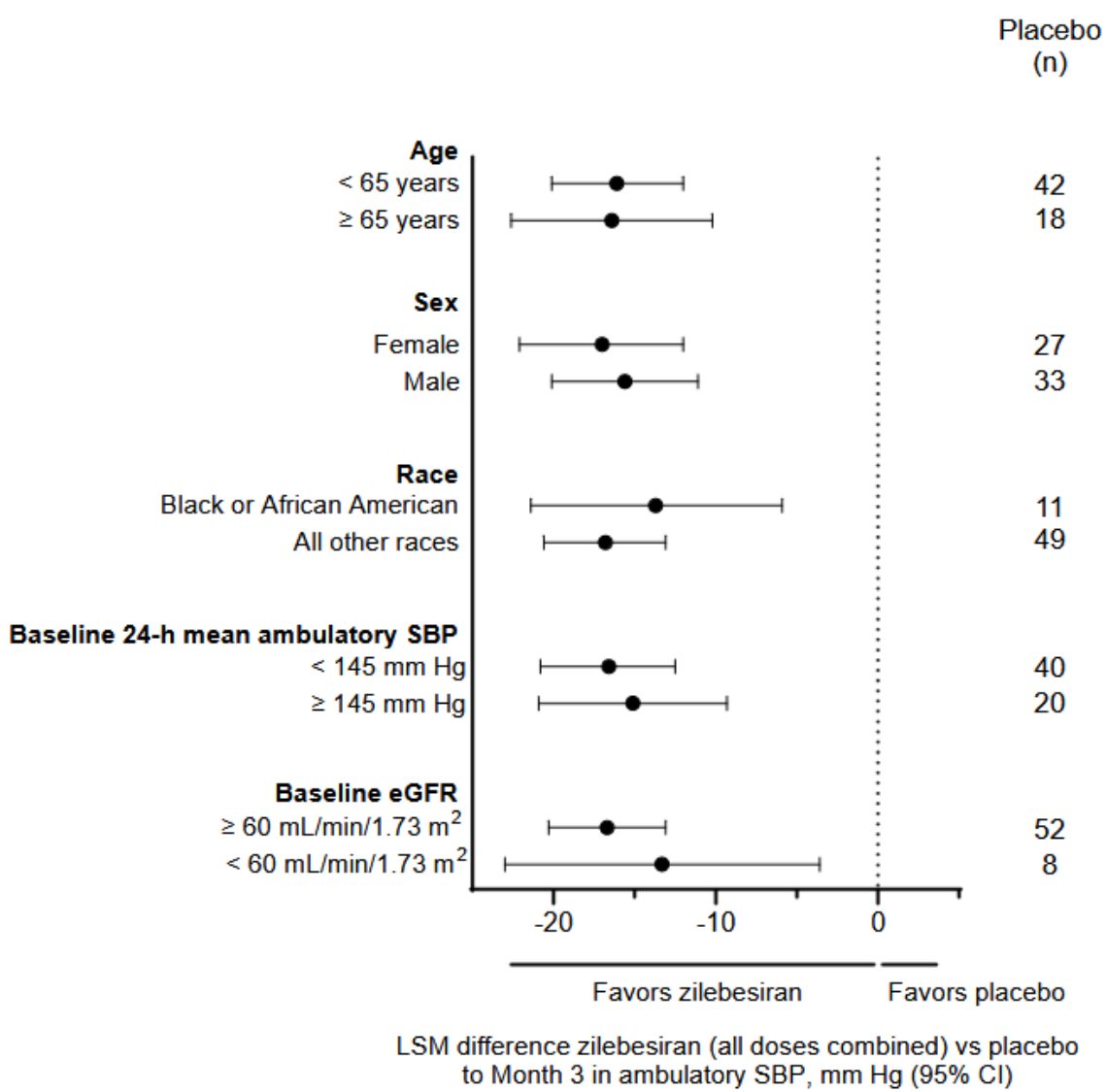
Toyouz RM. New Engl J Med, 2023

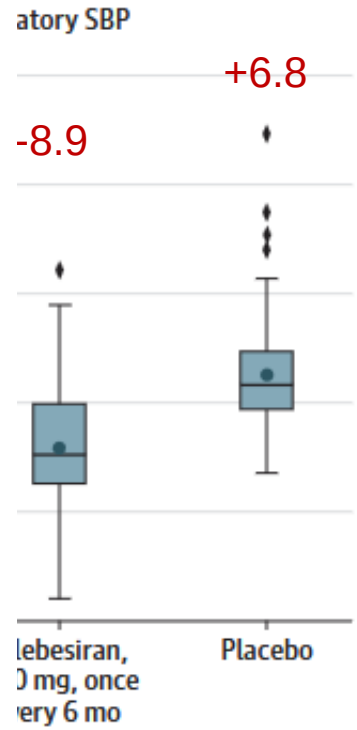
KARDIA-1 trial: zilebesiran for mild to moderate hypertension

377 adults with HTN
medication were ra
months, 300 mg onc

ground antihypertensive
ns, 300 mg once every 6
o once every 3 months.







Bakris GL, JAMA, 2024

KARDIA-2 trial: zilebesiran for inadequately controlled hypertension

- Patients with untreated or uncontrolled HTN despite 1 or 2 antihypertensive agents were randomized in 4:7:10 ratio to receive open-label treatment with **indapamide 2.5 mg once daily, amlodipine 5 mg once daily, or olmesartan 40 mg** once daily for 4 weeks.

