Υπερκαλιαιμία στην ΧΝΝ

Σύγχρονη θεραπευτική διαχείριση

Παντελής Σαραφίδης

Αναπληρωτής Καθηγητής Νεφρολογίας Α.Π.Θ.,
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DOI statement

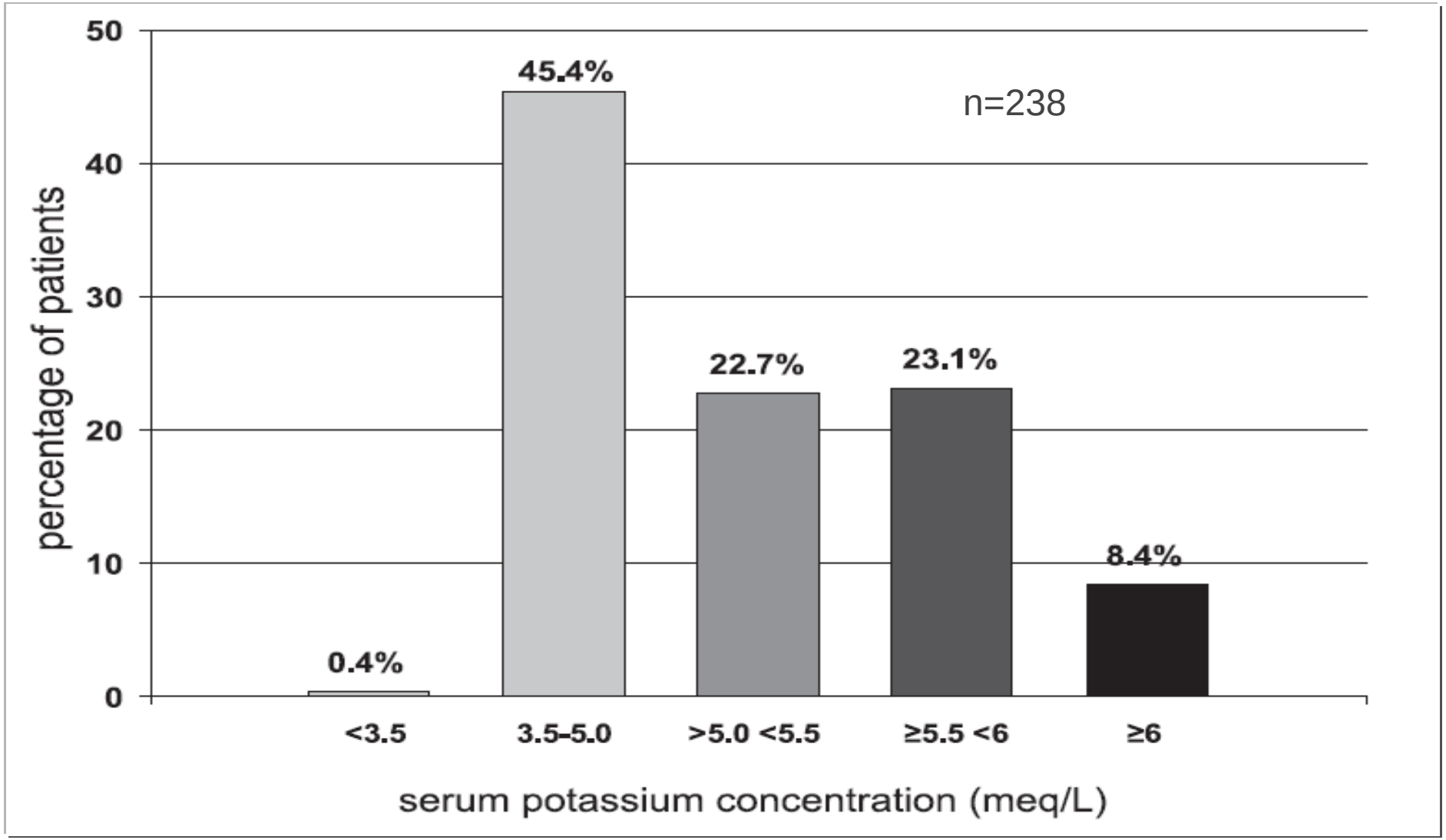
Doctor Sarafidis has served as an Advisor for Elpen, Genesis Pharma, Astra-Zeneca, Menarini, Innovis Pharma, Winmedica and as a Speaker for Amgen, Boehringer Ingelheim, Mediquest India, Menarini, Winmedica, Bayer and Genesis.

He has received grant support for an Investigator-Initiated Study from Astra-Zeneca and served as a Member of Steering Committee and of Endpoint Adjudication Committee for FIGARO and FIDELIO Studies of Bayer.

He is an Associate Editor for the Journal of Human Hypertension and a Theme Editor for Nephrology Dialysis and Transplantation.

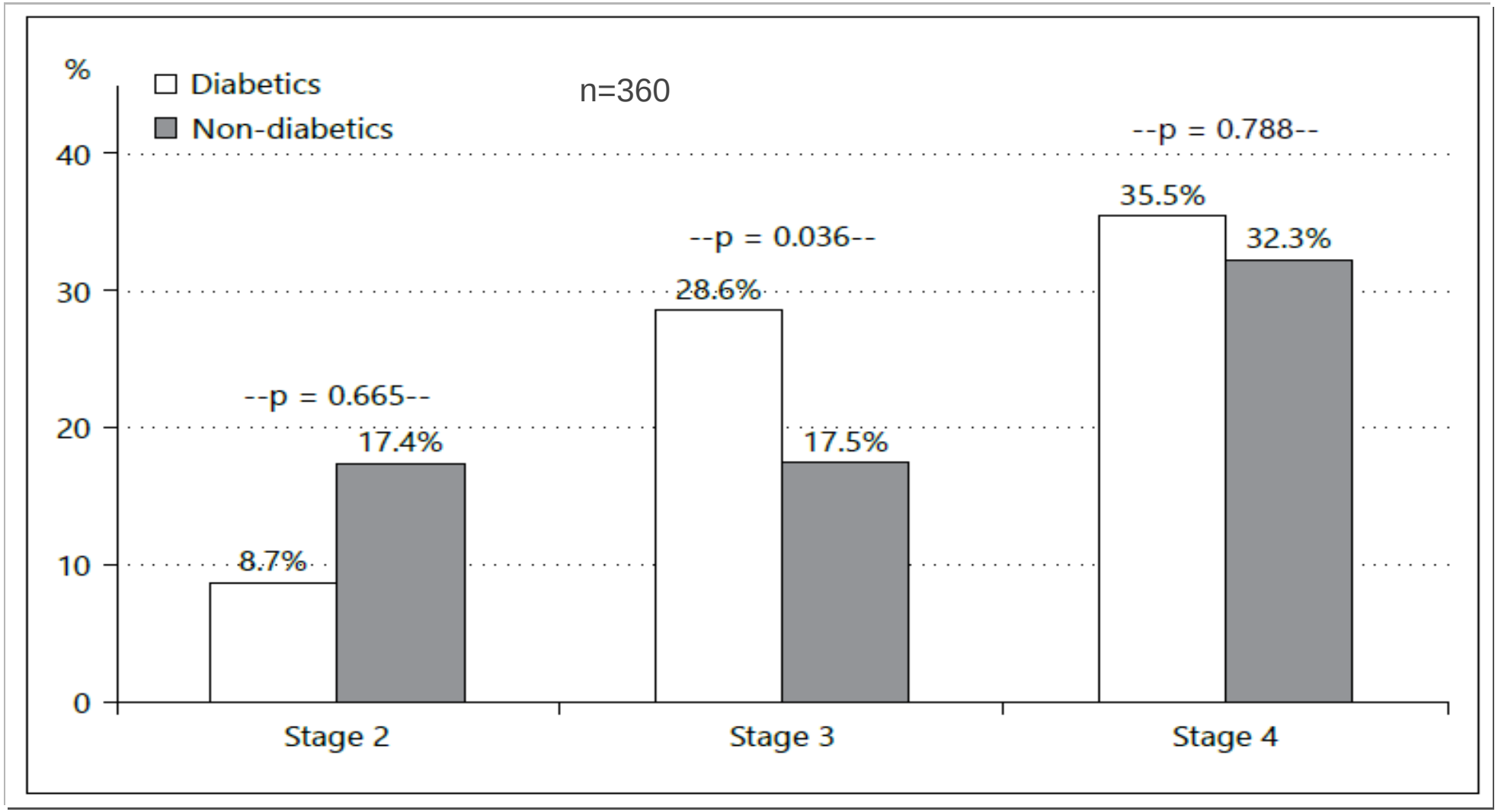
Υπερκαλιαιμία στη ΧΝΝ: Εισαγωγή

Hyperkalemia in predialysis patients (eGFR <20 ml/min/1.73 m^2)



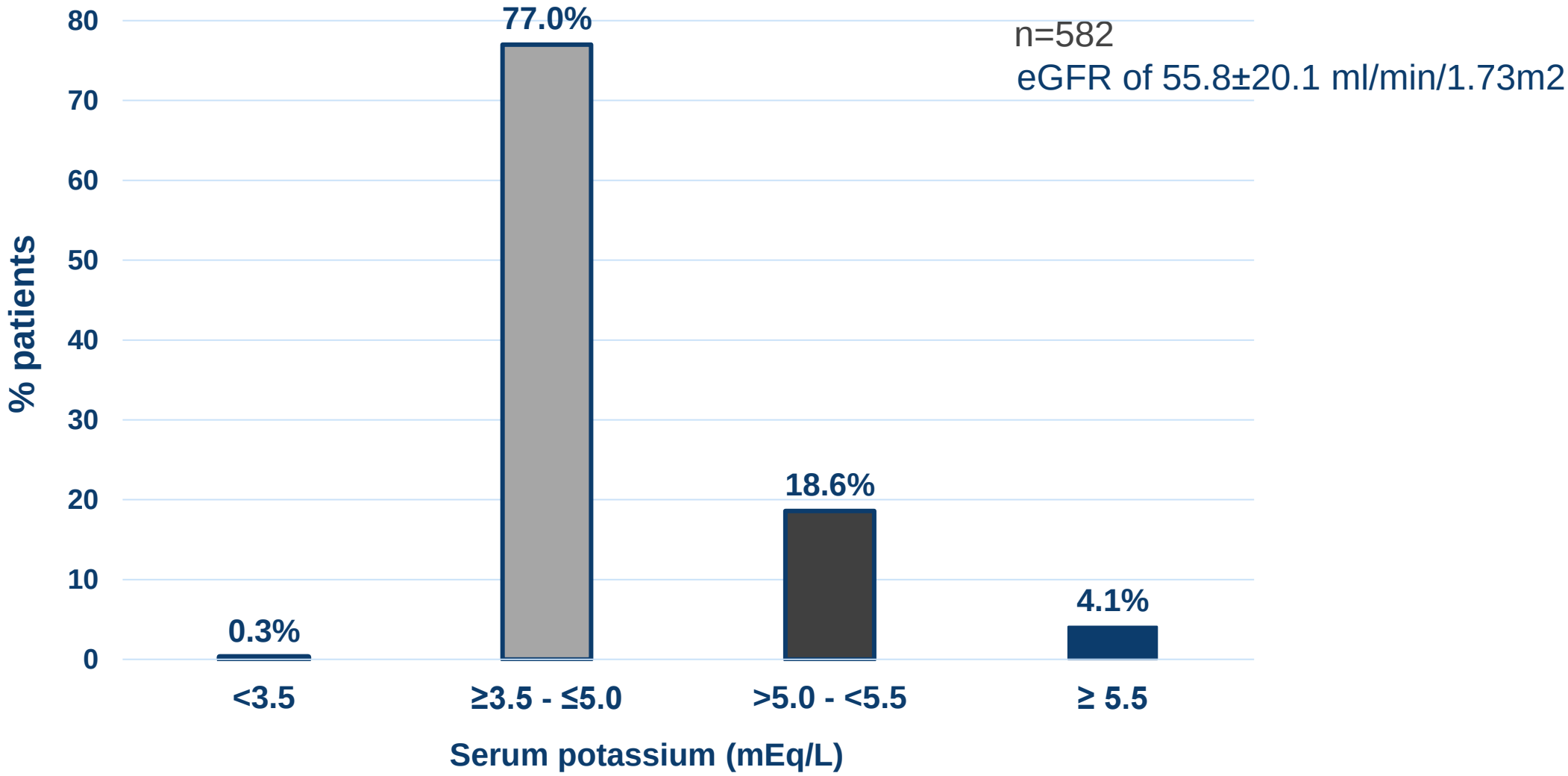
Sarafidis PA, et al. Clin J Am Soc Nephrol. 2012;7(8):1234-1241

Hyperkalemia in CKD patients Stage 2-4



Loutradis C, et al. Am J Nephrol 2015

Hyperkalemia in kidney transplant recipients



Smirli M, et al. Clin Kidn J 2021

RAASIs ARE RECOMMENDED BY MULTIPLE ORGANIZATIONS FOR THE PREVENTION OF HEART FAILURE AND KIDNEY FUNCTION DECLINE

Class IA recommendation

- ACEi is recommended, in addition to a BB, for symptomatic patients with HF[1–3]*
- ACEi/ARB is recommended for treatment of hypertension[4,5]† and ACEi/MRA for HF in patients with DM[4]
- ARB is recommended when ACEi is not tolerated[1,2]
- MRA is recommended for patients with HF*, who remain symptomatic despite treatment with an ACEi, and a BB[2]

Highest tolerated targeted doses recommended[1,2]

Slow the progression of kidney disease[4]

- Reduce proteinuria[6,7]
- Valuable in CKD and indicated in proteinuria[6–8]
- More effective at reducing kidney function decline than other BP-lowering drugs[6]

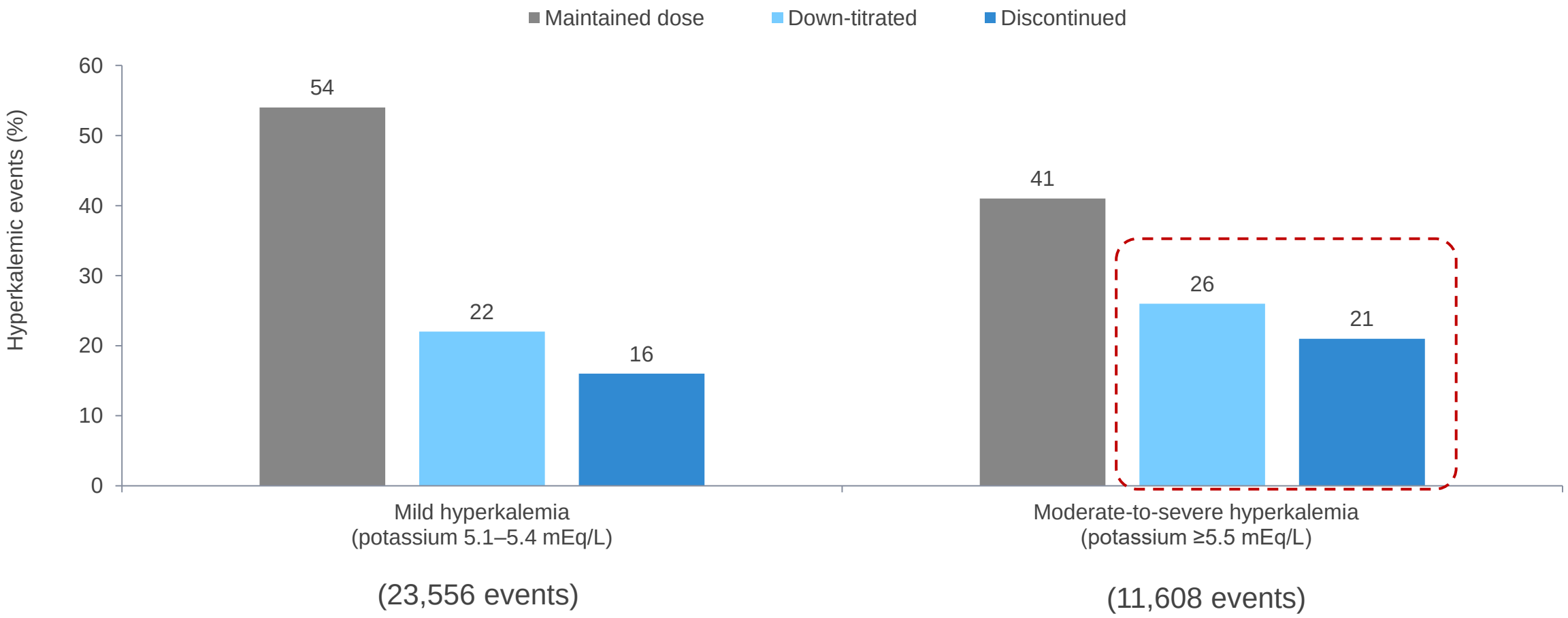
Titrated to the highest approved dose that is tolerated[9]

* With reduced ejection fraction; † Class A level of evidence.

