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## A Multidisciplinary Approach to Managing Potassium Levels in Patients with Heart Failure When Optimizing RAASi Therapy in Complex Cases

### Announcer:

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### Dr. Bayés-Genís:

Hyperkalemia is common in patients with heart failure on RAASi [renin-angiotensin-aldosterone system inhibitor] therapy, especially in those patients where their condition is more advanced and complicated by other factors such as diabetes. Optimized therapeutic management is challenging and requires a multidisciplinary approach to improve outcomes. Today, we will be reviewing treatment options for a patient with heart failure and diabetes, who is at high risk for hyperkalemia.

This is CME on ReachMD, and I am Dr. Antoni Bayés-Genís.

### Dr. Rossignol:

And I am Dr. Patrick Rossignol.

So, Antoni, can you start us off with the patient case. Tell us about someone you've seen recently with HFrEF [heart failure with reduced ejection fraction] and diabetes who has a history of frequent hyperkalemia and was not on GDMT [guideline-directed medical therapy]. What are the challenges?

### Dr. Bayés-Genís:

Yeah. Thank you, Patrick. So let me start with a patient that is 65-year-old man that has HFrEF. It's in New York Heart Association Class II, with CKD 3b, diabetes mellitus, and a history of myocardial infarction. This patient has a key medications including GDMT, but probably not at the appropriate doses: carvedilol 50 mg, enalapril 10 mg, spironolactone 25 mg, and dapagliflozin 10 mg. In spite of that, the patient comes with symptoms of fatigue and on NT-proBNP we see 1,002 pg/mL. And looking to the kidney function, it's an eGFR of 38 mL/min/1.73 m<sup>2</sup> and a potassium of 5.6 mEq/L.

So we have this patient, Patrick, that is complicated. It's heart failure, it's kidney dysfunction, it's diabetes, and despite the medication, potassium is high. So these are the kind of patients where we have a high risk of mortality, both in the end of hyperkalemia as well as in the end of hypokalemia. But this patient is with a potassium of 5.6. So we know that normalizing potassium is associated with reduced risk of mortality in heart failure, and that's what we have to do to our patient.

There are a number of things that we can do. We as cardiologists often do increase furosemide dose. And increasing furosemide dose is very intuitive and is very quick, but we need to remember that high doses of loop diuretics limit the up-titration of RAASi, and in some studies, they were associated with worse outcomes. So this is something that we need to take consideration about, and later on I would like your opinion about this.

The second thing we can do is to reconsider RAASi option. This patient was on enalapril. We know that sacubitril/valsartan may be better in a patient with heart failure and CKD [chronic kidney disease] because it's more renal-protective – sacubitril/valsartan than enalapril – as well as potassium levels are better controlled with sacubitril/valsartan than enalapril. This was demonstrated by the PARADIGM study, and it's also very important to say that with sacubitril/valsartan in the presence of MRA, there is less hyperkalemia. So again, combining heart failure, diabetes, and the kidney, things go even better.

So, Patrick, do you agree in doing this change of switching enalapril to sacubitril/valsartan?

**Dr. Rossignol:**

Well, Toni, these points are all well taken. As a nephrologist, of course, I would avoid to titrate furosemide unless the patient is really congested. Switching from enalapril to sacubitril/valsartan is wise as well, but as a nephrologist, considering the hyperkalemia, which is already present here, I may already consider introducing, initiating a potassium binder. And by the way, we may discuss this later on, as this is now acknowledged by guidelines, most kidney and cardiology/heart failure guidelines.

**Dr. Bayés-Genís:**

Yeah. So you suggest that it is very important that we established a close correlation between the heart failure specialist and the nephrologist in order to implement probably patiromer as soon as possible.

**Dr. Rossignol:**

So, Toni, based on the clinical trial evidence, how should we manage these patients with HFrEF and diabetes?

**Dr. Bayés-Genís:**

Patrick, for some reasons this patient was not on what you suggested, so RAASi were discontinued, and particularly MRA [mineralocorticoid receptor antagonist] was discontinued, and the patient came back more symptomatic with elevated natriuretic peptides and a potassium again of 5.8 with this renal dysfunction of 38. So what we think it's the appropriate thing to do now is to incorporate patiromer because it's the right proposed – that you suggested. The evidence from the DIAMOND is very robust. And by incorporating patiromer, what we know is that we get a 26% less likely to have MRAs reduced or discontinued and 35% less likely to have MRA discontinued. So it looks like by incorporating patiromer, we can do over the long term a good control of potassium.

We did put patiromer to this patient and the patient did go well because patiromer controlled potassium. But I would like to know your opinion and the importance of the interaction between cardiology and nephrology once we have complex patients like these patients with heart failure, with CKD, and with diabetes.

