

Advances in Heart Failure

3rd PORTO MEETING
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ORGANIZATION

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FACULDADE DE MEDICINA
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PCO

NO
GET
DONE
EVENTS.

What is the relevance of novel potassium-binders?

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Disclosure

José Silva Cardoso (JSC) has consulted and received speaker fees, or advisory boards' participation fees, or investigational grants for Abbott, AstraZeneca Pharmaceuticals, Bial, Boehringer Ingelheim, Menarini, Merck Serono, Merck Sharp & Dohme, Novartis, Orion, Pfizer, Sanofi, Servier and Vifor

RAASi

Neuro-Hormonal Blockade

- ACEIs
- ARBs
- MRAs
- Renin-inhibitors

Neuro-Hormonal Modulation

- ARNIs

RAASi

A positive impact on CVD prognosis

RAASi

Impact on prognosis

Reduce morbi-mortality in HFrEF and CKD
and in other CVDs (HTN, CAD, DM).

RAASi

Class I recommendation

Highest tolerated targeted doses recommended

RAASi

Can cause hyperkalemia

Hyperkalemia in real-practice

The incidence can be as high as 50%
in unselected patients under RAASi

RAASi

Increase the risk of hyperkalaemia

Particularly high in patient with HF, CKD and DM

(~ 50% have 2 or more yearly episodes)

Hyperkalemia

Is associated to an increased mortality

Hyperkalemia

Serum K > 5.0 mmol/l

However in the RALES study

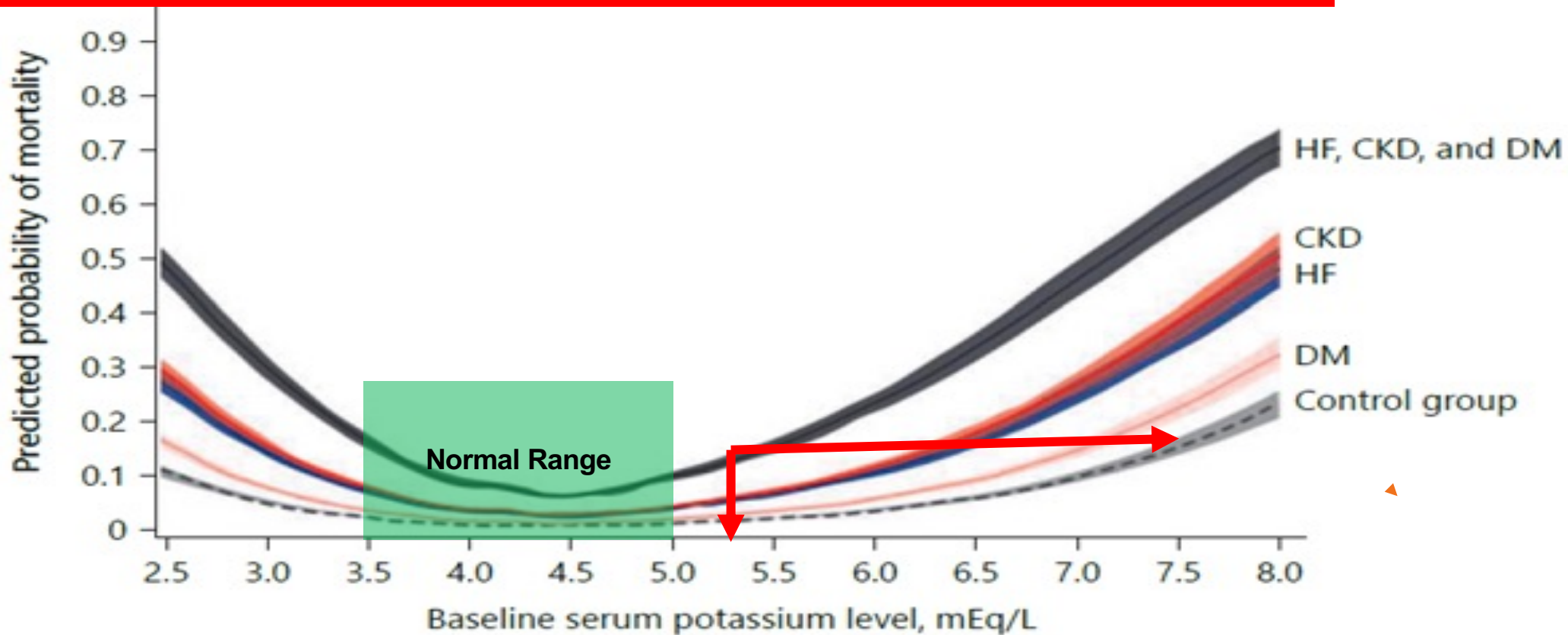
↑ mortality was observed only at K⁺ > 5.5 mmol/l

Hiperkalemia

The risk increases with age and co-morbidities

In pts with **HF+CKD+DM**, K=5.0-5.5 mEq/l

corresponds to a mortality risk similar that of controls with K = 7.5-8.0 mEq/l



The risk

- **Ventricular tachy-arrhythmias**
- **Sudden arrhythmic death**

Hyperkalemia

- leads to more frequent hospitalizations
- and increased mortality

Hyperkalemia

Mortality rate of up to 30%.