1. Yancy CW *et al. Circulation.* 2017;136:e137–61; 2. Ponikowski P *et al. Eur J Heart Fail.* 2016;18:891–975; 3. Lindenfeld J *et al. J Card Fail.* 2010;16:475–539; 4. Cosentino F, *et al. Eur Heart J.* 2020;41:255–323; 5. American Diabetes Association. *Diabetes Care.* 2020;43:S111–34; 6. KDIGO Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2013;3:1–150; 7. National Kidney Foundation. K/DOQI Clinical Practice Guidelines on Hypertension and Antihypertensive Agents in Chronic Kidney Disease. 2004. Available at: kidneyfoundation.cachefly.net/professionals/KDOQI/guidelines_bp/index.htm (accessed July 2020); 8. National Institute for Health and Care Excellence. Chronic kidney disease in adults: assessment and management. 2014 (updated 2015). Available at: nice.org.uk/CG182 (accessed July 2020); 9. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int Suppl.* 2020;98:S1–S115.

Nearly half of patients on maximum dose of RAASi were down-titrated to a sub-maximum dose or discontinued

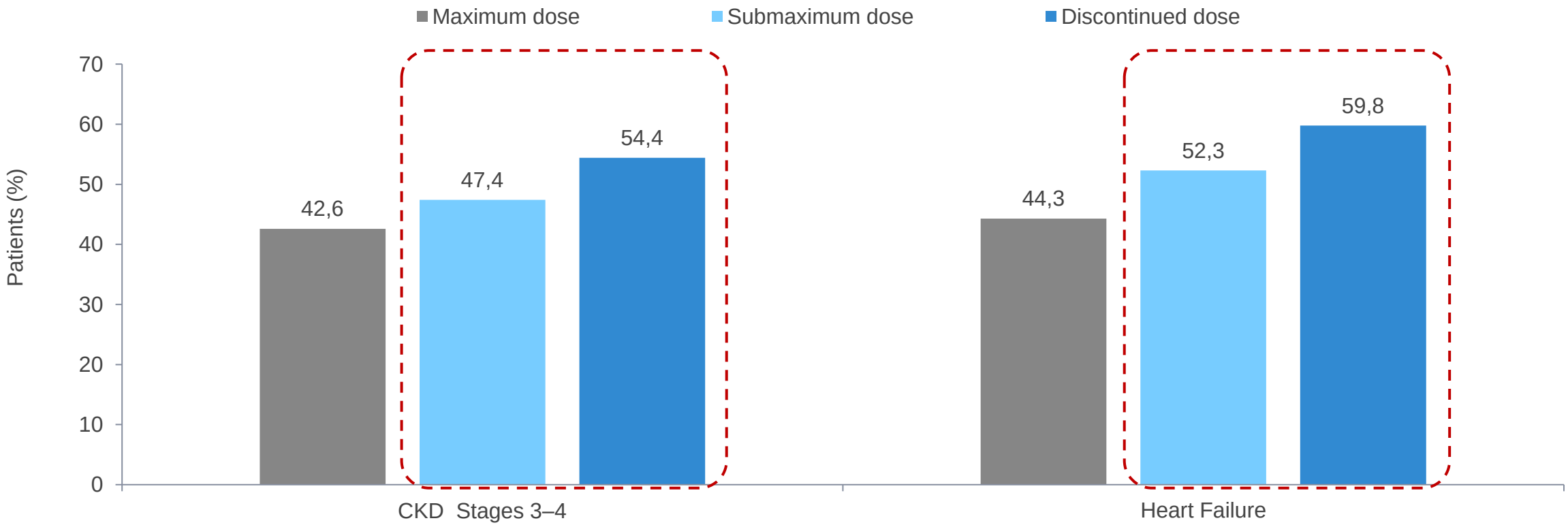
Changes in RAASi dose subsequent to hyperkalaemic events



Epstein M et al. Am J Manag Care 2015; 21:S212-S220.

Sub-maximum dosing and early discontinuation of RAASi is associated with poor patient outcomes

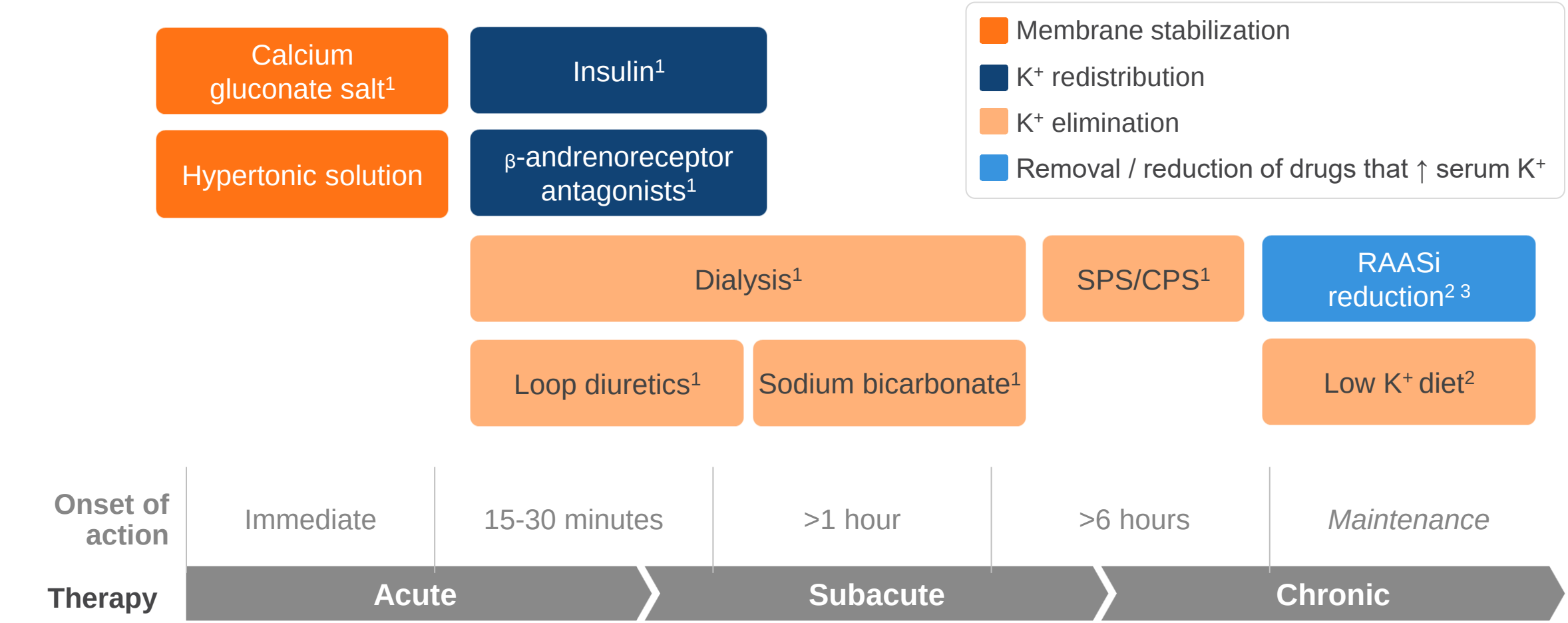
Patients who experienced adverse outcomes or mortality by prior RAASi dosing



Epstein M et al. Am J Manag Care 2015; 21:S212-S220.

(Προ)υπάρχουσες θεραπευτικές επιλογές για την αντιμετώπιση της υπερκαλιαιμίας

Treatment Options for Hyperkalemia



[1] Weisberg L. Crit Care Med. 2008; 36 (12):3246-3251. [2] Palmer BF, et al. N Engl J Med. 2004;351(6):585-592. [3] National Kidney Foundation. Guideline 11. www2.kidney.org/professionals/KDOQI/guidelines_bp/guide_11.htm. Accessed: February 2015.2

Note: SPS, sodium polystyrene sulfonate; CPS, calcium polystyrene sulfonate

Chronic Hyperkalemia Treatment

Dietary interventions
Patient education towards implementation of a potassium-restrictive diet
Discontinuation of potassium-based salt substitutes and herbal products
Pharmacotherapy interventions
Patient education to avoid use of over the counter medicines causing hyperkalemia (i.e., NSAIDs)
Disruption or reduction of dose of other agents causing hyperkalemia
Downward dose adjustment for ACEIs and ARBs according to the level of renal function
Proper use of diuretic agents according to the level of renal function to enhance renal potassium excretion
Correction of metabolic acidosis
Use of oral fludrocortisone in patients with proven hyporeninemic hypoaldosteronism
Use of potassium-exchanging resins to bind potassium in the gut

Sarafidis P, Georgianos P, Bakris G. Expert Opinion on Pharmacotherapy 2015

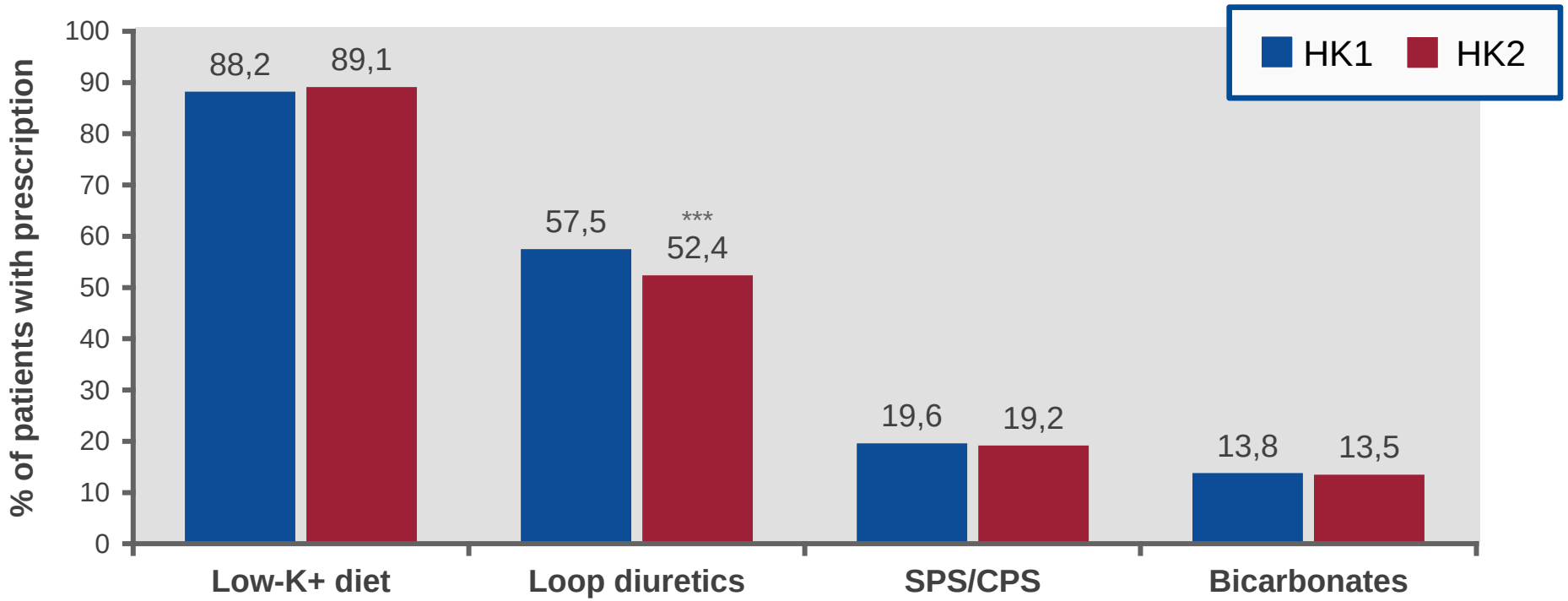
ΠΕΡΙΟΡΙΣΜΟΙ ΤΩΝ ΠΑΡΑΔΟΣΙΑΚΩΝ ΜΕΤΡΩΝ ΔΙΑΧΕΙΡΙΣΗΣ ΤΗΣ ΥΠΕΡΚΑΛΙΑΙΜΙΑΣ[1,2]

Διατροφή	Μπορεί να περιορίσει την κατανάλωση υγειϊνών τροφών
Μείωση των RAASi ή διακοπή	Μπορεί να οδηγήσει σε δυσμενή αποτελέσματα ή θνησιμότητα
Μη καλιοσυντηρητικά Διουρητικά	Μπορεί να αυξήσουν τον κίνδυνο ουρικής αρθρίτιδας, διαβήτη και υπο-ογκαιμίας Μπορεί να επιδεινώσουν τη νεφρική λειτουργία
Διττανθρακικό νάτριο	Μπορεί να οδηγήσει σε υπερνατριαιμία, υπερφόρτωση όγκου, και υπέρταση
SPS/CPS	Ανεπιθύμητες ενέργειες από το πεπτικό, όπως αιμορραγία, ισχαιμική κολίτιδα και διάτρηση Επιπλέον φορτίο νατρίου

- CPS = calcium polysterene sulfonate; HK = kyperkalaemia;
- RAASi = renin-angiotensin-aldosterone system inhibitor; SPS = sodium polystyrene sulfonate

- **1.** Dunn JD et al. *Am J Manag Care.* 2015;21:S307–315
- **2.** Rosano GMC et al. *European Heart Journal Supplements.* 2019;21(Suppl A):A28-33

LOW POTASSIUM DIET IS THE MOST COMMON HK INTERVENTION



Study information

A retrospective chart review of patients from 5 EU countries experiencing ≥2 HK episodes within a 12-month observational period*

1,457 patients

Baseline comorbidities/treatment

- **72%** with HTN
- **68%** with CKD
- **40%** with HF
- **36%** with T2DM
- **60.5%** receiving RAASI

* Serum K^+ ≥5.5 mEq/L. (On figure) Significant difference from HK1:***P <0.001.

Rossignol P, *et al. Clin Kidney J.* 2019; doi: 10.1093/ckj/sfz129.

Confidential. Do not distribute. Not to be left behind. © Vifor Pharma

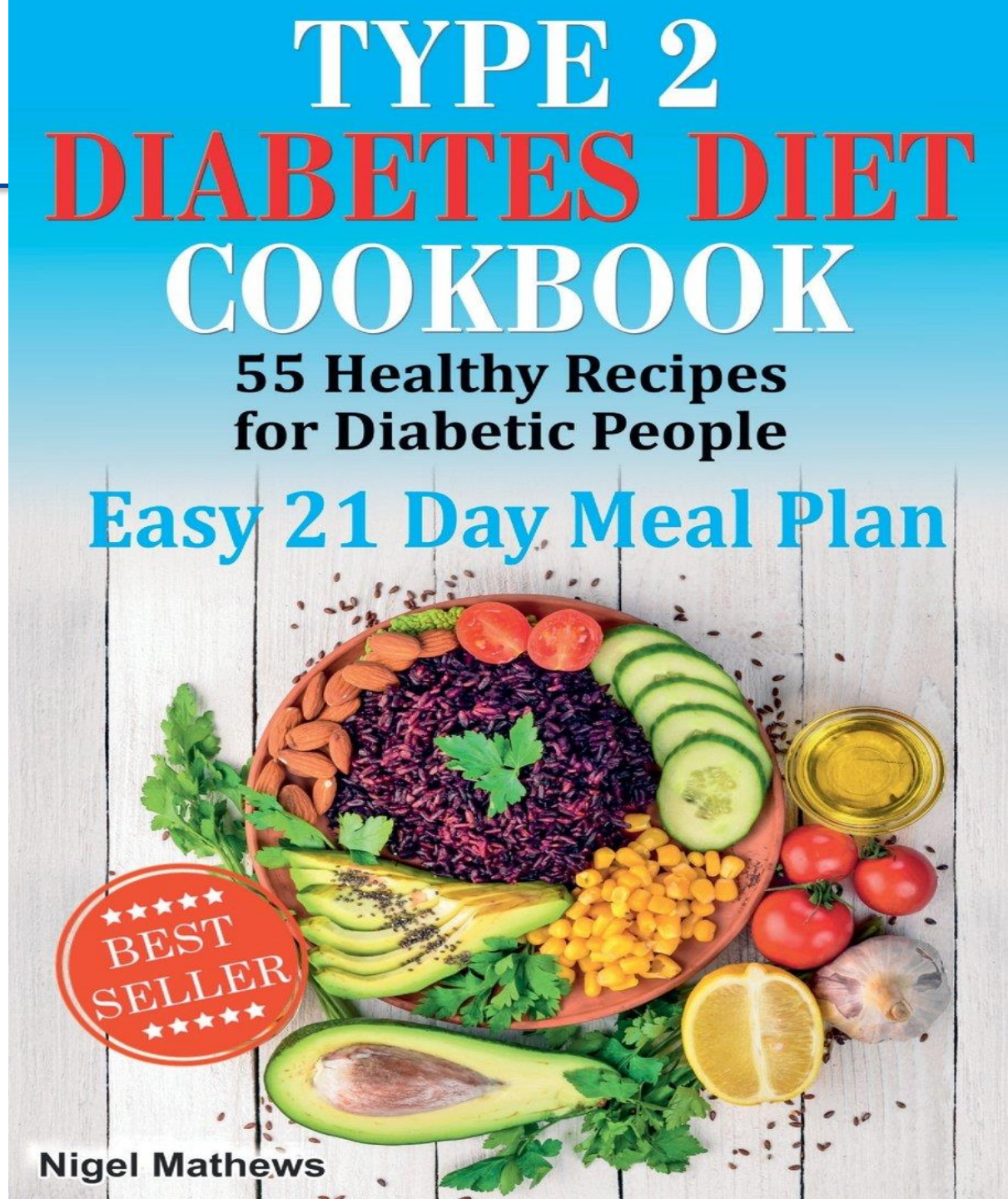
Γιατρέ και τι να φάω;

Όχι λιπαρά/γλυκά

Όχι κρέατα/πρωτεϊνη

Όχι αλάτι

Όχι φρούτα/λαχανικά!

