Transcript Details

This is a transcript of a continuing medical education (CME) activity. Additional media formats for the activity and full activity details (including sponsor and supporter, disclosures, and instructions for claiming credit) are available by visiting:
https://reachmd.com/programs/cme/a-new-option-for-cardiorenal-protection-for-patients-with-ckd-in-t2d/13809/

Released: 07/29/2022
Valid until: 07/29/2023
Time needed to complete: 15 minutes

ReachMD

www.reachmd.com
info@reachmd.com
(866) 423-7849

A New Option for Cardiorenal Protection for Patients with CKD in T2D

Announcer:
Welcome to CME on ReachMD. This activity, entitled “A New Option for Cardiorenal Protection for Patients with CKD in T2D” is provided by Medtelligence.

Prior to beginning the activity, please be sure to review the faculty and commercial support disclosure statements as well as the learning objectives.

Dr. Filippatos:
Hello to everyone. Do nonsteroidal mineralocorticoid receptor antagonists, or MRAs, added to maximum tolerated renin-angiotensin system inhibition reduce cardiovascular disease and kidney disease progression in patients with chronic kidney disease [CKD] and type 2 diabetes? And how do we translate this data into patient care? These are the questions posed by authors of the FIDELITY analysis and that we hope to answer here today as well.

This is CME on ReachMD, and I’m Dr. Gerasimos Filippatos from the University of Athens Department of Cardiology, and here today with me are Dr. Wang and Dr. Morales. Dr. Wang, welcome to this discussion.

Dr. Wang:
Thank you, Dr. Filippatos. It’s a great honor to join this panel discussion. My name is Angela Wang, and I’m a nephrologist by background, working in Hong Kong at the Queen Mary Hospital.

Dr. Filippatos:
Welcome, Dr. Morales.

Dr. Morales:
Hi. My name is Javier Morales. I’m a practicing internist in Long Island, New York. Thanks again for having me join you with this panel discussion.

Dr. Filippatos:
We have a lot to discuss today, so let’s begin. To start out our conversation, Dr. Wang, the FIDELITY analysis, published earlier this year, looked at the combined result, or the pooled result if you prefer, of the FIDELIO and FIGARO trials. What stood out to you among the results of this analysis?

Dr. Wang:
Thank you, Dr. Filippatos. I think that this is a very interesting, prespecified combined meta-analysis of both the FIGARO-DKD and the FIDELIO-DKD, and it’s very interesting that the aim is actually to look at the relationship between use of finerenone in relation to the composite cardiovascular and kidney endpoints in a range of patients with different eGFR [estimated glomerular filtration rate] for those subject with having diabetic kidney disease. And they defined the stages of kidney disease using the estimated eGFR categories and also using the urine albumin-to-creatinine ratios [UACR].

And the urine albumin-to-creatinine ratio is a very important measure because it is able to identify subjects who have high

cardiovascular risks despite having a relatively high eGFR. There are 2 key composite endpoints. One is the cardiovascular composite endpoint of this trial, which is the time to cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure. Also, this combined analysis looked at the key composite endpoint, which is the time to kidney failure, sustained more than 57% decrease in eGFR, or renal death. And what they've shown is the finerenone treatment, compared to the placebo treatment, reduces the risk of composite cardiovascular endpoint by 14% and the kidney composite by 23%. So the data show that the finerenone on top of the standard of care actually reduces the risk of clinically meaningful cardiovascular and kidney outcomes in patients with type 2 diabetes over a broad spectrum of chronic kidney disease. It is also important to actually look at the different outcomes that constitute the composite cardiovascular outcomes. In fact, it was essentially the reduction of hospitalization of heart failure, which is about 22%, as it was highly significant with a P of 0.003. So clearly, reduction in the hospitalization for heart failure is one of the key aspects or key benefits with the finerenone.

Dr. Filippatos:
So thank you, Angela. I think that, Javier, what was very important for me when I saw the results is, first of all, that 45% of this more than 13,000 patients, they had a history of cardiovascular disease, and 45% of them, they have preserved eGFR, and the only indication of chronic kidney disease was albuminuria.