Hyperkalemia

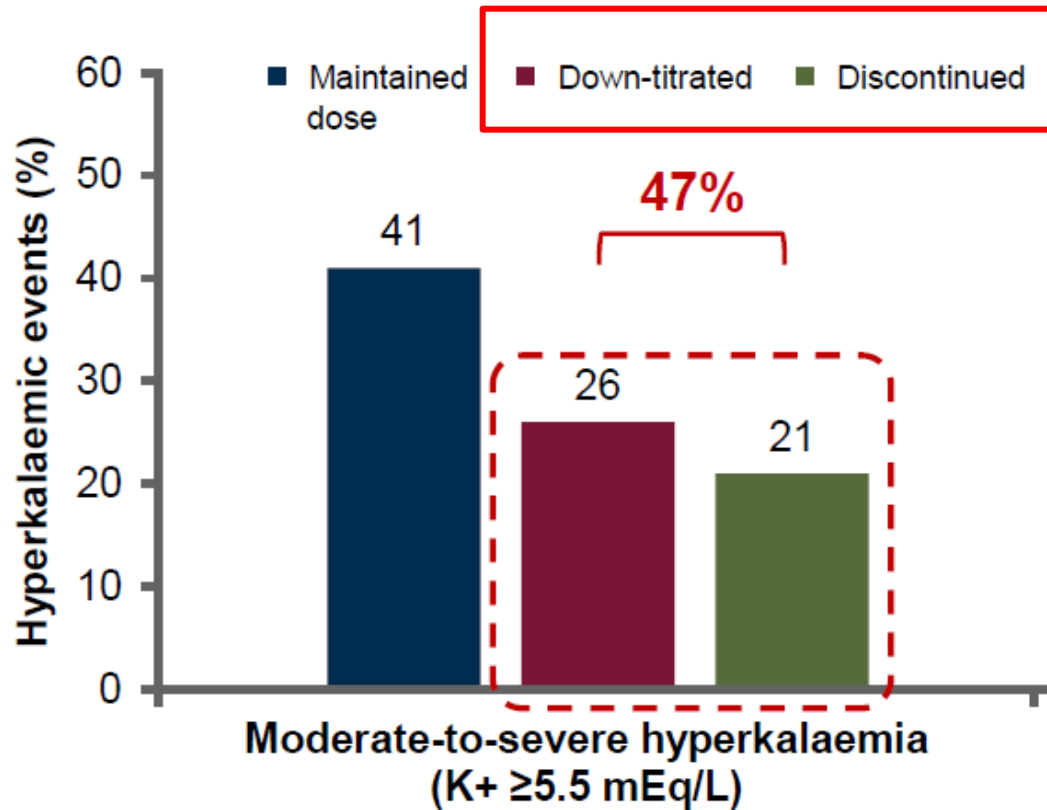
Impact on RAASi therapy

CVD guidelines and hyperkalaemia

In the presence of persistent hyperkalaemia

Guidelines recommend [RAASi down-titration/discontinuation](#)

Hyperkalaemia impact on RAASi therapy



RAASi permanent discontinuation

After hyperkalemia

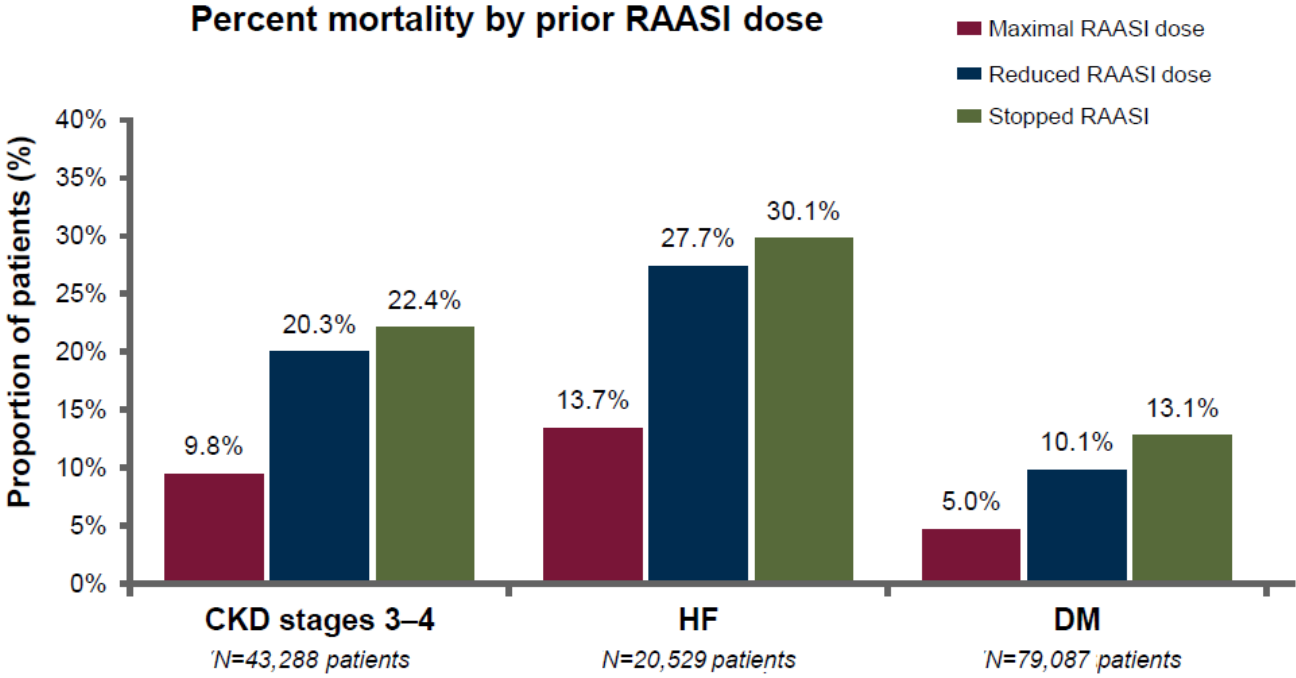
In clinical practice RAASi are seldom re-initiated
following an episode of hyperkalaemia.