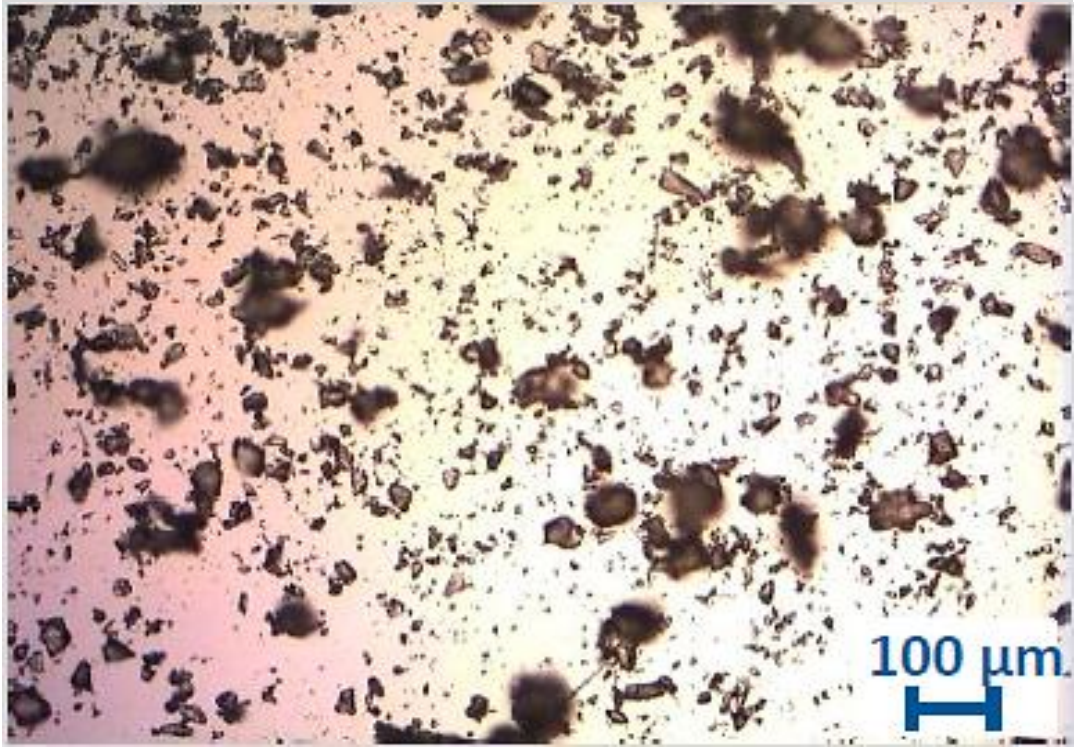


Kayexalate® (sodium polystyrene sulfonate) is indicated for the treatment of hyperkalaemia

Properties	Kayexalate®
Mechanism of action	Potassium binder that is ingested and exchanges sodium for potassium in the GI tract to reduce serum potassium levels[1]
Safety and tolerability	Intestinal necrosis warning, GI side effects[1]
Design / active pharmaceutical ingredient	Bulk gel material, non-uniform size, and fine, brown, clay-like consistency[1,2]
Counterion	Na^+-loaded, about 1/3 is delivered to the body[1]
Efficacy data	Efficacy and safety not studied in large, systematic, long-term trials[2]
Dosing	Average daily adult dose is 15–60 g/day[1]

Microscopic image of SPS showing irregular, non-uniform structure[2]

Kayexalate®



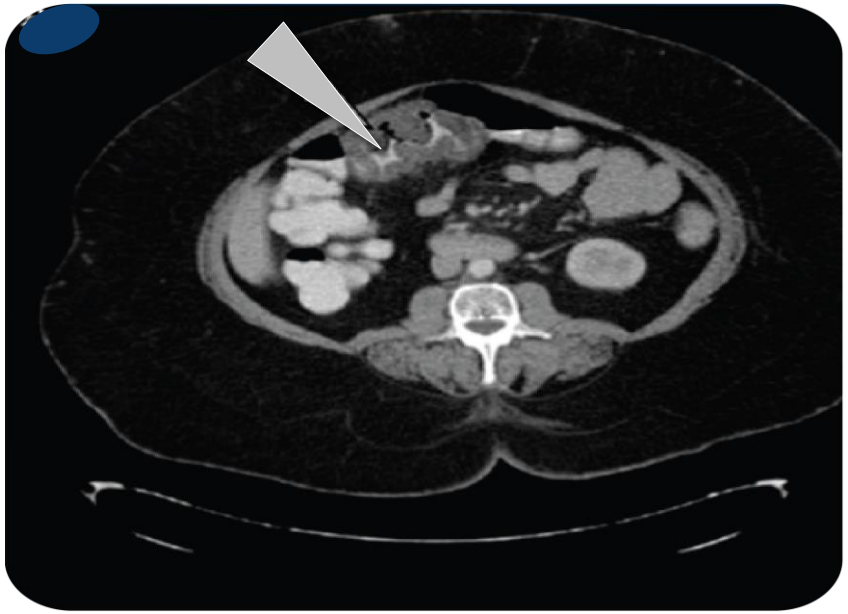
GI, gastrointestinal; SPS, sodium polystyrene sulfonate. Kayexalate® is a registered trademark of Sanofi-Aventis.

[1] Kayexalate® package insert. Bridgewater, NJ: Sanofi-Aventis, 2010; [2] Sterns RH et al. J Am Soc Nephrol 2010;21:733–5.

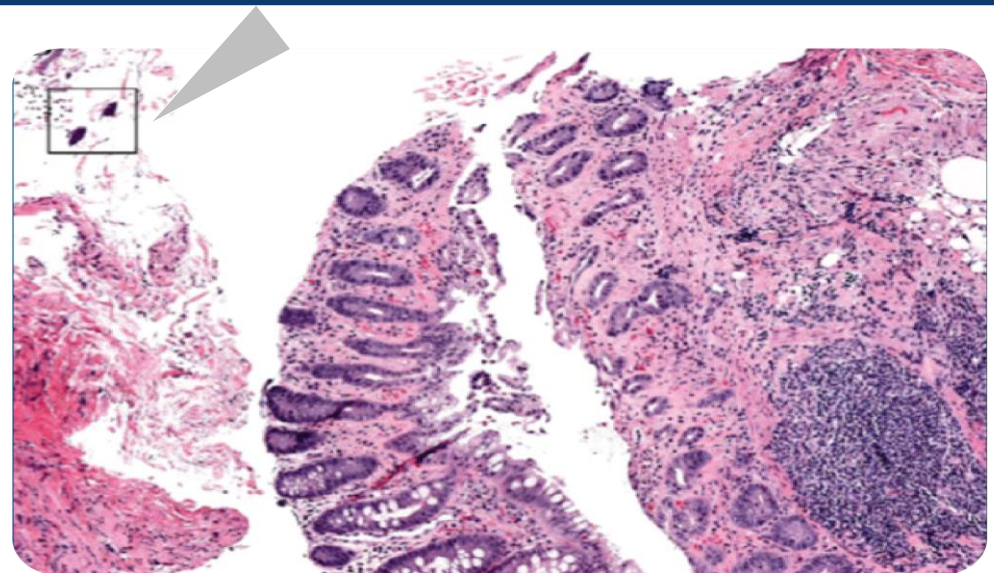
Gastrointestinal injury with kayexalate (65% with sorbitol)

Necrosis (62%), Ulceration (48%), Perforation (9%), and SPS Crystals (90%) – Death (33%)[1]

Circumferential wall thickening and pericolonic stranding on CT scan[2]*



Angulated basophilic crystals, a typical appearance of Kayexalate[2]



*Fragments of colonic mucosa have miniaturized crypts with leakage of RBCs and fibrin into the surrounding lamina propria[2] ***

* IV and oral contrast, a focal region of large bowel in the proximal transverse colon, near the hepatic flexure.
** a few normal-sized crypts are present at the bottom center for comparison.

[1] Harel Z, et al. Am J Med. 2013;126(3):264.e9-e24. [2] Bomback AS, et al. Am J Emerg Med. 2009;27(6):753.e1-e2.

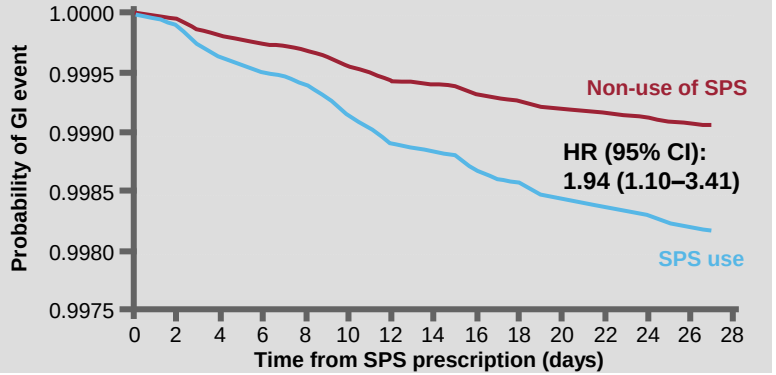
IN REAL-WORLD PRACTICE, SPS USE IS ASSOCIATED WITH A HIGHER RISK OF GI ADVERSE EVENTS

Study setting[1]

A population-based retrospective matched cohort study of adults (≥66 years) dispensed SPS (N=20,020)

1 Apr 2003 – 30 Sep 2015

Outcomes[1]



- **SPS use** was associated with a **1.9-fold higher risk of hospitalisation** for an **adverse GI event** within 30 days
- **Intestinal ischemia / thrombosis** was the most common type of GI injury

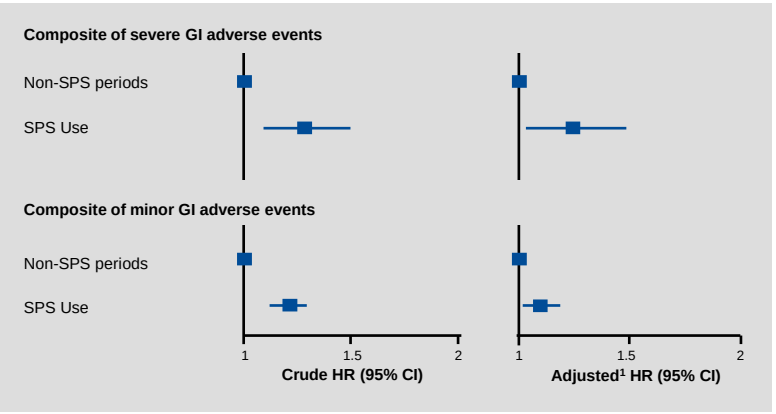
Study setting[2]

Observational study of SPS-naïve adults with CKD stage 4/5 following SPS initiation (N=19,530)

*Majority (**85**%) were prescribed lower dosages than per label recommendations*

2006 – 2016

Outcomes[2]



- **SPS initiation** was associated with a **1.25-fold higher incidence of severe adverse GI events** (95% CI 1.05–1.49)
- Most severe adverse GI events were ulcers and perforations
- **SPS initiation** was also associated with **higher incidence of minor GI events** (adjusted HR [95% CI] 1.11 [1.03–1.19])

1. Noel JA, *et al. JAMA Intern Med.* 2019; 179:1025−33; 2. Laureati P, *et al. Nephrol Dial Transplant* 2019; doi: 10.1093/ndt/gfz150.

Warning on Sodium Polystyrene Sulfonate Related to Sodium Load

WARNINGS

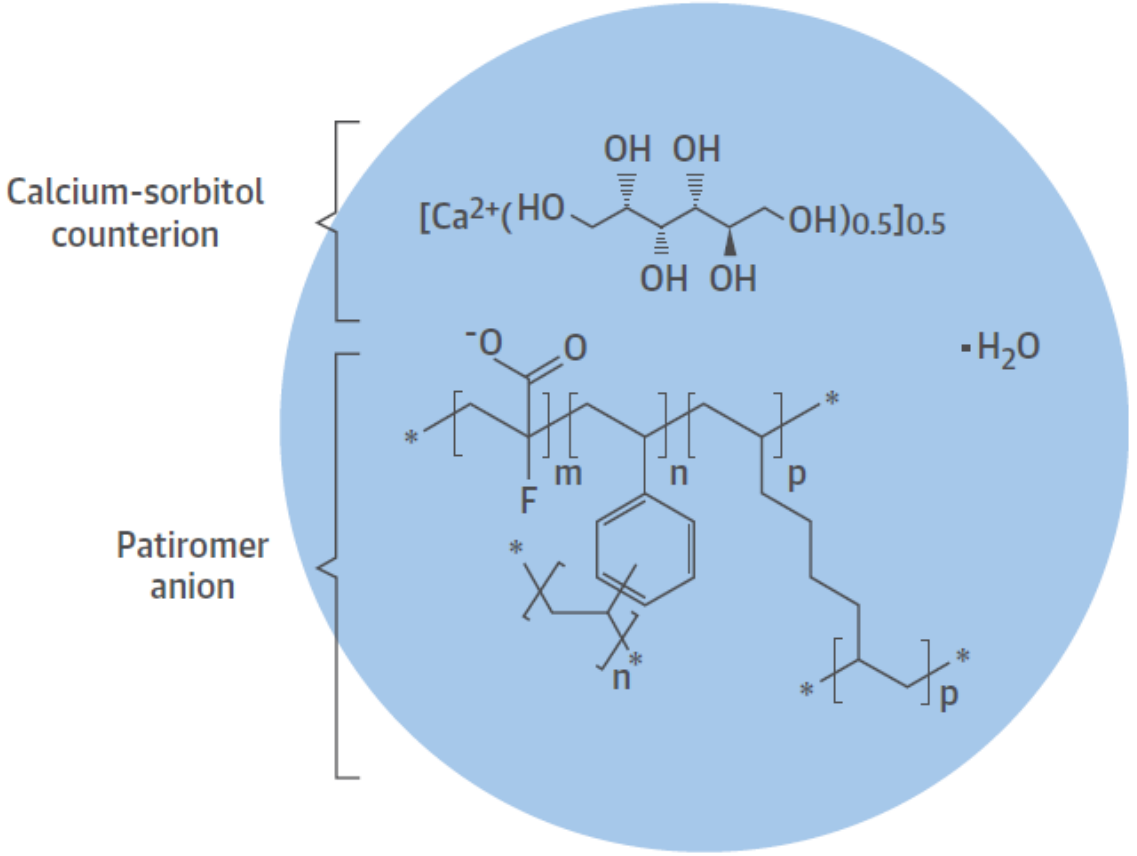
- Patients at risk from an increase in sodium load:
  - During the resin's action in the intestinal tract, sodium is released mole for mole with potassium uptake
  - A single dose of KAYEXALATE (15 grams) contains approximately 60 mmol of sodium
  - Since the resin is a source of sodium, caution is advised when KAYEXALATE is administered to patients who cannot tolerate even a small increase in sodium loads and for whom an increase in sodium load may be detrimental (i.e. severe congestive heart failure, severe hypertension, marked edema or renal damage)
  - In such instances compensatory restriction of sodium intake from other sources may be indicated and adequate clinical and biochemical control is essential
  - The calcium form of the resin may offer advantages in this situation