- Patients in each background therapy cohort with 24-hour ambulatory SBP 130-160 mmHg and at least 80% adherence to protocol-specified background therapy were randomized in a 1:1 ratio to receive a single subcutaneous dose of zilebesiran 600mg or matching placebo **(n=663)**.

A 24-h Mean ambulatory SBP

LSM difference (95% CI)	
Indapamide	-12.1 (-16.5 to -7.6); *P* <.001
Amlodipine	-9.7 (-12.9 to -6.6); *P* <.001
Olmesartan	-4.5 (-8.2 to -0.8); *P* = .018
LSM change from baseline (95% CI)	
Indapamide	
Zilebesiran	-15.7 (-18.9 to -12.6)
Placebo	-3.7 (-6.7 to -0.6)
Amlodipine	
Zilebesiran	-10.5 (-12.7 to -8.2)
Placebo	-0.7 (-3.0 to 1.5)
Olmesartan	
Zilebesiran	-7.7 (-10.3 to -5.1)
Placebo	-3.2 (-5.9 to -0.6)

Indapamide Amlodipine Olmesartan

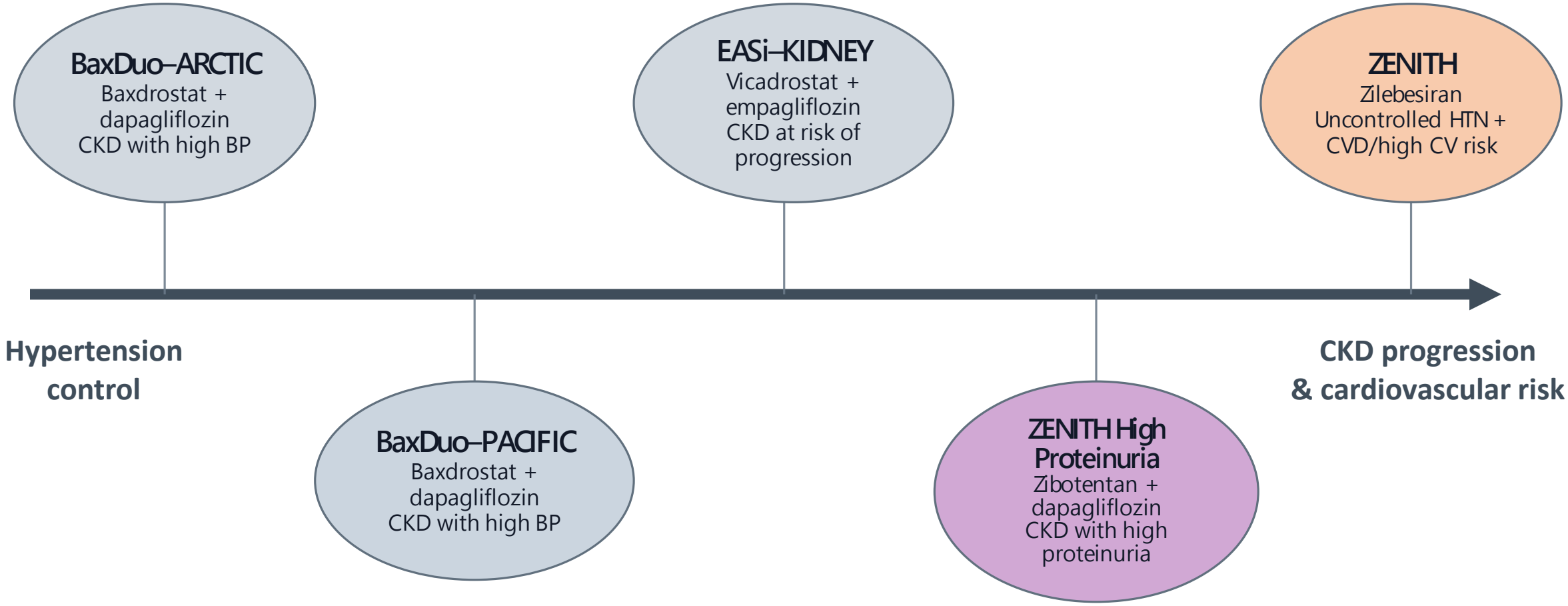
B Office SBP

LSM difference (95% CI)	
Indapamide	-18.5 (-22.8 to -14.20); *P* <.001
Amlodipine	-10.2 (-13.4 to -6.90); *P* <.001
Olmesartan	-6.7 (-10.2 to -3.3); *P* <.001
LSM change from baseline (95% CI)	
Indapamide	
Zilebesiran	-19.3 (-22.3 to -16.2)
Placebo	-0.8 (-3.8 to 2.3)
Amlodipine	
Zilebesiran	-11.5 (-13.8 to -9.2)
Placebo	-1.4 (-3.7 to 1.0)
Olmesartan	
Zilebesiran	-9.3 (-11.8 to -6.9)
Placebo	-2.6 (-5.1 to -0.1)

Indapamide Amlodipine Olmesartan

Bakris GL, JAMA, 2024

Ongoing trials of emerging BP-lowering therapies



Α΄ ΝΕΦΡΟΛΟΓΙΚΗ ΚΛΙΝΙΚΗ Α.Π.Θ.

Γ.Ν.Θ. ΙΠΠΟΚΡΑΤΕΙΟ

ARISTOTLE UNIVERSITY OF THESSALONIKI

Σας ευχαριστώ!