We don't measure – very often when we see a patient with the eGFR of 70 and a history of stroke or a PCI [percutaneous coronary intervention], we didn't measure UACR. I think now, with the results that Angela presented, probably we should slightly change our practice. What do you think?

Dr. Morales:
Well, first of all, when we're looking at kidney function, we have glomerular filtration rate; that really defines kidney function. However, the presence of albuminuria really correlates most with kidney damage, and oftentimes that kidney damage will occur before a decline in the GFR. So it's really important to make that distinction. And for years, as primary care providers, we always looked at GFR, and we always thought about using things like ACE [angiotensin-converting enzyme] inhibitors and angiotensin receptor blockers as agents in patients with diabetes to protect their renal function. And short of keeping them on these agents, there really wasn't much more to add on to that, other than the SGLT2 [sodium-glucose co-transporter 2] class, which really has made its mark globally and now, of course, looking at mineralocorticoid receptor antagonists [MRAs]. So I think that now, because of these study designs, I think urine albumin creatinine measurement is now an emerging strategy that's always been really under the radar.

Dr. Filippatos:
Yes, you are absolutely right, and I think that the best way to see what we do in everyday clinical practice is to discuss some patients and discuss some cases. And for the first case, we have a 59-year-old female who was diagnosed with type 2 diabetes 4 years ago. She has a BMI [body mass index] of 32, hypertension and dyslipidemia controlled by medication. And her current HBA1c is 6.9%. And she is being treated with dapagliflozin and SGLT2 inhibitor and the GLP-1 inhibitor semaglutide. As well, irbesartan, an angiotensin receptor blocker. Her eGFR is 50 with a UACR of 400 mg/g.

So let me start with you, Javier – Dr. Morales. What do you think? Should we add in a steroidal or nonsteroidal MRA to this patient's current treatment?

Dr. Morales:
All of these therapies that have demonstrated reduction in proteinuria – and all of a sudden, now we have a urine albumin creatinine ratio of 400, even with a GFR of 50. Obviously, there's a fair amount of inflammation that may be going on but could be driving and potentially worsening this patient's renal function as time goes on. So for years, we've always looked at progressive kidney failure as really related to 3 different things. And that is hemodynamics and blood pressure fluctuation with glomerular filtration pressure being affected. There's the metabolic factor with glycemic variability. Sometimes that can actually produce a little bit of inflammatory changes. And then, of course, inflammation itself.

So taking these into consideration with the urine albumin creatinine ratio of 400 mg/g, the cat's out of the bag and it's running down the street, so it's just about curtailing this and preventing it from getting worse. So obviously, this would be a person that would benefit from going on some sort of mineralocorticoid receptor antagonism. So for the most part, we have nonsteroidal therapies and we have steroidal-based therapies. So why would I want to use a nonsteroidal instead of a steroidal-based? Well, it's quite simple, and it's all based on half-life. So if we're dealing with a steroidal-based agent, they have a much, much longer half-life. They have less specificity for the mineralocorticoid receptor. They have greater anti-androgenic effects. And, in addition, have a greater risk of hyperkalemia. And when we look at that pivotal trial – the FIDELIO study – and we looked at potassium in particular, I mean, potassium went up maybe by about 0.2 mmol or so, so there was really a negligible effect on potassium.

So for me, it winds up being a safer agent with a lower half-life with demonstrable renal benefit, and to boot, the secondary endpoint.

And I know, Dr. Filippatos, you being a cardiologist can certainly appreciate the reduction in major adverse cardiovascular events that was noted in this population of patients.

Dr. Filippatos:
Yes, thank you. Angela any comments for this case?

Dr. Wang:
I think this is actually the typical patient population that were being recruited in the FIDELIO-DKD trial. So therefore, the patient actually needs additional treatment with the nonsteroidal MRAs, which is actually very well evidenced in the FIDELIO-DKD and also in the FIDELITY meta-analysis.

Dr. Filippatos:
You are absolutely right.

