Gebruik van kaliumbinders in de klinische praktijk

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Disclosures

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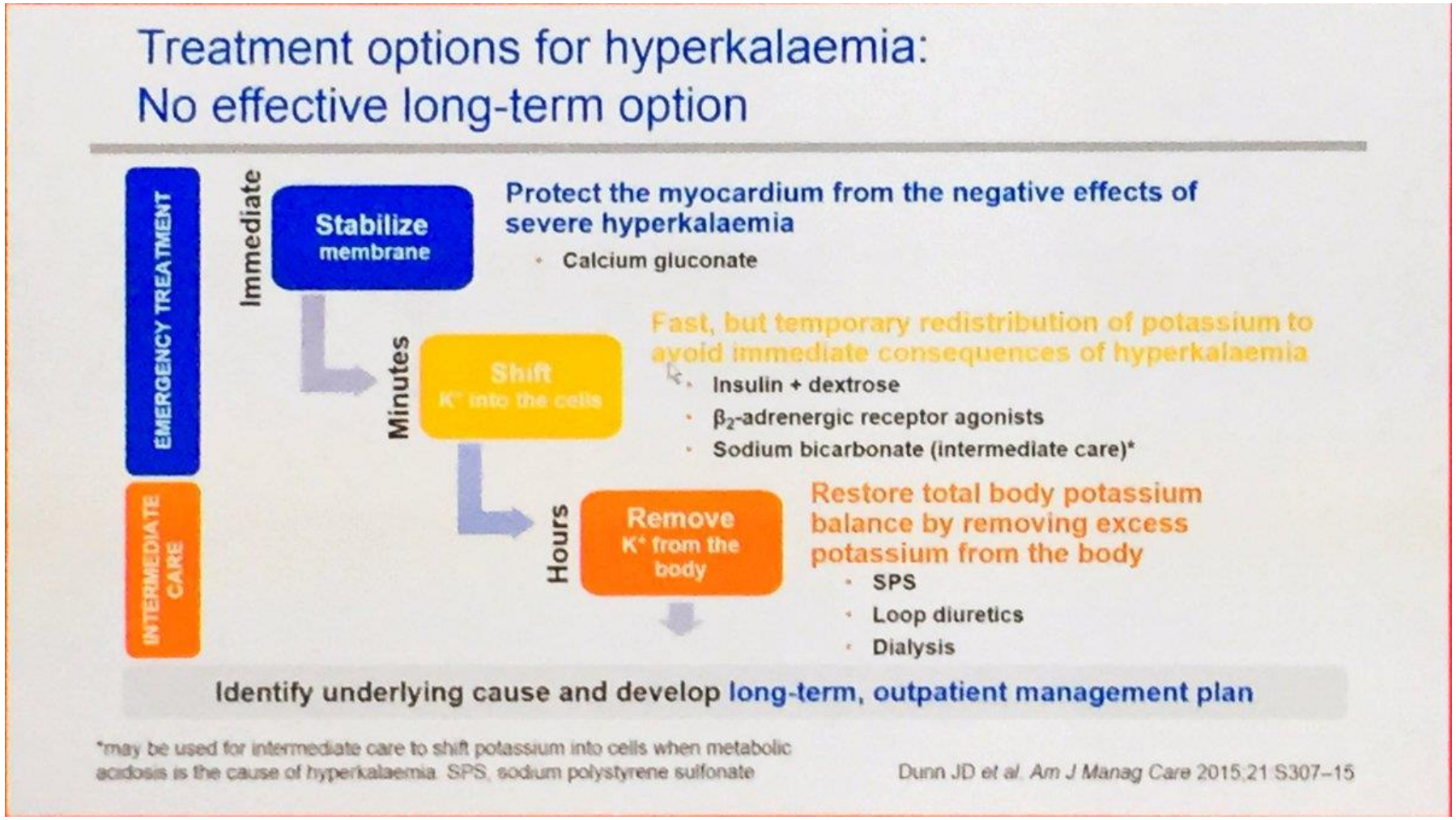
- Vifor Pharma, Novartis, AstraZeneca, Pharmacosmos, Pharma Nord