Kayexalate PI November 2010.
http://www.fda.gov/Safety/MedWatch/SafetyInformation/ucm186845.htm

Πατιρομέρη:
Μοριακή Δομή και Μηχανισμός Δράσης

Chemical Structure of Patiromer

Chemical structure of active ingredient



m = number of 2-fluoro-2-proprenoate groups
n, p = number of crosslinking groups
H_2O = associated water
*Indicates an extended polymeric network

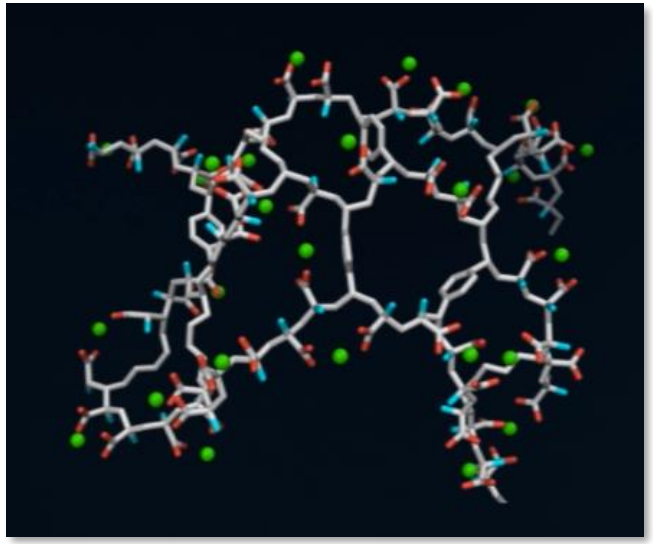
m = 0.91
n + p = 0.09

From patiromer (Veltassa) prescribing information (Relypsa, Inc., Red Wood City, California). Ca = calcium; F = fluorine; O = oxygen; OH = hydroxide.

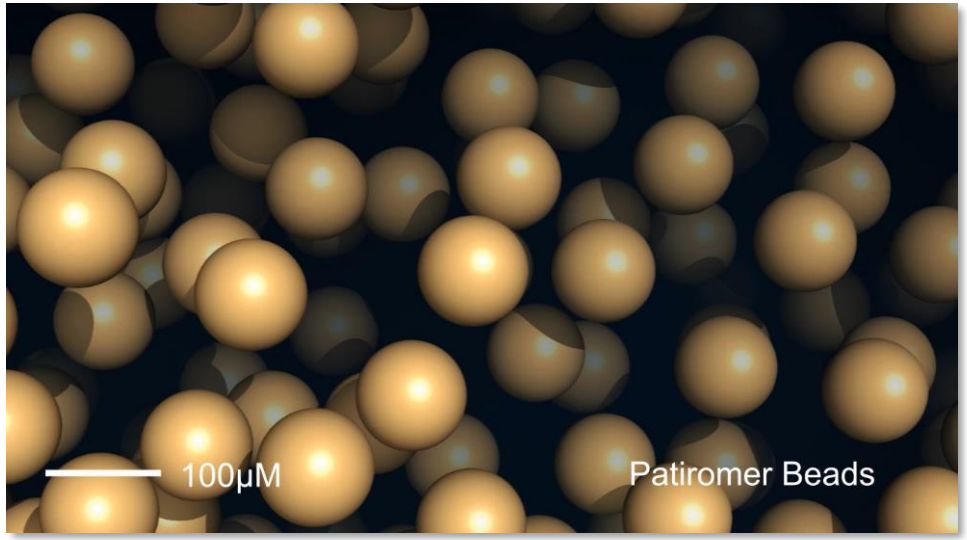
C Sarwar, L Papadimitriou, B Pitt et al, Hyperkalemia in Heart Failure, JOURNAL OF THE AMERICAN COLLLEGE OF CARDIOLOGY, VOL. 68, NO. 14, 2016

Patiromer Is a Non-absorbed K^+ Binder

- Patiromer is a novel, spherical, non-absorbed polymer
  - High-capacity K^+ binder
  - Average bead size (100 µM) is too large for patiromer to be absorbed from the GI tract, enabling patiromer to be passed through the entire GI tract and absorb more K^+
  - Uniform spherical shape, size, and low-swelling beads ratio



High-capacity polymer



Uniform, spherical patiromer beads

GI: gastrointestinal; K^+: potassium.

Li L, et al. *J Cardiovasc Phamacol Ther.* 2016;21(5):456-465.

Patiromer versus Kayexalate in light microscopy

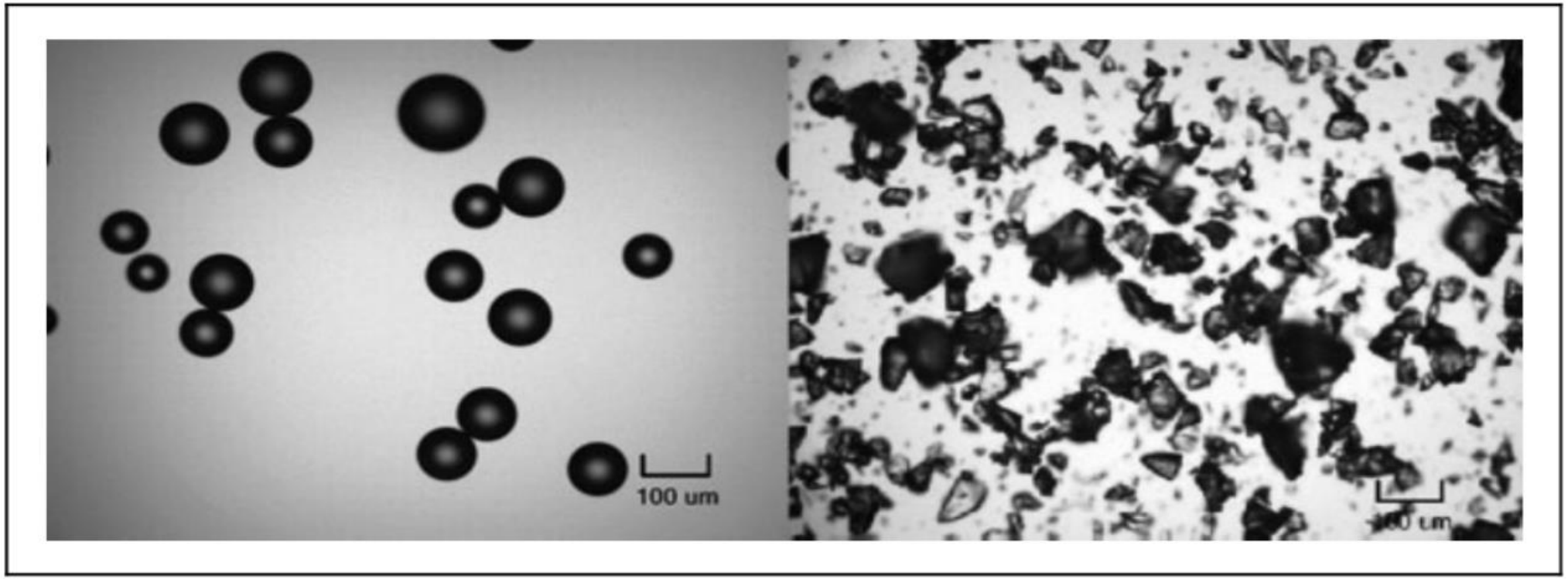


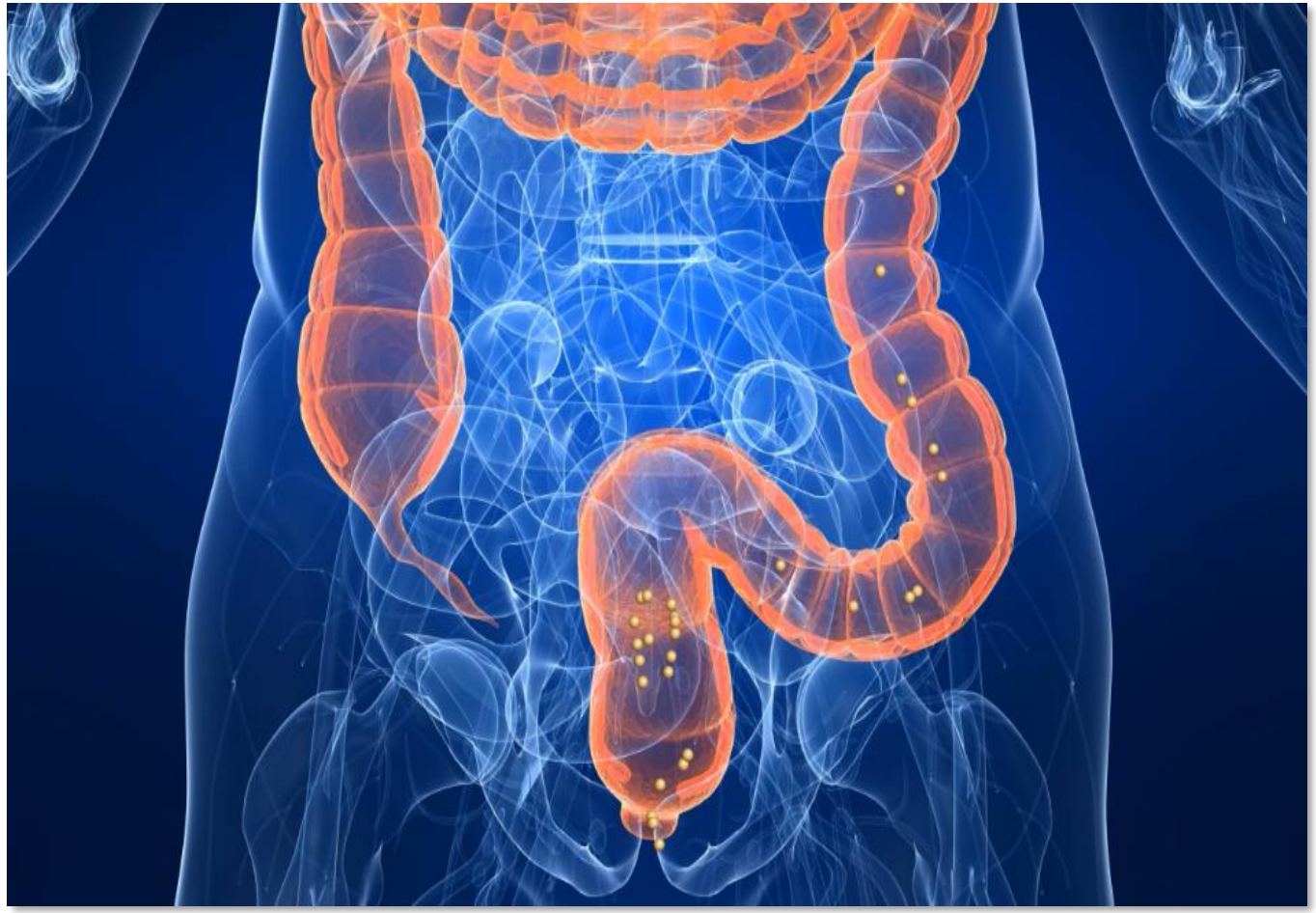
Figure 3. Light microscopy images (×100 magnification) of RLY5016S (left) and sodium polystyrene sulfonate (right).

Lingyun Li, Stephen D. Harrison, M. Jamie Cope, et al, Mechanism of Action and Pharmacology of Patiromer, a Nonabsorbed Cross-Linked Polymer That Lowers Serum Potassium Concentration in Patients With Hyperkalemia, Journal of Cardiovascular Pharmacology and Therapeutics 2016, Vol. 21(5) 456-465

Patiromer Is Designed to Bind Potassium Predominantly in the Colon

Patiromer travels through the GI tract over 24-72 hours

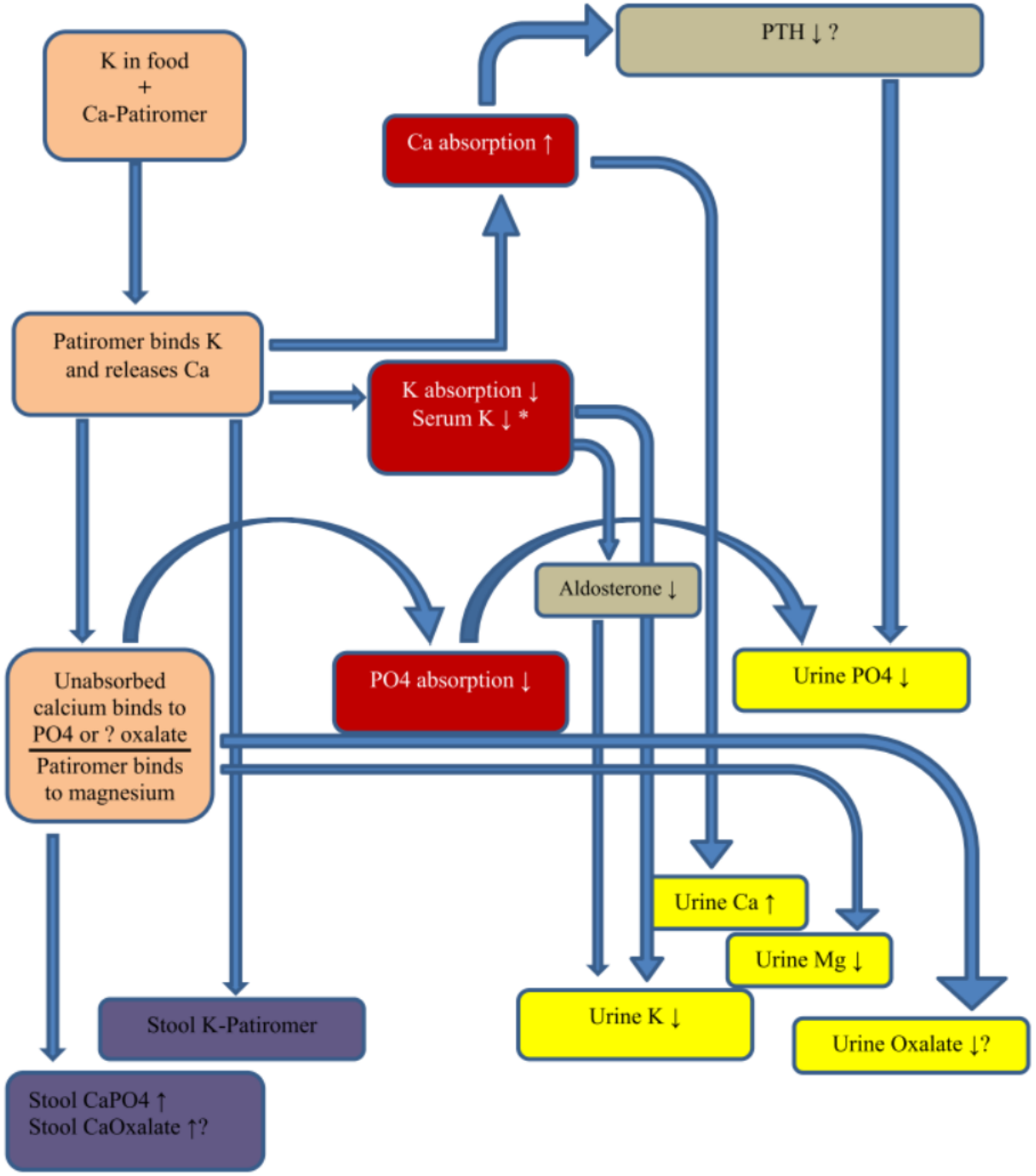
- Patiromer is fully ionized at the physiologic pH of the colon for optimal ion exchange
- Carboxylate groups of patiromer bind to K^+, which is primarily in the colon due to upregulation of BK channels in colonic epithelial cells
- Patiromer beads are excreted, leading to removal of excess K^+ and reduction of serum K^+ levels



GI: gastrointestinal.