For those just tuning in, you are listening to CME on ReachMD. I'm Dr. Gerasimos Filippatos, and here with me today are Dr. Angela Wang and Dr. Javier Morales, and we're reviewing case studies to help put into practice the results of the FIDELITY analysis on the use of nonsteroidal MRAs in patients with CKD and with type 2 diabetes.

Let's turn our attention to our second patient, a patient with heart failure. We have a 60-year-old male with diabetes for 8 years who presents with an ejection fraction that is approximately 45, so he's in heart failure with mildly reduced injection fraction. UACR of 150 mg/g, eGFR of 30, potassium of 4.8, sodium of 138, and he's on sacubitril/valsartan, empagliflozin, carvedilol, and furosemide.

So we are at a decision point here. Do we start an MRA? And if so, do we start the steroids – a steroid-based MRA or a nonsteroidal MRA? Dr. Wang, what do you think?

Dr. Wang:
One thing it reflects from the nephrologist's point is that the patient has an eGFR of 30, which means that the patient already has advanced CKD. And then the patient still has some degree of albuminuria, although not as high as the previous case. And he also has active cardiovascular disease with a midrange ejection fraction. So I'm aware that according to the European Society of Cardiology Heart Failure Guidelines, that an MRA is given the IIb grading for use within heart failure midrange ejection fraction. And for this particular case, I would actually use a nonsteroidal MRA rather than a steroid-based MRA. The nonsteroidal MRA is much better evidenced, both from the FIDELIO, FIGARO, and also the combined analysis, FIDELITY trial meta-analysis.

Dr. Filippatos:
So, Dr. Morales – Javier?

Dr. Morales:
What I like about this particular case is the question of SGLT2 versus nonsteroidal mineralocorticoid receptor antagonist, and which one should you use first and why? And, you know, looking at the data, if you're looking at the FIDELITY trial, it winds up that about 7% of patients that were in this combined data were on SGLT2s or GLP-1 receptor agonists, and it basically showed benefit. And in terms of the SGLT2s, there was a subset analysis that was actually done using a model with the CREDENCE study. And what they did was they took these patients that were on the CREDENCE trial and they selected out their cardiovascular risk factors and they plotted them head-to-head against finerenone. The SGLT2 had a 30% reduction. It was 28% for the finerenone group. So it's kind of interesting because, I mean, I don't think anybody's really going to argue about 2%, but the take-home point is that these agents are really beneficial in terms of the potential of reduction in major adverse cardiovascular events and, even more importantly, heart failure hospitalizations, because we do know that patients with decreased GFR tend to have a 5.6 times increase in heart failure hospitalizations.

Dr. Filippatos:
So I think that was a fascinating conversation, but before we wrap up, Angela, Javier, do you have any take-home message that you would like to share with our audience?

Dr. Wang:
I think one of the really key messages is that we really should perform urine albumin screening among the patients with type 2 diabetes in order to identify patients that are at risk of adverse cardiovascular and kidney outcomes earlier for earlier intervention. I think the nonsteroidal MRAs should be initiated in early stages of kidney disease, as shown by the entire spectrum of CKD with the type 2 diabetes in the trials.

Dr. Morales:
For the most part, we're underutilizing the urine albumin creatinine ratio, so we should be checking it a little bit more. Now we have agents that work. Between the nonsteroidal and the steroidal-based mineralocorticoid receptor antagonists, the nonsteroidal

mineralocorticoid receptor antagonist finerenone has demonstrated significant benefit in terms of curtailing the natural progression of chronic kidney disease.

Dr. Filippatos:
I think it is clear that we have a new therapy in this area. We have an answer to why we should measure UACR. We have an answer to "so what?" for those with preserved eGFR.

I want to thank Dr. Wang and Dr. Morales. I want to thank you all for being here and looking forward to our next discussion.

Announcer:
You have been listening to CME on ReachMD. This activity is provided by Medtelligence.

To receive your free CME credit, or to download this activity, go to ReachMD.com/Medtelligence. Thank you for listening.