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/new-insights-into-the-management-of-ckd-in-t2d-the-role-of-mra-therapies/13097/

Released: 01/07/2022
Valid until: 01/07/2023
Time needed to complete: 15 minutes

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

New Insights into the Management of CKD in T2D: The Role of MRA Therapies

Announcer:
Welcome to CME on ReachMD. This activity, entitled “New Insights into the Management of CKD in T2D: The Role of MRA Therapies” 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. Rossing:
Achieving optimal outcomes from treating patients with chronic kidney disease and type 2 diabetes remains a challenge due to the multidisciplinary response needed to prevent progressive renal dysfunction. Early diagnosis and regular screening of chronic kidney disease and type 2 diabetes sets the stage for clinicians to optimize drug therapy to prevent progression to end-stage kidney disease or ESKD. This also allows for the aggressive management of comorbid hypertension and other cardiovascular risk factors. Although advances in diabetes care have substantially reduced the incidence of related complications, new strategies and therapies for managing progression to end-stage kidney disease remain an unmet need.

This is CME on ReachMD, and I’m Dr. Rossing.

Dr. Filippatos:
I’m Dr. Filippatos.

Dr. Weir:
And I’m Dr. Matthew Weir.

Dr. Rossing:
Today we are going to look at the unmet needs in the management of chronic kidney disease and type 2 diabetes and delve into the role of MRAs, or mineralocorticoid receptor antagonists, in the treatment spectrum and review recent findings from clinical trials.

As I mentioned, achieving optimal outcomes in the treatment of patients with chronic kidney disease and type 2 diabetes remains a challenge, and we need to embrace multidisciplinary component in managing progression to chronic kidney disease.

So first, to you, Dr. Filippatos. Can you take us through current cardiorenal outcomes and the challenge that you face when treating patients with chronic kidney disease and type 2 diabetes? How does multidisciplinary approach factor in?

Dr. Filippatos:
Thank you very much Dr. Rossing. Thank you, Peter. Let me start from the last part of your question. The majority of patients with chronic kidney disease and type 2 diabetes are being seen not only by a nephrologist, but also by a diabetologist, and as we’ve learned from a recent trial, as we confirmed the recent trial, at least 40%-50% of these patients have a history of cardiovascular disease and are being seen by cardiologists. And of course, most of them have a GP, have a primary care physician. So it is necessary to have a multidisciplinary approach.

I think the second problem, as you pointed out, is that these patients with chronic kidney disease and type 2 diabetes are at high risk for cardiovascular morbidity and mortality and kidney disease progression despite recent advances in therapy. Most of these patients are on ACE inhibitors and beta-blockers, and many of these patients, they receive SGLT2 inhibitors. However, chronic kidney disease progression with diabetes is not only driven by the metabolic factors and hemodynamic factors, but also by inflammation and fibrosis. And these cause overactivation of mineralocorticoid receptors [MR]. And the previous therapies don't target the MR. So this overactivation has been suggested to contribute to cardiovascular disease progression and to kidney progression in these patients with chronic kidney disease and diabetes.

Let me just point it out, something that we know, we have worked together with other experts in multidisciplinary approach into clinical trials, the FIDELIO and FIGARO. These trials in patients with chronic kidney disease and diabetes evaluated finerenone and novel nonsteroidal MRA, which is thought to contribute to inflammation and fibrosis. And the FIDELIO randomized 5,000 patients with late-stage chronic kidney disease and included a primary kidney composite, that on the top of the ACE inhibitors or ARBs led to an 18% relative reduction in the primary composite kidney endpoint versus placebo. And also, FIGARO, where in over 7,000 patients with early-stage chronic kidney disease, finerenone reduced the risk of the cardiovascular composite primary endpoint by 13% compared with placebo.

So I think we have challenges. We have opportunities, and I'm looking forward to discuss this further.

Dr. Rossing:
Yeah, thank you very much. The use of nonsteroidal MRAs provide an opportunity to prevent deterioration in renal function and improve outcomes in patients with chronic kidney disease and type 2 diabetes. Dr. Weir, I'd like to follow up with your thoughts on this and ask what did we learn from recent clinical trials, and how can we apply this to patient care?

Dr. Weir:
Well, as Dr. Filippatos said, cardiorenal risk reduction is the name of the game in people with type 2 diabetes, chronic kidney disease. More likely than not, they will die of a cardiovascular event before they reach end-stage renal disease, so everything that is possible needs to be done, including full-dose statin. Obviously, the bedrock of our therapies, highest tolerated dose of ACE or ARB. We now know SGLT2 inhibitors, as well as also finerenone, provide an incremental risk reduction opportunity in this regard for both cardiac and renal events. So I think, really, we now have 3 opportunities to reduce the rate of cardiorenal disease progression. Optimally, we should be able to use them all in our patients to make our best effort to slow the disease process.

Dr. Rossing:
And could you perhaps comment upon how do we identify those patients that would benefit from this therapy?

Dr. Weir:
Well, I think the major issues we need to focus on are obviously the trajectory change of their kidney function, as well as changes in urinary albumin or urinary protein excretion. And again, this need not be a 24-hour collection. A spot urine protein-to-creatinine ratio or a spot urinary albumin-creatinine ratio can be extremely valuable and can be monitored just like the blood pressure and the kidney function to assess and evaluate the impact of our therapeutic initiatives. And so goes the albuminuria, so goes the patient. And this has been an important observation in many of the clinical studies.