Therapeutic options for Hyperkalemia



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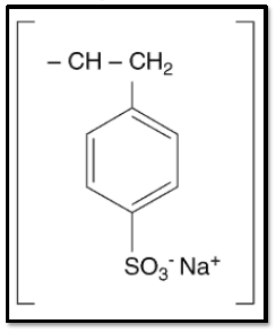
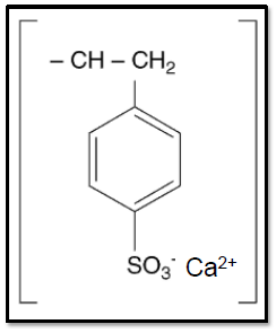
Other therapeutic options for the treatment of HyperK

Dietary potassium restriction	• Potassium is a common ingredient in many foods
RAASi reduction	• Limiting the dose or discontinuing treatment of drugs known to be effective in these populations
Diuretics	• Efficacy depends on residual renal function
Resonium / Kayexelate	• Warnings related to serious gastrointestinal adverse events

Kayexalate



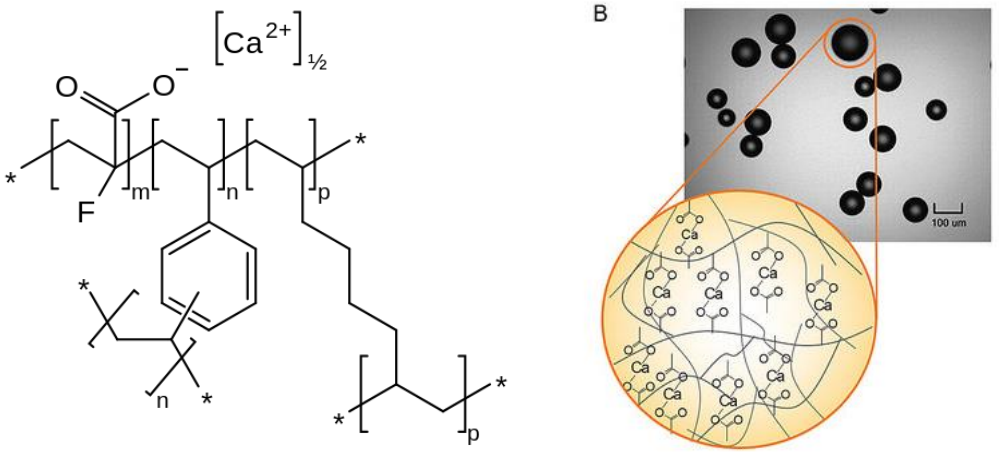
RESONIUM CALCIUM®

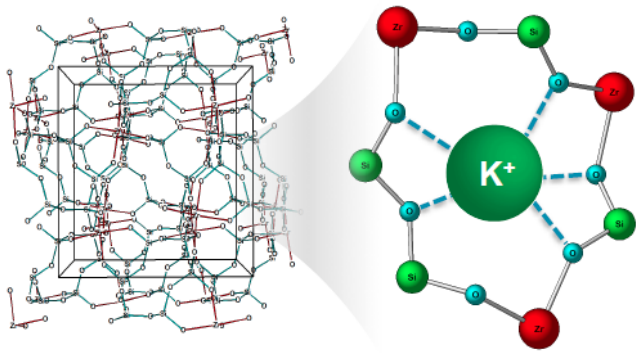


Given the non-selective binding and side effects there is a clinical need for hyperkalemia treatment that is effective, safe and well-tolerated

<u>2 novel potassium binders</u>:

- **Patiromer**
- **ZS-9**





Original Investigation

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

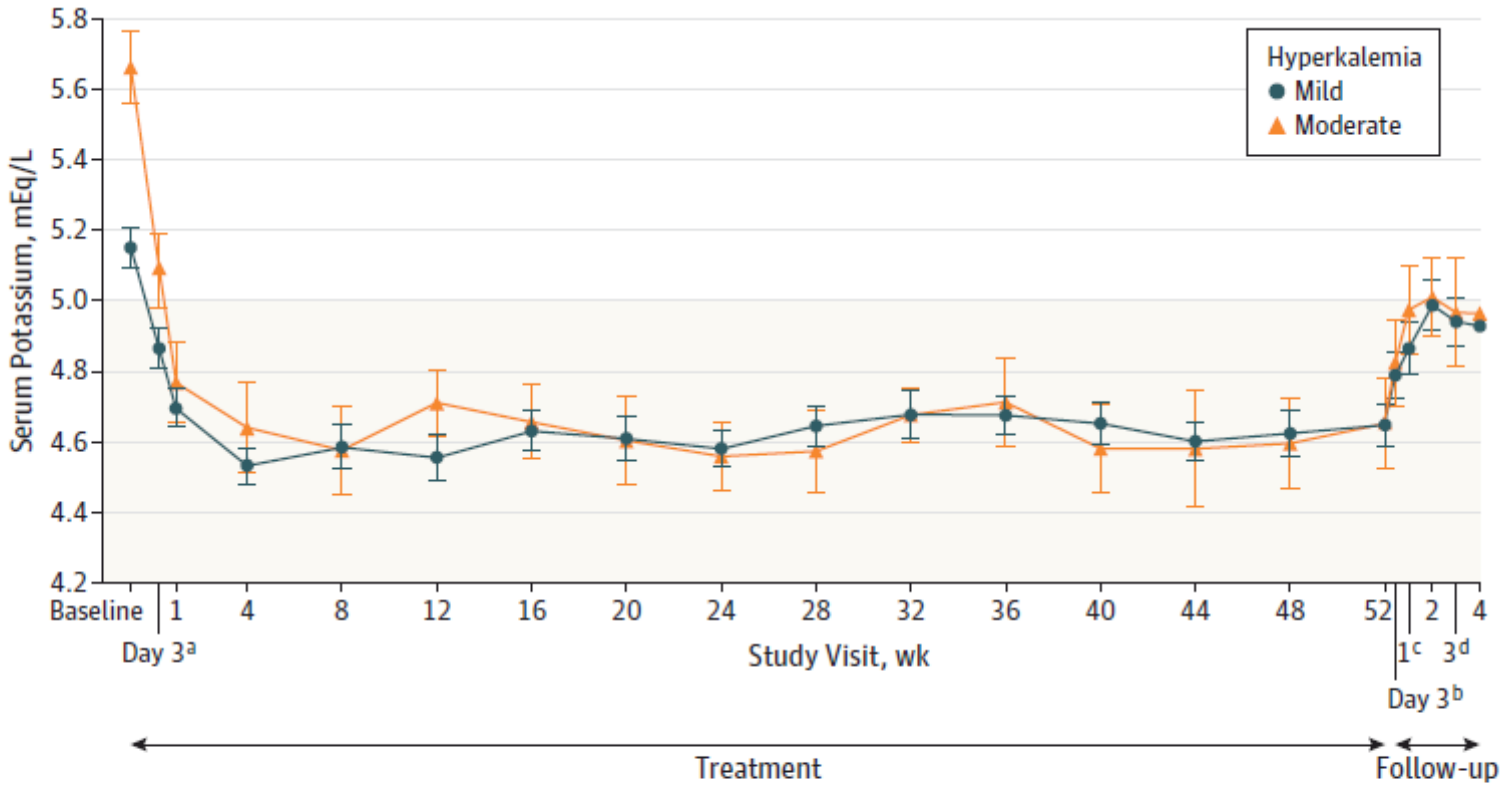
George L. Bakris, MD; Bertram Pitt, MD; Matthew R. Weir, MD; Mason W. Freeman, MD; Martha R. Mayo, PharmD; Dahlia Garza, MD; Yuri Stasiv, PhD; Rezi Zawadzki, DrPH; Lance Berman, MD; David A. Bushinsky, MD; for the AMETHYST-DN Investigators

- Effect of patiromer on serum potassium

  - Diabetes (type 2), N=306
  - eGFR 15-60 ml/min
  - RAASi
  - Potassium > 5 mmol/L

- Endpoints: Efficacy: Change in K+ (baseline – week 4)
  Safety: adverse events during 1 year FU

AMETHYST-DN trial



No. of patients

Hyperkalemia																	
Mild	218	204	199	192	175	168	161	161	163	158	156	151	148	149	145	131	126
Moderate	83	83	73	70	65	62	62	62	61	53	53	53	52	49	49	48	47