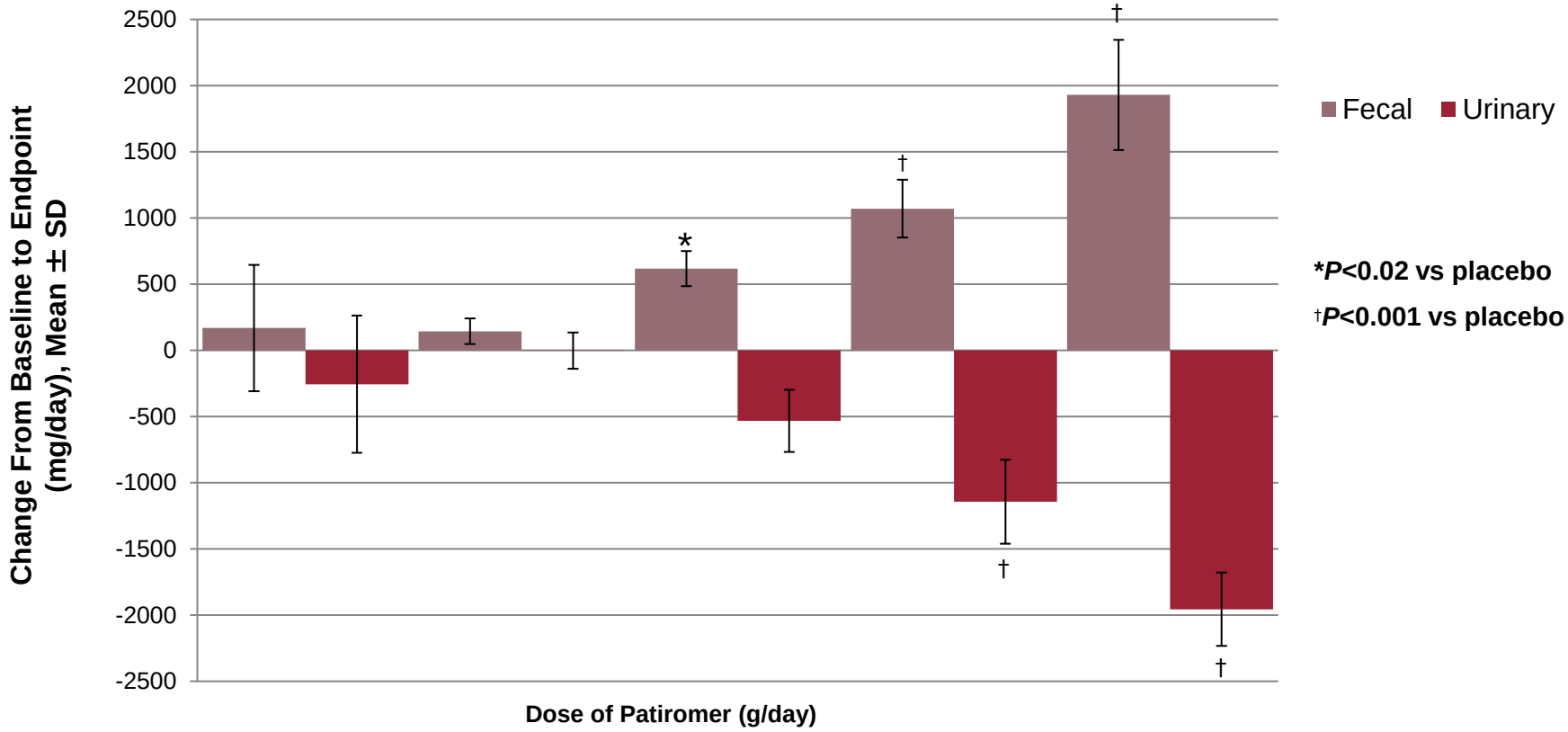
Li L, et al. *J Cardiovasc Phamacol Ther.* 2016;21(5):456-465.

Mode of action of Patiromer



Emmett & Mehta Clin J Am Soc Nephrol, 11: 1723–1725, 2016

Patiromer Increases Fecal and Decreases Urinary K^+ Excretion



*P<0.02 vs placebo

†P<0.001 vs placebo

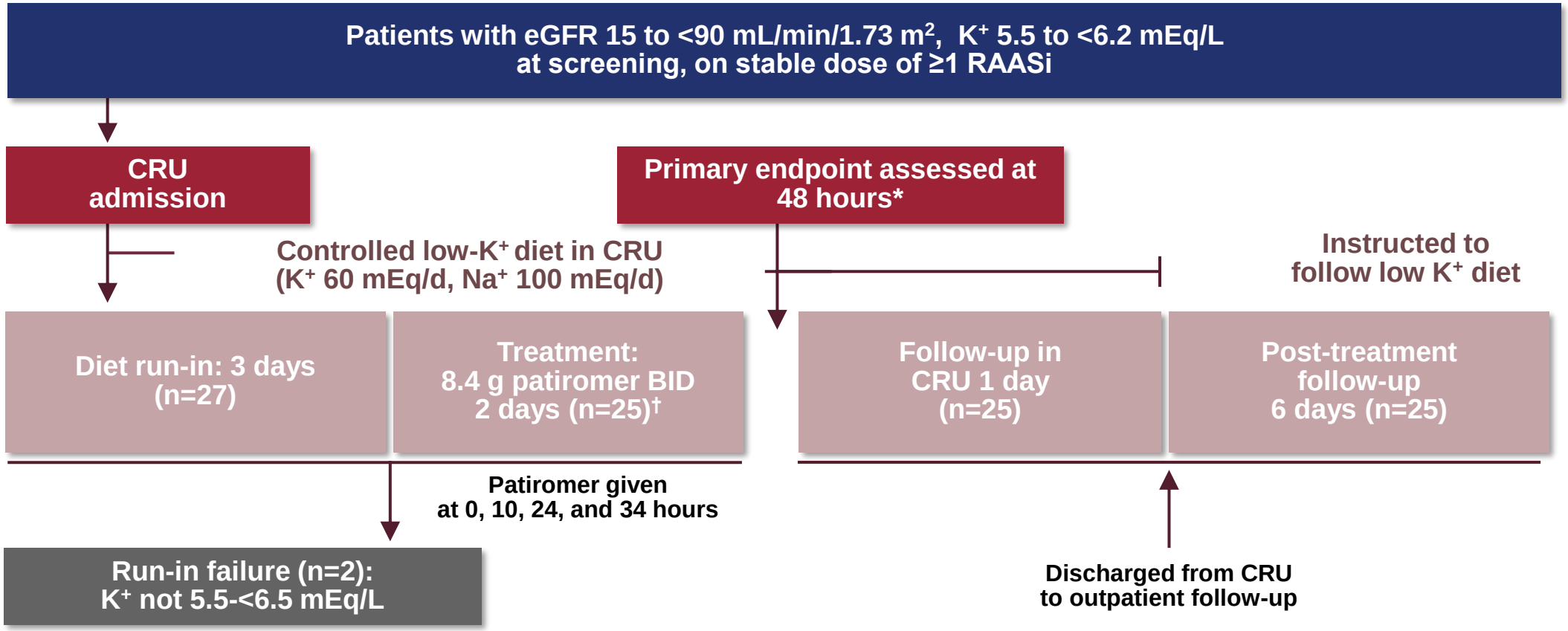
	Placebo n=8	**0.8** n=6	**4.2** n=6	**8.4** n=6	**16.8** n=6
Baseline Fecal Excretion	768.1±297.9	758.1±91.5	794.0±198.9	676.5±114.5	862.0±172.6
Baseline Urinary Excretion	3644.9±468.3	3493.7±570.4	3447.2±446.6	3765.5±325.8	3748.8±248.5

K^+: potassium; SD: standard deviation.

Li L, et al. *J Cardiovasc Phamacol Ther.* 2016;21(5):456-465.

Πατιρομέρη:
Κλινικές μελέτες αποτελεσματικότητας και ασφάλειας

Phase II: Study Design



The 3-day run-in ensured the identification of patients with chronic or persistent hyperkalemia and also that patients with spurious (ie, due to hemolysis), transient, and/or postprandial hyperkalemia were excluded

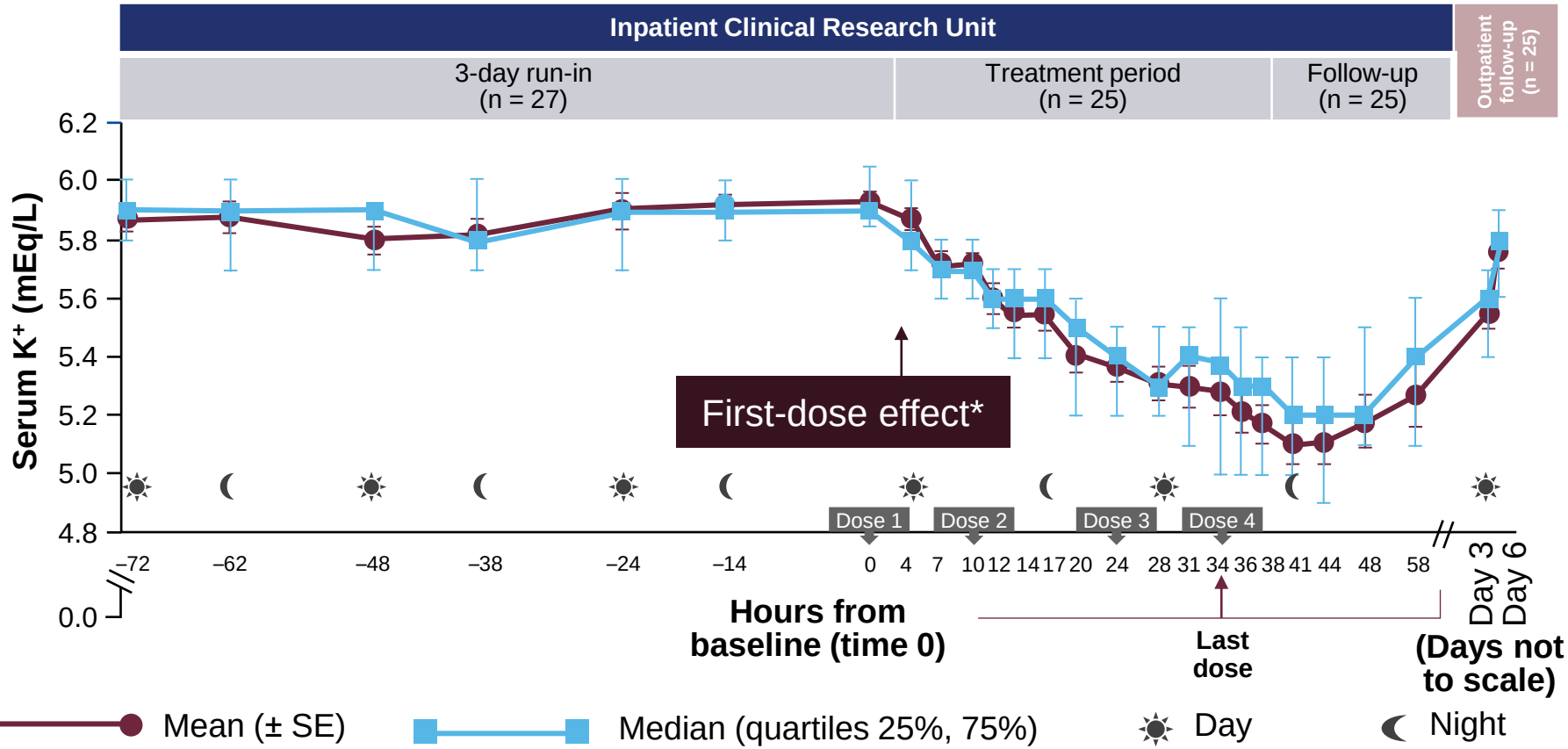
*Sequential testing procedure starting at 48 hours and working back in time to determine earliest time point at which change from baseline serum K^+ was significant.

†Patients with serum K^+ 5.5 to <6.5 mEq/L after the 3-day low K^+ diet run-in entered the treatment phase.

BID: twice daily; CRU: clinical research unit; eGFR: estimated glomerular filtration rate; K^+: potassium; Na^+: sodium; RAASi: renin-angiotensin-aldosterone system inhibitor.

Bushinsky DA, et al. *Kidney Int*. 2015;88(6):1427-1433.

Observed Serum Potassium (mEq/L) Over Time

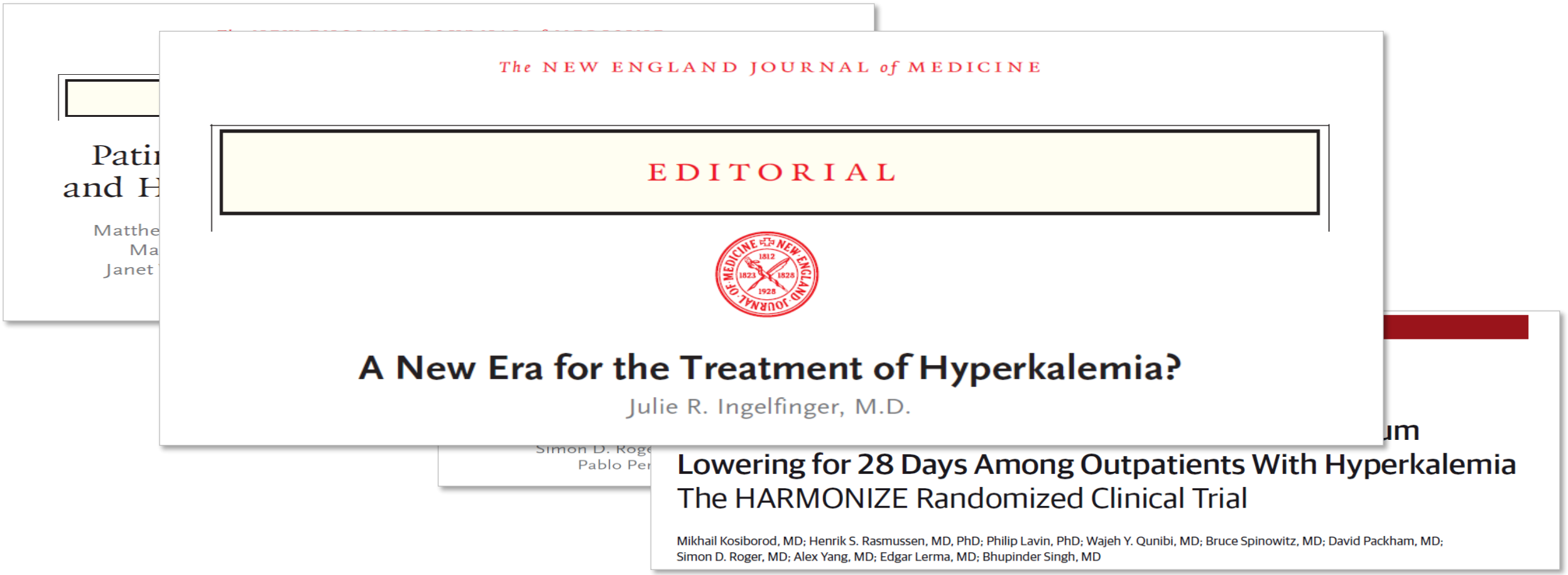


Significant reductions occurred at all assessments from 7 to 48 hours ($P \leq 0.004$ at 7 and 10 hours; $P < 0.001$ for 12 to 48 hours)

*Earliest timepoint where mean change from baseline in serum K^+ was significant; significant reduction seen at 7 hours (before the second patiromer dose).
Data presented as median (quartiles 25%,75%), mean (SE).

K^+: potassium; SE, standard error.