**Dr. Rossignol:**

Sure, Toni. I would mention that a dialogue between cardiologist and nephrologist is of the utmost importance around because patients with heart failure are frequently presenting with CKD, with diabetes, and we really have to pay attention to any worsening kidney function, which by itself may be associated with worse outcomes. That said, worsening kidney function might be multifactorial, it might need to boost the hydration, overhydration, and we have to keep in mind that we have to keep our patients on the highest tolerated dose of GDMT. And then, once again, we have now the possibility owing to the viability of new potassium binders, such as patiromer as you nicely showed us, to get patients on the highest tolerated dose of GDMT with maintaining normal potassium, which we know is by itself associated with better outcomes.

**Dr. Bayés-Genís:**

This is very interesting, Patrick, because sometimes the approach to patients by cardiologists and by nephrologists is different, and our first approach would be just to increase diuretics and probably switch RAAS inhibitors. Now, with your interaction, what you're telling us is that we should go for patiromer just from the very beginning, and that's what we're starting to do. And this patient, in the second visit when patiromer was initiated, potassium could be under good control. MRAs were, again, reinitiated at the high dose, and sacubitril/valsartan was again put up to the maximum tolerated dose. So I think that by incorporating patiromer, the patient did super good.

For those just tuning in, you're listening to CME on ReachMD. I am Dr. Antoni Bayés-Genís, and here with me today is Dr. Patrick Rossignol. We are discussing the importance of maintaining normokalemia and improving outcomes in patients with HFrEF and diabetes.

**Dr. Rossignol:**

Well, I think that this is indeed an outstanding opportunity to get our patients optimized. As soon as potassium is indeed normalized owing to the initiation of patiromer, we may take advantage of this, of getting the patient up-titrated, something which certainly could not do before because the patient was initially presenting with hyperkalemia. But now that the patient is getting normalized, owing to the initiation of patiromer, we have now the possibility to get the patient further up-titrated, and we know from several trials that the higher

the dose is, the better the outcomes.

Okay, so, Toni, why is it important to avoid hyperkalemia when treating patient with HFREF, and what is the impact of maintaining normokalemia in these patients?

**Dr. Bayés-Genís:**

Yeah. In heart failure, it is very important to avoid hyperkalemia because we know that hyperkalemia tends to push the doctors to reduce GDMT, and particularly to reduce RAASi, and this has an impact on the patient and also on biomarkers because we see very often that by reducing the GDMTs, sometimes NT-proBNP may be up or down, and this is just conflicting the evolution of the patient. So in my view, what we have to do is try to keep NT-proBNP as low as possible by maintaining GDMT as high as possible, and in this regard, patiromer is a super good drug to keep GDMT, as we know today, at the maximum tolerated doses.

**Dr. Rossignol:**

Discontinuing RAASi should be really the last resort after we have initiated a new potassium binder, such as you showed us with patiromer, and get the patient normalized. We should have more chances to get the patient up-titrated with a RAASi, and at least RAASi maintained, because we know for sure that RAASi discontinuation is associated with worse outcomes, hyperkalemia. RAASi discontinuation is by itself associated with worse outcomes, so just initiate patiromer and get the GDMT up-titrated.

**Dr. Bayés-Genís:**

Yeah. I think that if we have to discuss additional aspects, Patrick, particularly related to cost, we need to remember that every time that a patient is admitted, that is a burden for the healthcare system. So the cost of an admission is very significant. And the short- and the long-term goals for us is always the same. It's to keep the patient safe and at home with potassium under control, and this we can do with introduction of patiromer.

It is true that if the patient goes with symptomatic hypertension, then probably we need to play with the doses of RAASi to avoid inappropriate dosaging, but in general, if we go by a slow titration, in our experience, that goes well.

**Dr. Rossignol:**

I may add that there are already several published modelizations showing that potassium normalization is associated with cost, with better management for healthcare resources. But even more importantly, avoiding hospitalizations is associated with better quality of life for our patients, and this is, of course, something we are all aiming at.

**Dr. Bayés-Genís:**

Well, this has certainly been a fascinating conversation, but before we wrap up, Dr. Patrick Rossignol, can you share your one take-home message with our audience?

**Dr. Rossignol:**

Sure, Toni. We should aim at achieving the highest tolerated dose of GDMT, and for this purpose, we should take advantage of using patiromer as shown today to get this enabled.

**Dr. Bayés-Genís:**

Thank you, Patrick. My take-home message would be that there should be more interaction between cardiologists and nephrologists, number 1, and number 2, that we should consider potassium binders earlier to be able to keep GDMT at the highest recommended doses.

And that's all the time we have today. So I want to thank our audience for listening and thank you, Dr. Patrick Rossignol for joining me and for sharing all of your valuable insights. It was great speaking with you today.

**Dr. Rossignol:**

You're welcome, Antoni.

**Announcer:**

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