Adverse Event	Total (n = 304)
Worsening of CKD	28 (9.2)
Hypomagnesemia[c]	26 (8.6)
Worsening of hypertension	24 (7.9)
Constipation	19 (6.3)
Diarrhea	17 (5.6)
Hypoglycemia[c]	10 (3.3)

NB: no placebo group

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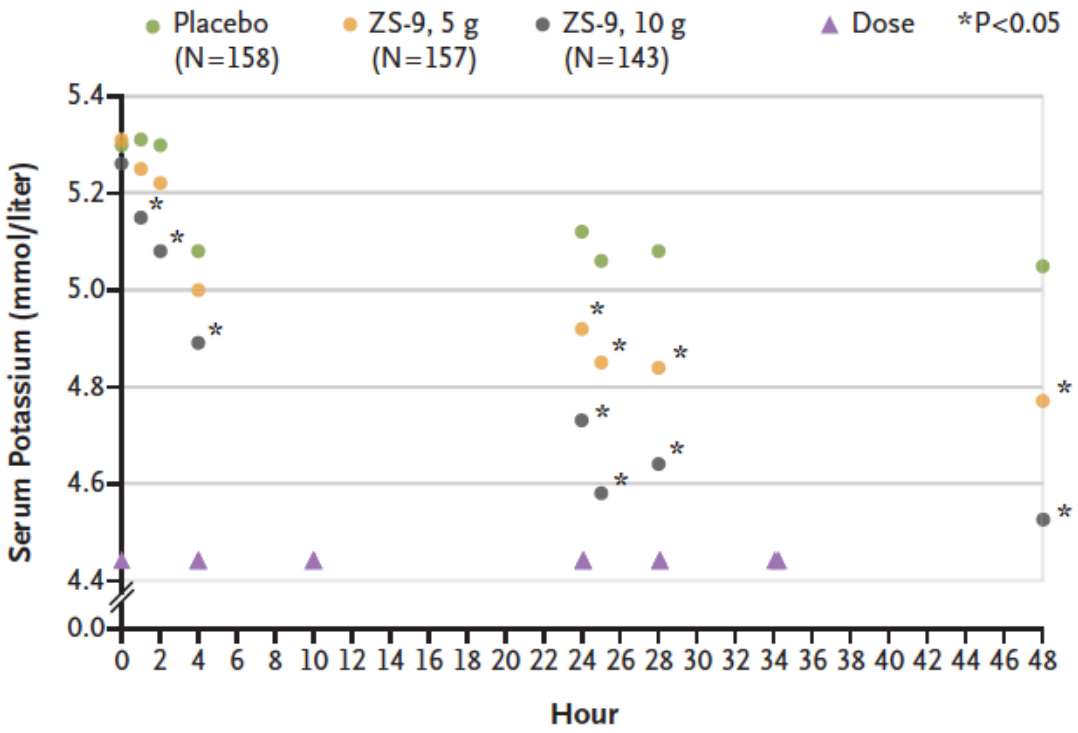
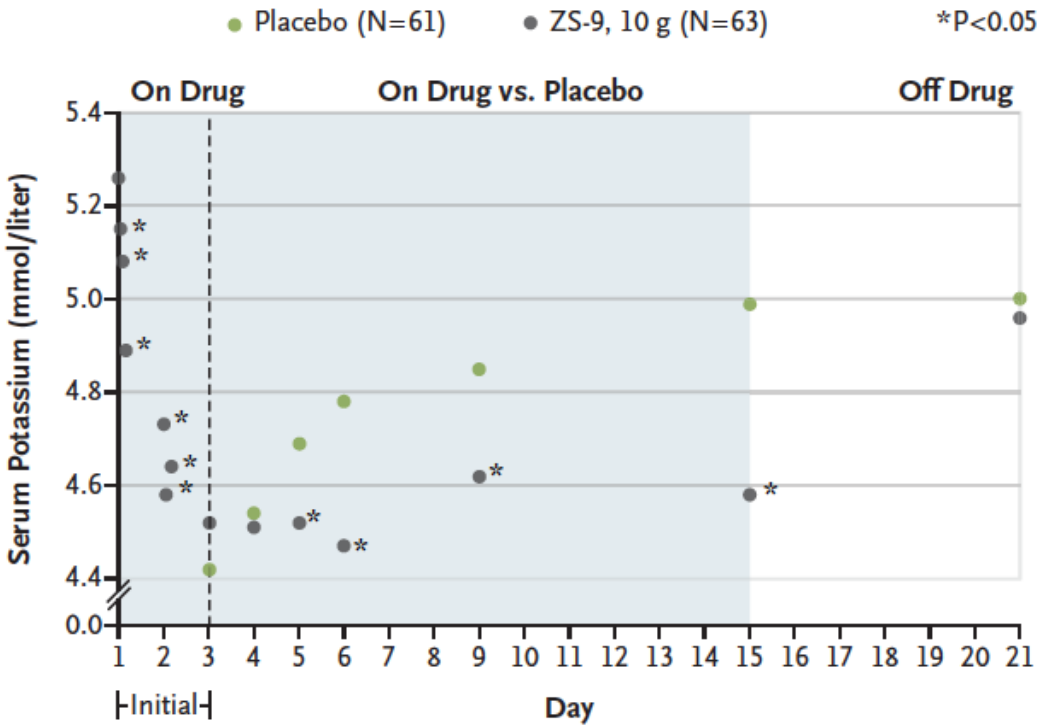
JAMA 2015