Bushinsky DA, et al. *Kidney Int.* 2015;88(6):1427-1433.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The NEW ENGLAND JOURNAL of MEDICINE
EDITORIAL
A New Era for the Treatment of Hyperkalemia?
Julie R. Ingelfinger, M.D.
Simon D. Roge
Pablo Per
um
Lowering for 28 Days Among Outpatients With Hyperkalemia
The HARMONIZE Randomized Clinical Trial
Mikhail Kosiborod, MD; Henrik S. Rasmussen, MD, PhD; Philip Lavin, PhD; Wajeh Y. Qunibi, MD; Bruce Spinowitz, MD; David Packham, MD;
Simon D. Roger, MD; Alex Yang, MD; Edgar Lerma, MD; Bhupinder Singh, MD

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JANUARY 15, 2015 VOL. 372 NO. 3

Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors

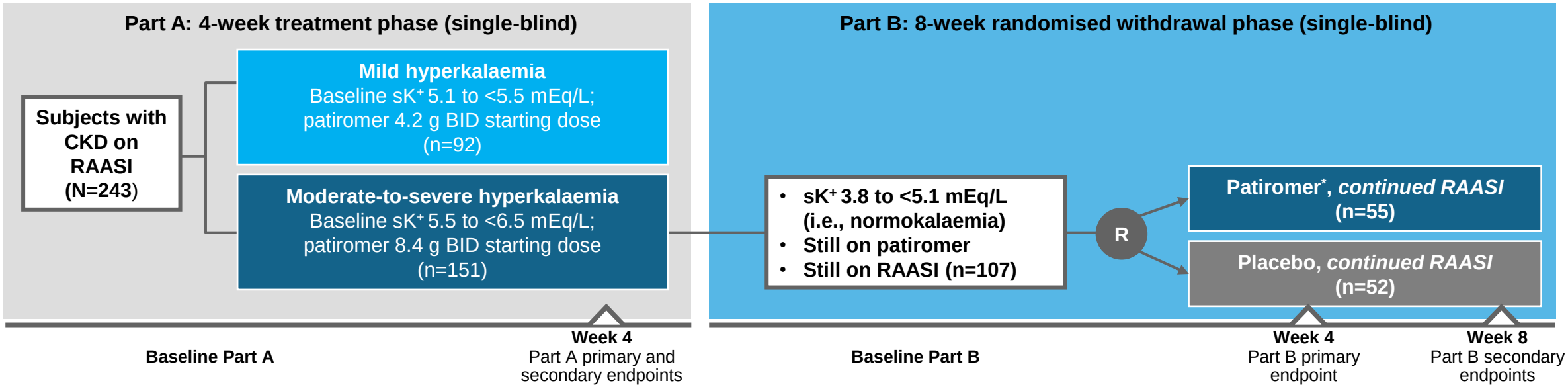
Matthew R. Weir, M.D., George L. Bakris, M.D., David A. Bushinsky, M.D., Martha R. Mayo, Pharm.D., Dahlia Garza, M.D., Yuri Stasiv, Ph.D., Janet Wittes, Ph.D., Heidi Christ-Schmidt, M.S.E., Lance Berman, M.D., and Bertram Pitt, M.D., for the OPAL-HK Investigators*

Study Objectives	**Part A:** •	To evaluate the efficacy and safety of patiromer for the treatment of hyperkalemia.
	Part B: •	To evaluate the effect of withdrawing patiromer on serum potassium control;
	•	To assess whether chronic treatment with patiromer prevents the recurrence of hyperkalemia To provide placebo-controlled safety data.

The NEW ENGLAND JOURNAL of MEDICINE

Weir M, Bakris G, Bushinsky D et al, Patiromer in Patients with Kidney Disease and Hyperkalemia Receiving RAAS Inhibitors, N Engl J Med (2015) 372, 211-221

OPAL-HK STUDY DESIGN



Part A: 4-week treatment phase (patients with hyperkalaemia)

- **Primary endpoint:** Mean change in sK+ from baseline to Week 4
- **Secondary endpoint:** Proportion of normokalaemic patients (sK+: 3.8–<5.1 mEq/L) at Week 4

Part B: 8-week randomised withdrawal phase (patients with normokalaemia)

- **Primary endpoint:** Treatment group differences in median change in sK+ from start of Part B to Part B Week 4 or first visit where sK+ was <3.8 or ≥5.5 mEq/L
- **Secondary endpoint:** Proportion of patients with mild (sK+: ≥5.1 mEq/L) or moderate/severe (≥5.5 mEq/L) hyperkalaemia

Inclusion criteria

CKD 3/4 (eGFR 15–<60 mL/min/1.73 m^2) with hyperkalaemia (sK+ 5.1–<6.5 mEq/L) using RAASI

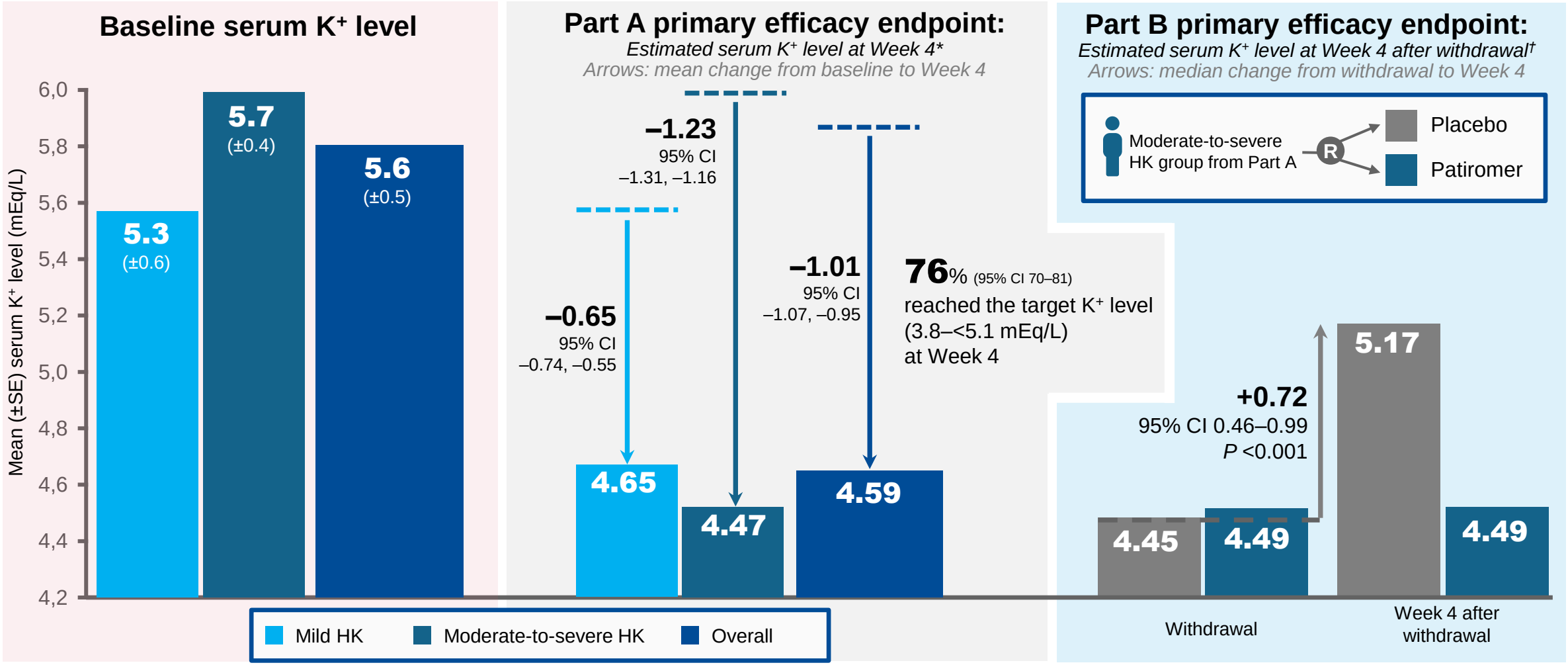
Baseline comorbidities/ treatment

- **100%** with CKD
- **97%** with HTN
- **57%** with T2DM
- **42%** with HF
- **100%** receiving RAASI

* Dose adjusted as needed by treating physician.

Weir MR, *et al. N Engl J Med.* 2015;372:211–21. Figure adapted from Weir MR, et al. Presented at: the American Society of Hypertension 2015 Annual Scientific Meeting.

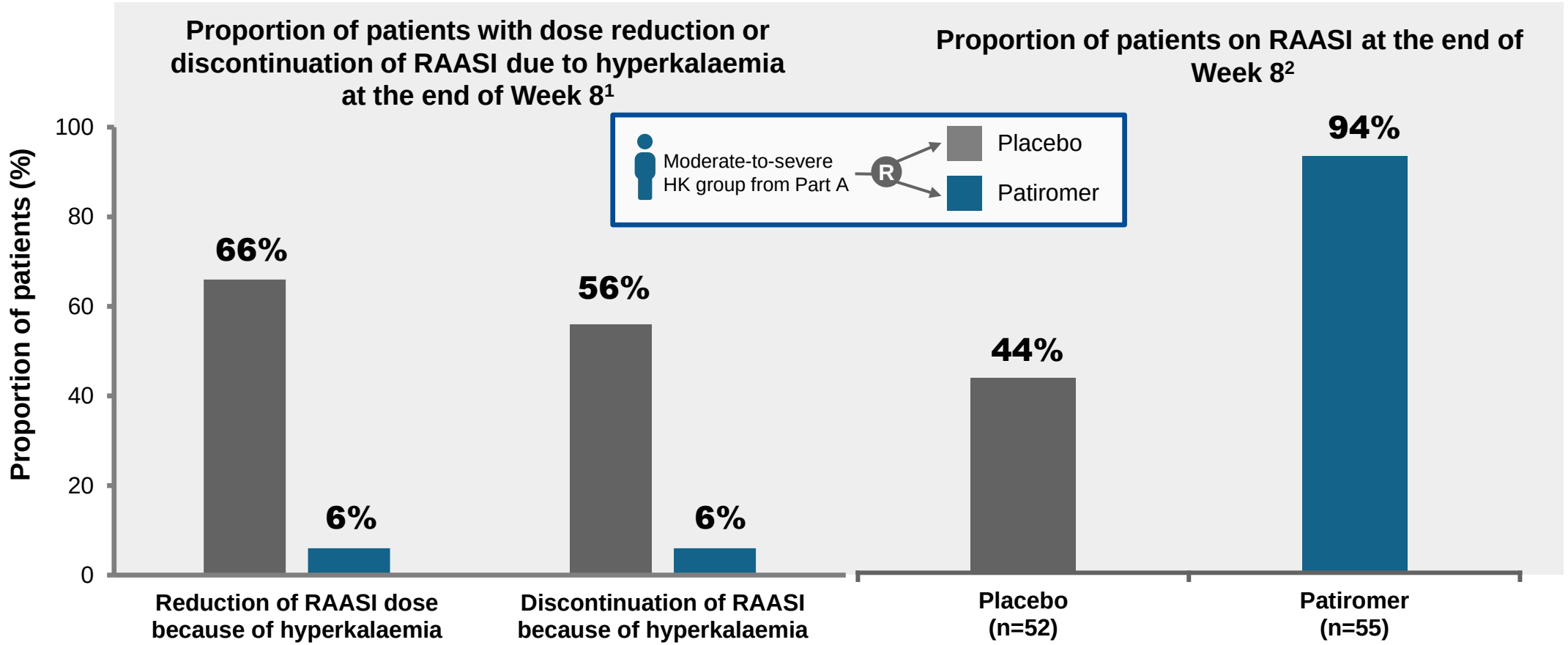
OPAL-HK: PATIROMER WAS EFFECTIVE AND HAD A DURABLE RESPONSE IN PATIENTS WITH CKD



* Serum K+ level was estimated by adding mean change in serum K+ level (from baseline to Week 4) to baseline serum K+ level. † Serum K+ level was estimated by adding median change in serum K+ level (after withdrawal to Week 4 of withdrawal) to serum K+ level measured at start of Part B.

Weir MR, *et al. N Engl J Med.* 2015;372:211–21.

OPAL-HK DEMONSTRATES RAASI ENABLEMENT WITH PATIROMER IN HYPERKALAEMIC CKD PATIENTS



1. Data on file. Redwood City, CA. Relypsa, Inc. Data source: Humedica, Cambridge, MA; 2. Weir MR, *et al. N Engl J Med.* 2015;372:211–21.

Original Investigation

Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease
The AMETHYST-DN Randomized Clinical Trial

George L. Bakris, MD; Bertram Pitt, MD; Matthew R. Weir, MD; Mason W. Freeman, MD; Martha R. Mayo, PharmD; Dahlia Garza, MD; Yuri Stasiv, PhD; Rezi Zawadzki, DrPH; Lance Berman, MD; David A. Bushinsky, MD; for the AMETHYST-DN Investigators

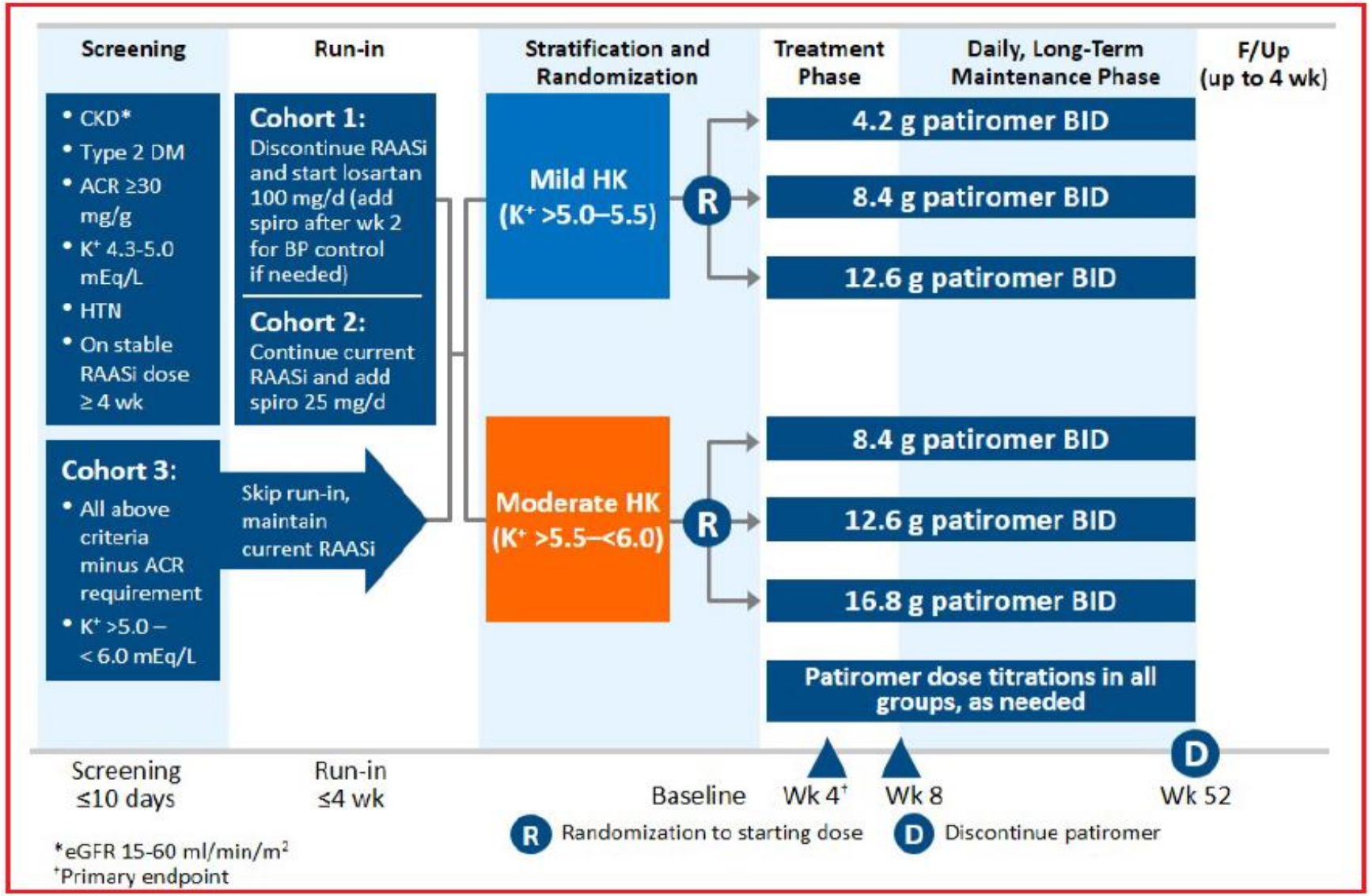
JAMA July 14, 2015 Volume 314, Number 2

OBJECTIVES To select starting doses for a phase 3 study and to evaluate the long-term safety and efficacy of a potassium-binding polymer, patiromer, in outpatients with hyperkalemia.