Dr. Rossing:
And I think that's a good – I mean, important learning, that we can identify the people if we screen for albuminuria and screen for GFR, which was an important part of the inclusion criteria for these trials.

Dr. Filippatos:
If you allow me, some – what you said and what Dr. Weir said is extremely important, and this also refers to your first question about the multidisciplinary approach. What is a routine clinical practice for you as a nephrologist and as diabetologist is not routine clinical practice for the majority of cardiologists. What we've seen in this FIGARO and FIDELIO trials, and what I've learned, and I think something that is not very well known to most cardiologists is that we have a high percentage of patients included in this trial, that is more than 40%, that they have EGFR above 60. 45% of these patients have a history of cardiovascular disease so are being seen by a cardiologist, and the only evidence of the chronic kidney disease, and these are patients of high risk, is albuminuria. And this is not routinely clinically tested by cardiologists in most places in the world. I think this is a very important message that we've learned from this trial, at least I've learned as a cardiologist.

Dr. Rossing:
I think that's a really important learning, that we need to look out for albuminuria, and as you say, although we have been talking about that in relation to blocking the renin-angiotensin system in previous times, that has not been adopted widely, and it really needs to be

implemented, as you said, also by cardiologists. So I think that was an important learning.

And maybe we could move to some of the recent highlights that were presented at the American Heart Association's 2021 scientific sessions. And the big question for me is, what have we learned from the FIGARO and FIDELIO-DKD? So, Gerasimos, what can you tell us about the recently presented data? And what would be the goal for these studies going forward?

And for those just tuning in, you're listening to CME on ReachMD. I'm Dr. Rossing, and here with me today are Drs. Gerasimos Filippatos and Matthew Weir. We are discussing new insights into the management of chronic kidney disease and Type 2 diabetes, and how MRA therapies fit into our treatment armamentarium.

Dr. Filippatos:
At AHA, Peter, we focused on the effect of finerenone on heart failure outcomes in FIDELIO-DKD, and also outcomes by history of heart failure at baseline. As you know, patients with systolic – with heart failure with reduced ejection fraction heretofore have been excluded from the trial, but 7.8% of patients had a history of heart failure at baseline. These persons were patients with ejection fraction above 40%, and the aim of this analysis that has been presented and published simultaneously in *Circulation* was to evaluate new-onset heart failure and heart failure outcomes for these patients with and without a history of heart failure at baseline. And what we found is that the incidence of new-onset heart failure in patients without a history of heart failure was significantly lower with finerenone than with placebo, and this has been reduced by finerenone by 32%, and there was no interaction between those with and without history of heart failure. And something that I think is also important, and this is something that has been presented previously, is that both in FIGARO but also in the FIDELITY, that was the pooled analysis of FIGARO and FIDELIO, the 2 trials, where we've seen similar effect on heart failure outcomes, is that the effect was at least similar in those who were on SGLT2 inhibitors. I think this is an information, clinically relevant, that could be applied immediately in everyday clinical practice.

Dr. Rossing:
Thank you very much. And, Dr. Weir, would you comment on the recent data and where you see finerenone in the treatment landscape going forward?

Dr. Weir:
Well, as Dr. Filippatos mentioned, 8% of the population in the FIGARO study were on SGLT2 inhibitors, and about 5% in the FIDELIO study were on SGLT2 inhibitors, and they all demonstrated incremental benefits with the finerenone treatment. And so that is why I would clearly state that these 3 therapies – the bedrock of ACE or ARB in highest tolerated dose, plus finerenone, plus SGLT2 inhibitor – are a remarkable step in improvement over the past 20 years when we've only had ACE or ARB before.

And just a final thought on my part to leave you with is people with diabetic kidney disease often lose GFR at a rate of 5 mL per minute per year. Full-dose ACE or ARB drops that to 4 mL per minute per year, which is still very rapid and 4 times faster than the normal attrition of kidney function. So by using SGLT2 inhibitors and finerenone, we can cut that even further and much more substantially, and as Dr. Filippatos mentioned, also have major inroads in reducing the likelihood of incident heart failure and adverse outcomes.

Dr. Rossing:
Well, thanks, and that's really an important and fascinating conversation. Before we wrap up, maybe I could ask Dr. Filippatos and you, Dr. Weir, on just one brief take-home message. What would that be to the audience?

Dr. Filippatos:
Chronic kidney disease and type 2 diabetes – these patients are at high risk. Even when we see EGFR above 60, these patients with just albuminuria, they are at high risk of cardiovascular event. Approximately 50% of these patients are being seen just by a cardiologist and a diabetologist. It's a message for the cardiologists: check also for albuminuria where we see these patients because now you can answer the question of, "So, what?" You have therapies for these patients.

Dr. Rossing:
Thank you. And Dr. Weir, a final comment?

Dr. Weir:
I would just say, earlier identification and education is critical, and we as healthcare providers need to do the best we can to provide these newer therapies for our patients. Get familiar with them, get comfortable, and get them into our patients.

Dr. Rossing:
I think that's really good comments, and I don't think I have much more to add, and now our time has also run out. So thank you very much to our audience for listening, and thanks both to Dr. Filippatos and Dr. Weir for joining me and for sharing all your valuable insights and expertise. It was really great speaking to you today, and good-bye.

Dr. Filippatos:
Thank you for the invitation, Peter.

Dr. Weir:
Likewise, thank you.

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.