Effect of ZS-9 on Potassium





- N=753
- K+ 5.0-6.5
- Endpoint: change K+

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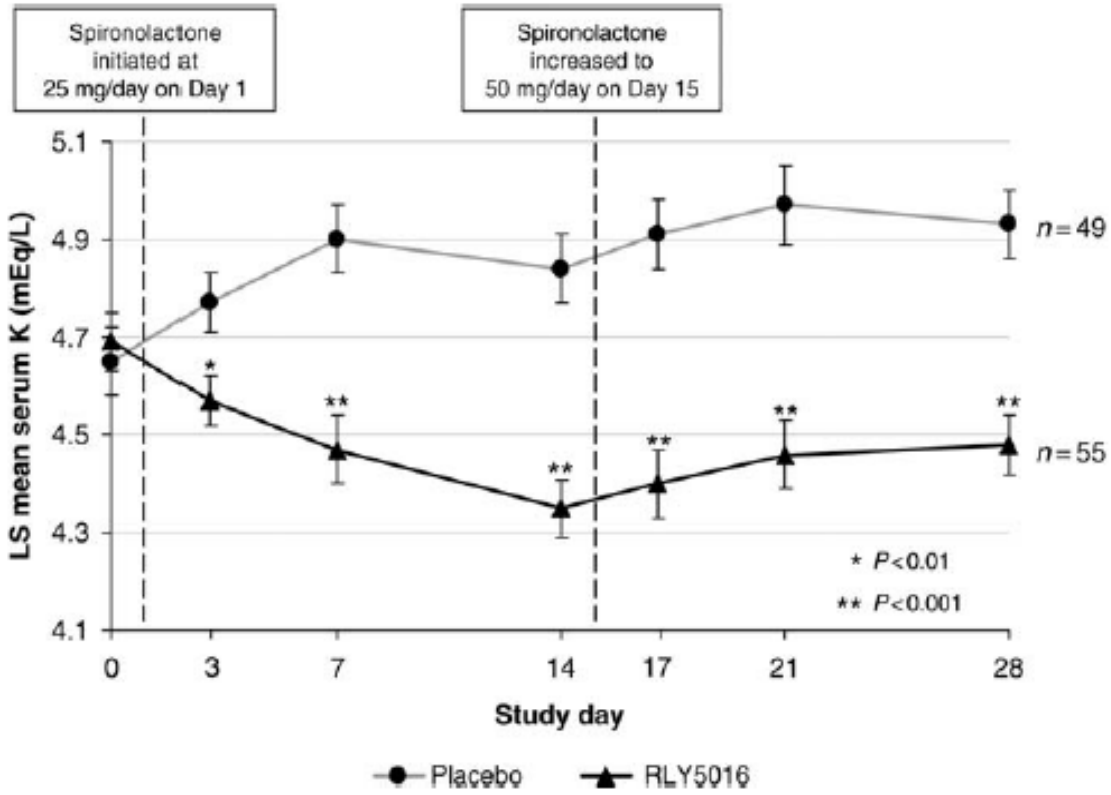
Packham et al. NEJM 2015