JAMA The Journal of the American Medical Association

Bakris G, Pitt B, Weir M et al, Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease The AMETHYST-DN Randomized Clinical Trial, JAMA. (2015) 314(2), 151-161

Amethyst-DN: Study design

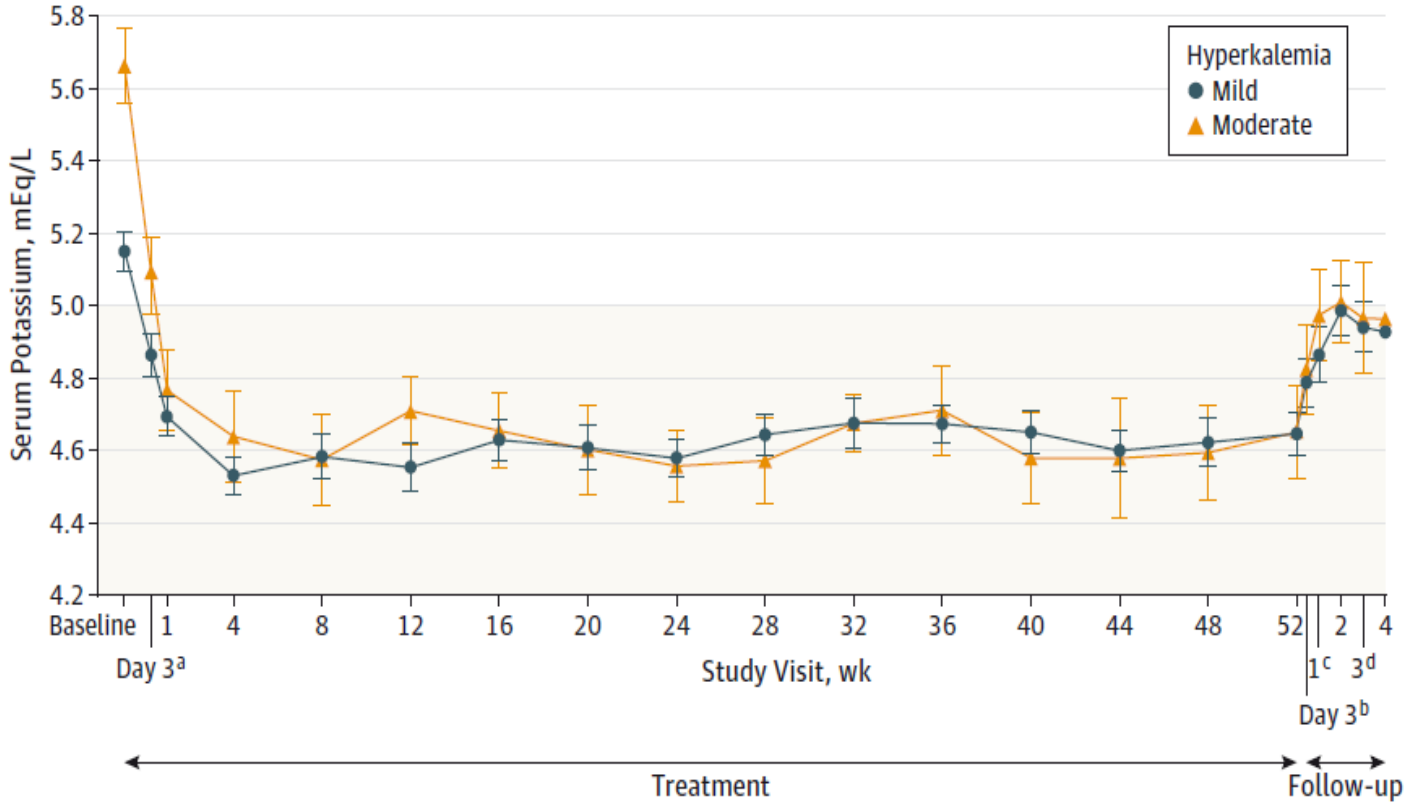


Bakris G, Pitt B, Weir M et al, Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease The AMETHYST-DN Randomized Clinical Trial, JAMA. (2015) 314(2), 151-161

JAMA The Journal of the American Medical Association

Study results: efficacy

Least Squares Mean (95% CI) Serum Potassium Levels Over 52 Weeks and During Posttreatment Follow-up in Patients With Mild or Moderate Hyperkalemia (Post Hoc Mixed-Effects Models for Repeated-Measures Analysis)



Bakris G, Pitt B, Weir M et al, Effect of Patiromer on Serum Potassium Level in Patients With Hyperkalemia and Diabetic Kidney Disease The AMETHYST-DN Randomized Clinical Trial, JAMA. (2015) 314(2), 151-161

JAMA The Journal of the American Medical Association

SAFETY SUMMARY OF PATIROMER: POOLED ANALYSIS OF OPAL-HK AND AMETHYST-DN

	N=547
≥1 AE	340 (62.2)
Severe AE	41 (7.5%)
Most common AEs*	**n (%)**
Constipation	45 (8.2)
Worsening of CKD	35 (6.4)
Hypomagnesaemia	35 (6.4)
Diarrhoea	27 (4.9)
Worsening of hypertension	28 (5.1)
Anaemia	18 (3.3)
Headache	12 (2.2)
Nausea	14 (2.6)
Hyperglycaemia	13 (2.4)
≥1 patiromer-related AE	116 (21.2)

Adverse events (cont'd)	N=547
Most common related AEs*	**n (%)**
Constipation	38 (6.9)
Hypomagnesaemia	30 (5.5)
Diarrhoea	15 (2.7)
≥1 SAE	47 (8.6)
Severe SAE	38 (6.9)
Patiromer-related SAE	0
AE leading to discontinuation of patiromer	51 (9.3)
SAE leading to discontinuation of patiromer	24 (4.4)
AE resulting in death†	15 (2.7)
Prespecified laboratory values of interest	**N=547**
Serum K^+ <3.5 mEq/L	26 (4.8)
Serum Mg^{2+} <1.4 mg/dL	57 (10.6)
Serum Mg^{2+} <1.2 mg/dL	13 (2.4)

* Presented as n (%) and AE incidence per 100 person-years and occurring in >2% of patients. † One additional patient died after 35 days on placebo during the randomised withdrawal phase of OPAL-HK; the patient previously had received 4 weeks of patiromer during the initial treatment phase of the study. No SAEs of hypokalaemia or hypomagnesaemia were reported. None of the SAEs were attributed to patiromer.

Pitt B and Garza D. *Expert Opin Drug Saf*. 2018;17:525−35.

AMBER Study Design

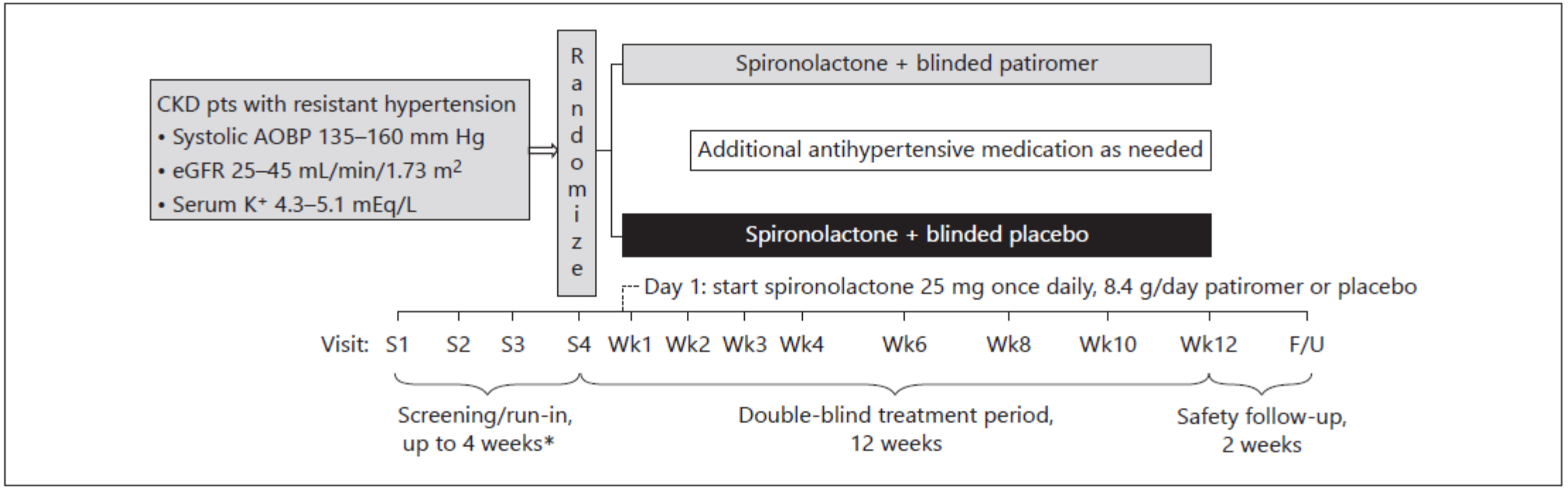


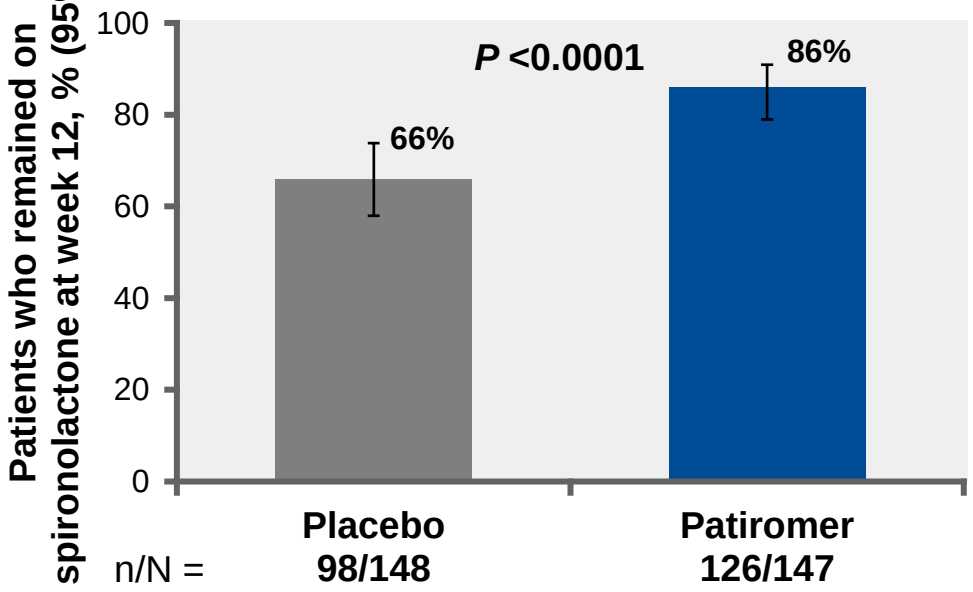
Fig. 1. AMBER study design. AOBP, automated office blood pressure; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HBP, home blood pressure. * To ensure eligibility criteria, stable medication, and competent use of HBP monitor.

- * Patients who completed 12 weeks of study treatment and had not had any event are censored at Week 12.
  Agarwal R, *et al. Lancet.* 2019;394:1540–50.

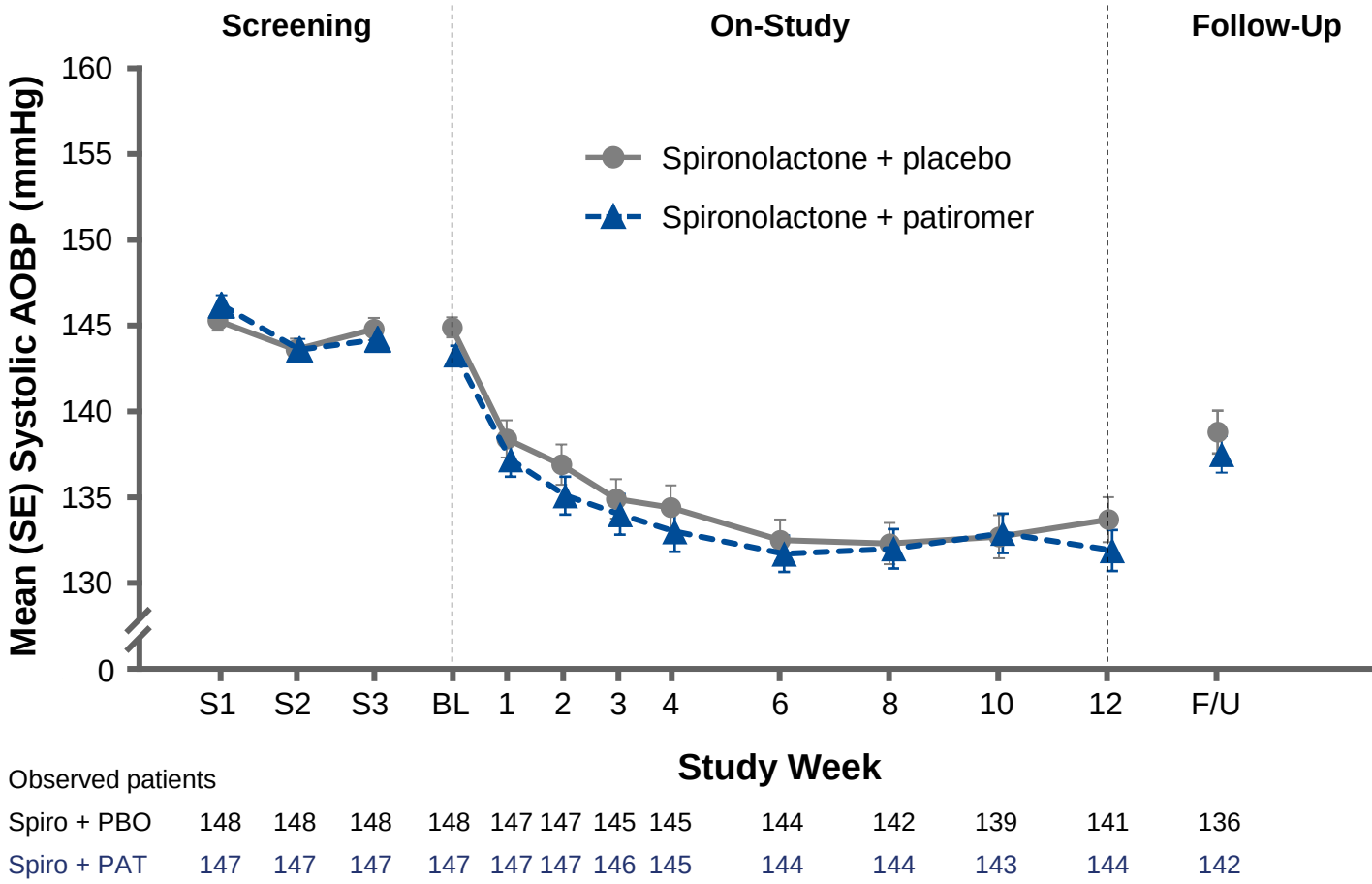
AMBER Key Results: ITT Population

Primary Endpoint: Patients who remained on spironolactone at Week 12

LS mean (95% CI) difference between groups: 20% (95% CI 10–29)



Secondary end-point: Systolic AOBP over time

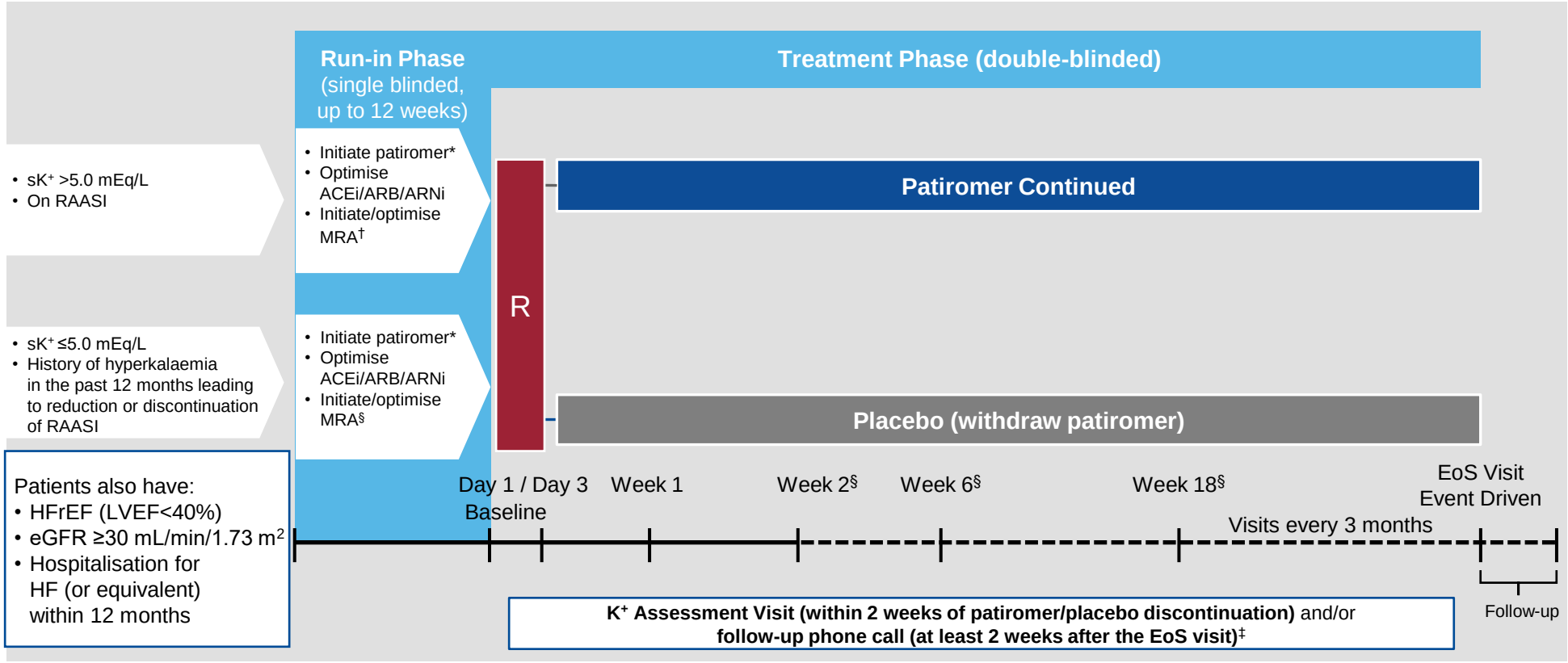


Observed patients													
Spiro + PBO	148	148	148	148	147	147	145	145	144	142	139	141	136
Spiro + PAT	147	147	147	147	147	147	146	145	144	144	143	144	142

* Patients who completed 12 weeks of study treatment and had not had any event are censored at Week 12.