RAASi down-titration/discontinuation

Impact on prognosis

RAASi down-titration/discontinuation

a two to three-fold increase in mortality



RAASi and hyperkalemia

The dilemma

The dilemma

1. RAASi improve long-term prognosis in a dose-dependent manner
2. They can cause hyperkalemia: which worsens short-term prognosis
3. This leads to RAASi downtitration/withdrawal
4. Which worsens long-term prognosis

Potassium binders

The hypothesis

K-binders

The hypothesis

1. K-binders reduce kalemia
2. Thus they may enable RAASi
3. As a consequence K-binders may improve long term prognosis

The ESC suggestion

To consider novel potassium binders (*patiromer and SZC*) for the management of RAASi-associated hyperkalaemia.

Patiromir and SZC

Both drugs can:

- reduce serum K levels
- and prevent recurrent hyperkalaemia.

Additionally, patiromer showed enabling of RAASi optimization in high-risk patients.

Patiromir

Impact in HFrEF prognosis

The impact of patiromir RAASi-enabling capacity in [HFrEF](#)
[prognosis](#) is being evaluated in the DIAMOND study

Management of RAASi-associated hyperkalaemia

A proposed algorithm

Management of RAASi-associated hyperkalaemia

A proposed algorithm

	Normokalaemia	Chronic hyperkalaemia			
1. Serum K ⁺	Column A 3.5–5 mEq/L	Column B Mild 5.1–5.5 mEq/L		Column C Moderate 5.6–6 mEq/L	Column D Severe >6 mEq/L
2. Patients undergoing RAASi optimization	Not on maximal tolerated RAASi dose	Not on maximal tolerated RAASi dose	Not on maximal tolerated RAASi dose <i>but</i> previous hyperkalaemia when up-titrating RAASi <i>or</i> HF and/or CKD 3b–4 ^a and/or DM	Whether on or not on maximal tolerated RAASi dose	Whether or not on maximal tolerated RAASi dose
3. Actions	Initiate/up-titrate RAASi	Initiate/up-titrate RAASi	Initiate/up-titrate novel potassium binders/patiromer ^b until serum K ⁺ ≤5.0 mEq/L ⁽³⁾	Initiate/up-titrate novel potassium binders/patiromer ^b until serum K ⁺ ≤5.0 mEq/L ⁽³⁾	Discontinue/Reduce RAASi and
	Monitor K ⁺⁽¹⁾	Monitor K ⁺⁽¹⁾	Monitor K ⁺⁽²⁾	Monitor K ⁺⁽²⁾	Initiate/up-titrate novel potassium binders/patiromer ^b until serum K ⁺ ≤5.0 mEq/L ⁽³⁾
	K ⁺ ≤5 ↓ K ⁺ >5 see columns B, C, or D	K ⁺ ≤5.5 ↓ K ⁺ >5.5 see columns C or D	If K ⁺ ≤5.0 up-titrate RAASi and maintain novel potassium binders/patiromer ^{b(3)}	If K ⁺ ≤5.0 up-titrate RAASi and maintain novel potassium binders/patiromer ^{b(3)}	
4. Follow-up	Maintain RAASi on maximal tolerated doses, monitor K ⁺ and renal function, and check for additional causes of hyperkalaemia (K ⁺ diet content, salt substitutes, drugs impairing renal function and K ⁺ excretion)				

Conclusion

What is the relevance of novel potassium-binders?

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1. RAASi improve CVDs long-term prognosis in a dose-dependent manner
2. They can cause hyperkalemia leading to RAASi downtitration/withdrawal
3. The latter worsens long-term prognosis
4. K⁺ binders reduce serum K⁺ levels and prevent recurrent hyperkalaemia.
5. Patiromer showed enabling of RAASi optimization in high-risk patients.
6. An algorithm for the Management of RAASi-associated hyperkalaemia was presented