Enablement of RAASi therapy

Evaluation of the efficacy and safety of RLY5016, a polymeric potassium binder, in a double-blind, placebo-controlled study in patients with chronic heart failure (the PEARL-HF) trial

Bertram Pitt[1*], Stefan D. Anker[2,3], David A. Bushinsky[4], Dalane W. Kitzman[5], Faiez Zannad[6], and I-Zu Huang[7], on behalf of the PEARL-HF Investigators



- N=104, chronic HF
- History of Hyper K+
- CKD: GFR<60 ml/min/1.73m2
- Patiromer vs Placebo
- Efficacy Endpoint: change in K+
- Safety endpoint: AE

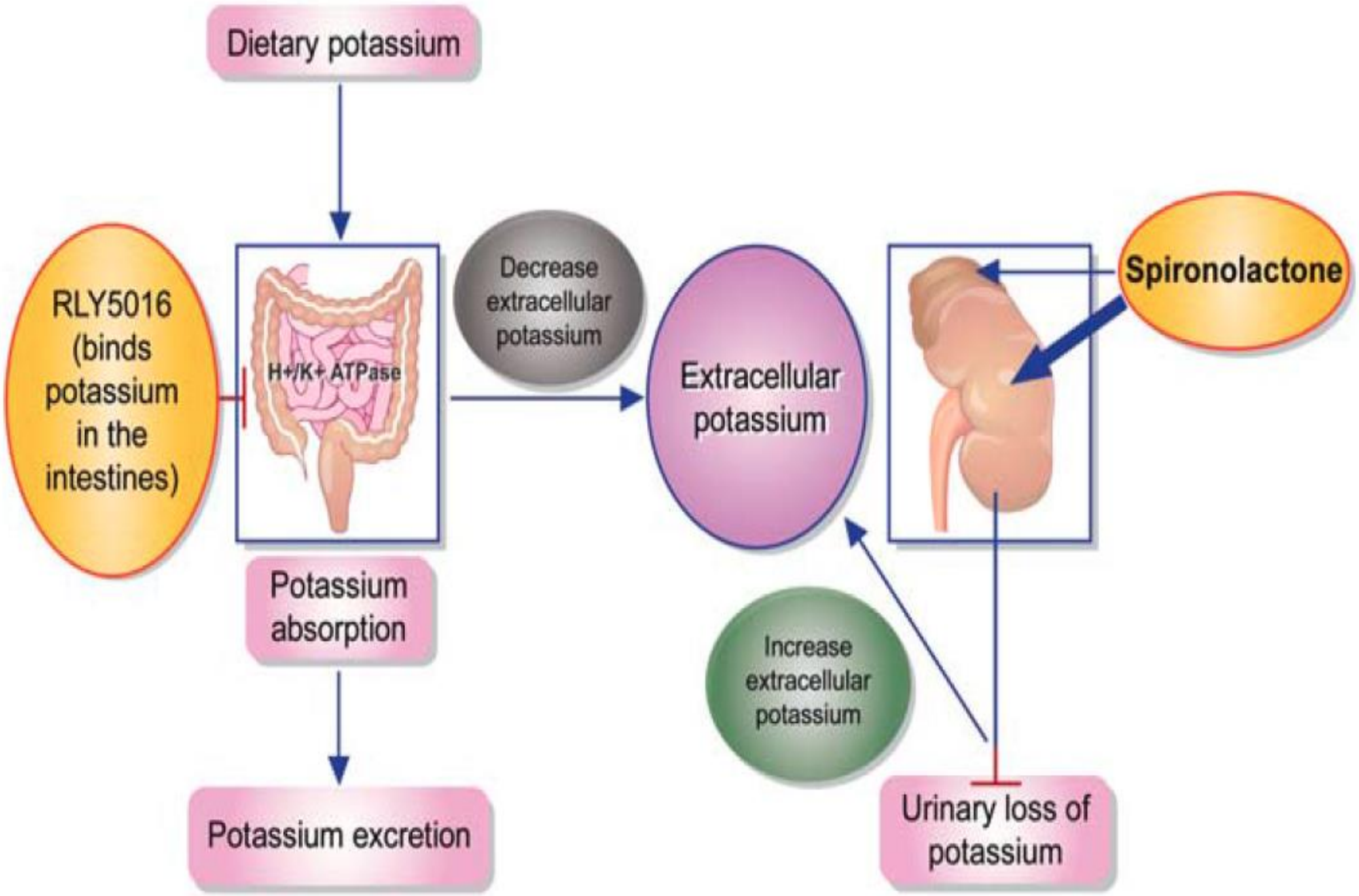
Eur Heart J 2011

Efficacy & Safety

Baseline eGFR (mL/min)	No. (%) of patients with hyperkalaemia (serum potassium > 5.5 mEq/L) at any study visit		
	RLY5016 30 g/day	Placebo	*P*-value
<60	1/15 (6.7)	5/13 (38.5)	0.041
≥60	3/40 (7.5)	7/36 (19.4)	0.125
All patients (eGFR = 81 ± 33)	4/55 (7.3)	12/49 (24.5)	0.015