Agarwal R, *et al. Lancet.* 2019;394:1540−50.

DIAMOND: THE CARDIOVASCULAR OUTCOME STUDY FOR PATIROMER



Study endpoints

Primary

- Time to first occurrence of CV death or CV hospitalisation

Secondary

- Proportion of subjects on ≥50% of guideline-recommended target dose of RAASI medications
- Total HF hospitalisations
- KCCQ

Objective: To determine if patiromer treatment of patients who develop HK while receiving RAASI will result in RAASI continuation per HF treatment guidelines and thereby decrease the occurrence of CV death and CV hospitalisation events compared with placebo

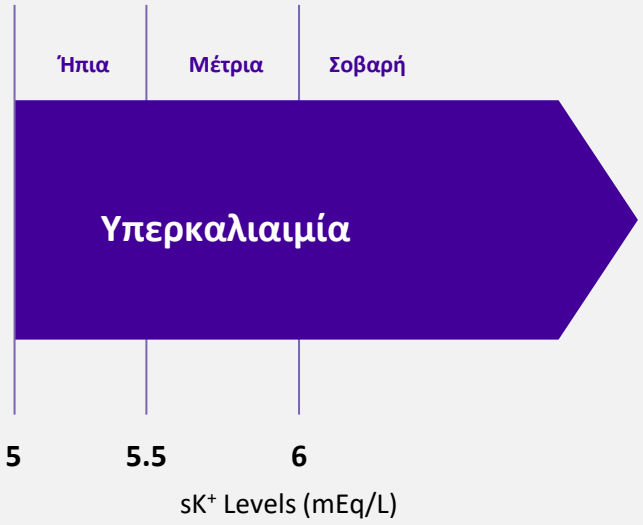
* Start at 8.4 g/day and up-titrate as necessary up to 25.2 g/day. Subject must return within 1 week (± 3 days) after patiromer initiation or dose adjustment to assess K^+ levels; † Initiate selected MRA, up-titrate to 50 mg/day; ‡ If the K^+ Assessment Visit is at 2 weeks after the EoS Visit, then the follow-up phone call is not required; § If there are changes to ACEi, ARB, ARNi and/or MRA dose or sK^+ varies outside of the intended range, unscheduled weekly or monthly visits should occur until stability returns.
NCT03888066. Available at: clinicaltrials.gov/ct2/show/NCT03888066 (accessed July 2020).

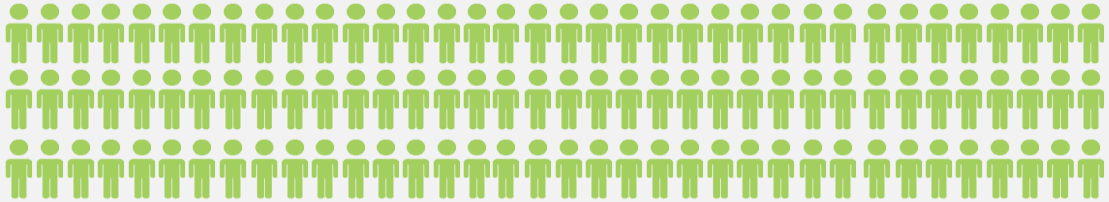
Πατιρομέρη: Κλινικές ενδείξεις και τρόπος χρήσης

PATIROMER : ΘΕΡΑΠΕΥΤΙΚΗ ΕΝΔΕΙΞΗ[1-3]

Το Patiromer ενδύκνειται για την θεραπεία της υπερκαλιαιμίας σε ενήλικες ασθενείς.[1]

extra info





Πάνω από 100,000 ασθενείς στην καθημερινή πρακτική πραγματικού κόσμου[3]

Συνολικά, στις κλινικές μελέτες φάσης 2 και φάσης 3 του Patiromer

99.4%
Λάμβανε θεραπεία με RAASi στην αρχή της παρατήρησης[1]

81.2%
Είχε ΧΝΝ με eGFR <60 mL/min/1.73 m^2
(Η πλειοψηφία είχε ΧΝΝ 3/4)[1]

72.8%
Είχε ΣΔ[1]

48.7%
Είχε ΚΑ[1]

XNN = Χρόνια Νεφρική Νόσο; eGFR = estimated glomerular filtration rate; , ΚΑ=Καρδιακή Ανεπάρκεια
RAASi = renin-angiotensin-aldosterone system inhibition; sK⁺ = serum potassium , ΣΔ=Σακχαρώδη Διαβήτη

1. Vifor. Patiromer SmPC. 2019
2. Rastegar A and Soleimani M. *Postgrad Med J*. 2001;77(914):759-64
3. Data on file March 2019. Relypsa, Inc

PATIROMER : ΔΟΣΟΛΟΓΙΑ ΚΑΙ ΤΡΟΠΟΣ ΧΟΡΗΓΗΣΗΣ[1,2]

Προτεινόμενη δόση έναρξης

8,4 g Μια φορά ημερησίως

Η ημερήσια δόση προσαρμόζεται με βάση το επίπεδο sK^+ καθώς και από τον επιθυμητό στόχο sK^+

Μέγιστη ημερήσια δόση 25.2 g

8,4 g + 8,4 g + 8,4 g

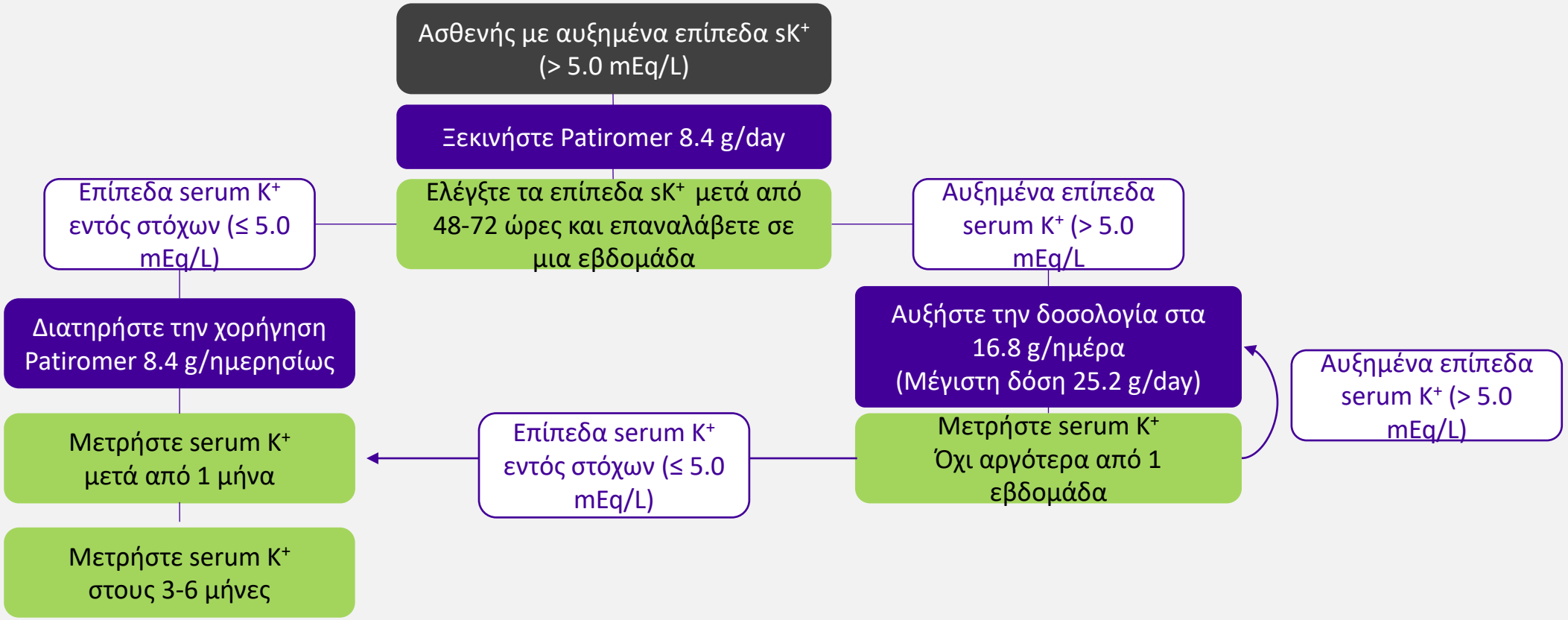
Η ημερήσια δόση μπορεί να αυξηθεί ή να μειωθεί κατά 8,4 g, αναλόγως των αναγκών του ασθενή.

Εάν παραληφθεί μια δόση, θα πρέπει να ληφθεί **το συντομότερο δυνατό** την ίδια ημέρα (αλλά **όχι μαζί με την επόμενη δόση**)

sK^+ = serum potassium

1. Vifor. Patiromer SmPC. 2019
2. Vifor. Patiromer. CCDS. v2.0. 2018

PATIROMER : ΑΛΓΟΡΙΘΜΟΣ ΧΟΡΗΓΗΣΗΣ[1]



1. Pitt B and Rossignol P. *Pharmacol Res*. 2017;118:2-4

PATIROMER : Αλληλεπιδράσεις με αλλά φαρμακευτικά προϊόντα και άλλες μορφές αλληλεπίδρασης [1,2]

Σε ταυτόχρονη χορήγηση, υπήρξε μειωμένη βιοδιαθεσιμότητα μόνο με 3 φάρμακα (σιπροφλοξασίνη, λεβοθυροξίνη και μετφορμίνη)

Προληπτικό μέτρο

3 ώρες

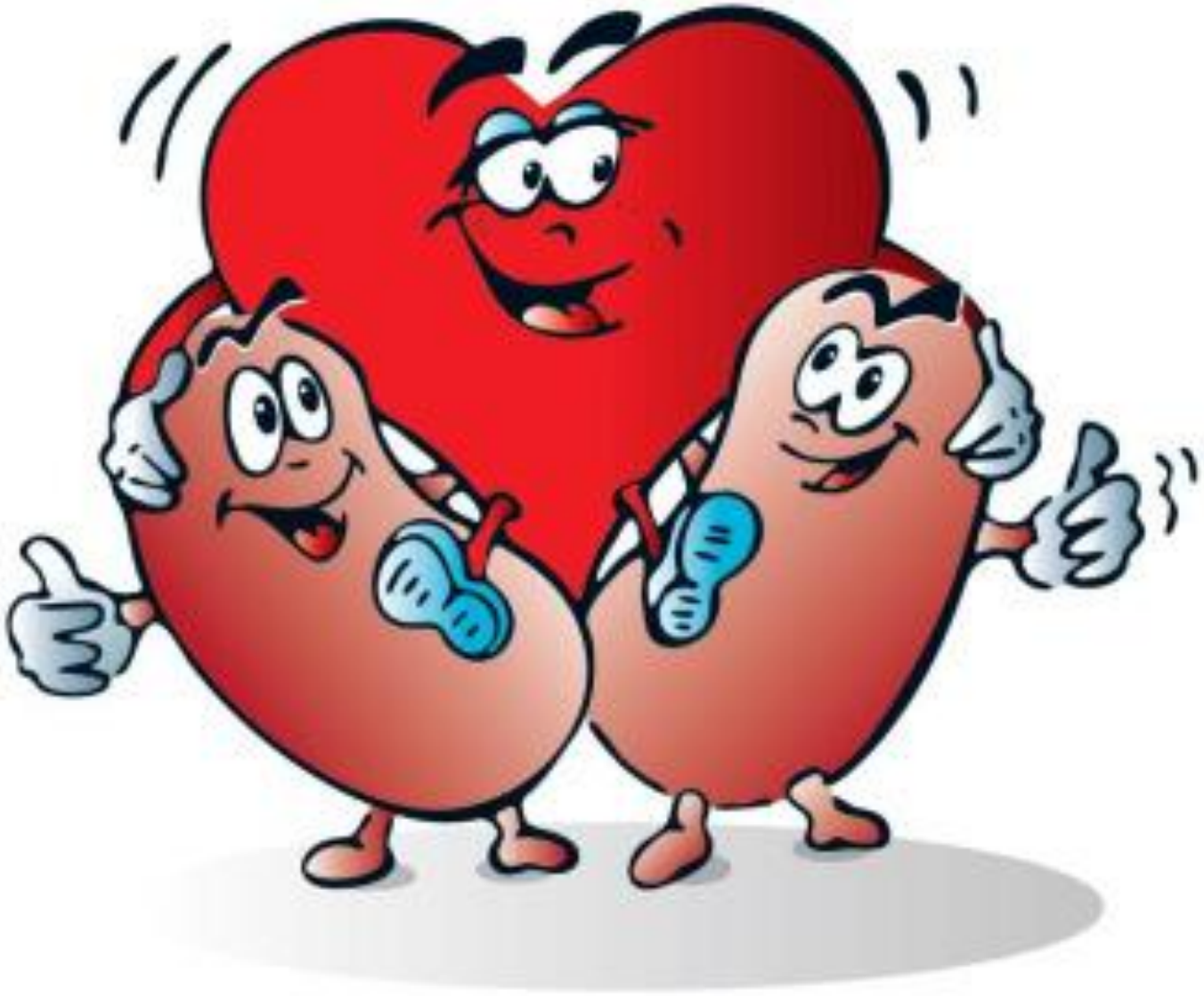
other oral drugs

1. Vifor. Patiromer SmPC. 2019
2. Lesko LJ et al. *J Cardiovasc Pharmacol Ther*. 2017;22(5):434-446

PATIROMER : ΠΡΟΦΙΛ ΑΣΦΑΛΕΙΑΣ[1]

	Συχνές (≥ 1/100 to < 1/10)	Σπάνιες (≥ 1/1,000 to < 1/100)	Βαρύτητα
Διαταραχές του γαστρεντερικού	Δυσκοιλιότητα **(6,2%)** Διάρροια **(3%)** Κοιλιακό άλγος**(2,9%)** Φούσκωμα **(1,8%)**	Ναυτία Έμετος	**Ήπια έως μέτρια** (Ανεξαρτήτως δόσης)
Μεταβολισμός και διατροφικές διαταραχές	Υπομαγνησιαιμία **(5,3%)**		**Ήπια έως μέτρια**

1. Vifor. Patiromer SmPC. 2019



Ευχαριστώ!