	No. (%) of patients		*P*-value
	RLY5016 30 g/day (*n* = 55)	Placebo (*n* = 49)	
Serum potassium >5.5 mEq/L[a]	4 (7)	12 (25)	0.015
Serum potassium <4.0 mEq/L	26 (47)	5 (10)	<0.001
Serum potassium <3.5 mEq/L	3 (6)	0 (0)	0.094
Serum magnesium <1.8 mg/dL	13 (24)	1 (2)	0.001
Spironolactone dose increased	50 (91)	36 (74)	0.019

Safety parameter	No. (%) of patients	
	RLY5016 (*N* = 56)	Placebo (*N* = 49)
Any adverse event	30 (54)	15 (31)
Gastrointestinal disorders	12 (21)	3 (6)
Flatulence	4 (7)	0
Diarrhea	3 (5)	1 (2)
Constipation	3 (5)	0
Vomiting	2 (4)	0
Any serious adverse event	2 (4)	2 (4)
Related serious adverse event	0	0
Any adverse event leading to discontinuation of study drug	4 (7)	3 (6)



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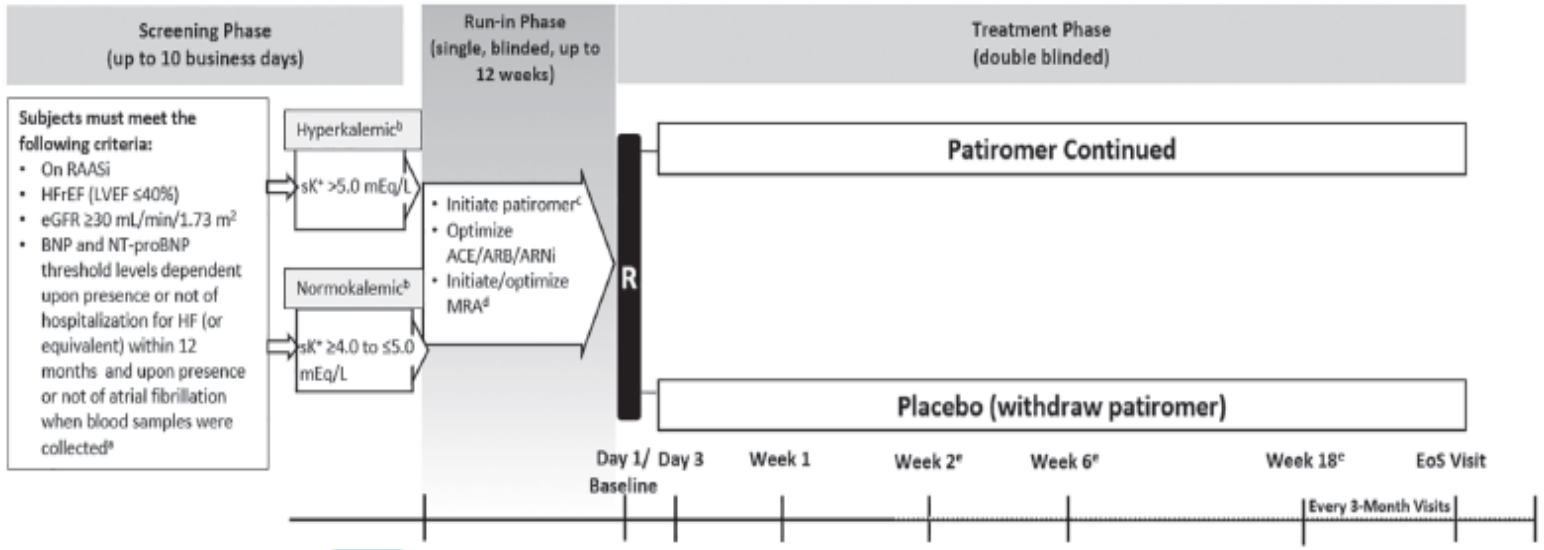
Van der Meer et al. Eur Heart J 2011

Patiromer for the management of hyperkalaemia in patients receiving renin–angiotensin–aldosterone system inhibitors for heart failure: design and rationale of the DIAMOND trial

Javed Butler[1]*, Stefan D. Anker[2], Tariq Jamal Siddiqi[3], Andrew J.S. Coats[4], Fabio Dorigotti[5], Gerasimos Filippatos[6], Tim Friede[7,8], Udo-Michael Göhring[5], Mikhail N. Kosiborod[9], Lars H. Lund[10], Marco Metra[11], Carol Moreno Quinn[5], Ileana L. Piña[12], Fausto J. Pinto[13], Patrick Rossignol[14], Peter Szecsödy[5], Peter Van Der Meer[15], Matthew Weir[16], and Bertram Pitt[17]

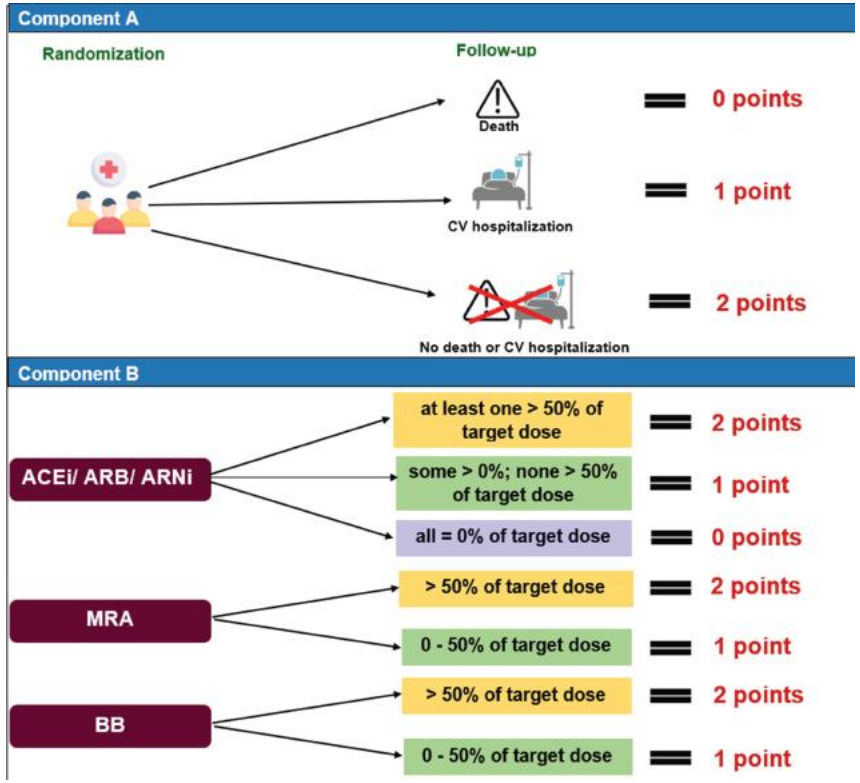
N=820 patients with HFrEF



Primairy Endpoint:

Change in Potassium

Secondary Endpoints:



DIAMOND

Eur J Heart Fail 2022

Conclusions

- Novel K-binding drugs have a favorable satefy profile and can be used chronic.
- Both drugs are highly efficient in lowering potassium
- Patiromer use resulted in more patients being able to use spironolacton
- DIAMOND study will learn us about the clinical efficacy of patiromer

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