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/no-patient-left-behind-advancing-ckd-associated-pruritus-care/26637/

Released: 01/31/2025
Valid until: 01/31/2026
Time needed to complete: 15 Minutes

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

No Patient Left Behind! Advancing CKD-Associated Pruritus Care

Announcer:
Welcome to CME on ReachMD. This activity, titled “No Patient Left Behind! Advancing CKD-Associated Pruritus Care” 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. McCafferty:
Patients with CKD-aP often face delays in diagnosis and treatment, coupled by potential side effects of some prescribed medicines. Join us as we analyze the burden of CKD-aP and evaluate the long-term outcomes and benefits of potential treatments.

This is CME on ReachMD, and I'm Dr. Kieran McCafferty.

Dr. Gallieni:
And I'm Dr. Maurizio Gallieni.

Dr. McCafferty:
So, Maurizio, studies show that patients with CKD-aP are often hesitant to discuss their pruritus symptoms, and there are potentially a variety of reasons behind that. What can you tell us about the prevalence and burden of CKD-aP?

Dr. Gallieni:
It is actually a very high prevalence, and we have new data showing that, in particular the CENSUS-EU data, which is a multinational study that was performed in Europe and recently presented at the American Society of Nephrology. This is a large cohort of patient that were tested with questionnaires including both a scale that measures the intensity of CDK-associated pruritus and also the effects that pruritus has on the quality of life.

And about 46% of patients show no itching. That means that more than half of them do have pruritus. And as you know, the intensity of pruritus can be mild, moderate, or severe. And if you combine the moderate and severe status, it's about 30% to 33%. So one-third of patients that will have, indeed, a quite disturbing pruritus affecting them.

Dr. McCafferty:
When I first got into CKD-aP, I thought that very few of my patients itched, and it's only when I went out and asked them directly, were they itchy, that I was surprised by how many of our patients suffer in silence, as it were, that they had CKD-aP for many years but haven't really mentioned it.

Dr. Gallieni:
And there is an additional very interesting finding of this study, is that if you consider just the patient with severe pruritus where you expect that they get some form of treatment, this is not the case. About 41% of patients with severe pruritus in the CENSUS-EU study is not receiving any treatment. And this means that there is a need for new treatments and effective treatments for this very bothering symptom.

Dr. McCafferty:
I couldn't agree more.

Dr. Gallieni:
And so we can now shift to treatments. What can you tell us about the selective kappa-opioid receptor agonist difelikefalin, which is indeed a new approved treatment?

Dr. McCafferty:
So as we've heard, CKD-aP is common and we've really struggled to have effective treatments for this for many, many years. And really, difelikefalin has really led the way in a novel therapy for CKD-aP. This was shown in 2 landmark studies, the KALM-1 and KALM-2 trials based in the US and globally. And what that showed was that difelikefalin was given as an intravenous bolus at the end of dialysis, 0.5 µg/kg, to patients versus placebo, and looked at the impact of the Worst Intensity Numerical Rating scale, which is a very simple question to ask your patients: In the last 24 hours, how itchy have you been? Naught being no itch, 10 being the worst itch imaginable. And we know that changes in the WI-NRS of more than 3 have clinically significant outcomes for our patients.

And so the KALM-1 and KALM-2 studies were both positive and both demonstrated that difelikefalin compared to placebo led to a statistically significant improvement in patient's itch, both in terms of the WI-NRS, but also in terms of other domains of patient questionnaires, in terms of lifestyle and physical functioning. And so this really represented a huge advance in our ability to manage CKD-aP in our hemodialysis cohort.

And other things, I guess, so we've now used difelikefalin; we use it routinely in our patients in the UK, where I'm based. And we're learning a little bit more about its use, both in terms of the initial study was in terms of 12 weeks, but we know that now the beneficial effects of difelikefalin are seen long term. We also know that if patients happen to stop difelikefalin for whatever reason, the itch returns, which is reassuring from a dose-response point of view. But also when they go back on difelikefalin, the beneficial effects of difelikefalin are seen again as patients' itch improves.

Other aspects of the use of difelikefalin, certainly patients, there was a question about, because of its action, was there any impact of concomitant opioid medication use in hemodialysis patients? So in other words, those patients who happen to be on opioid-based painkillers for other reasons, could they benefit from difelikefalin? And again, this was shown at a recent poster presented this year by Jim Burton, which revealed that whether or not patients were on opioid-based medications, there was no difference in the beneficial effects of difelikefalin. So we're quite keen to get difelikefalin used in patients who have moderate to severe CKD-aP and hemodialysis patients.

In the trials, when we first tried to use it, one of the inclusion criteria was a persistent and moderate to severe pruritus, as evidenced by the WI-NRS over a weeklong period. And to try and make it easy as possible for patients to use it, we looked to see whether or not the previous one off yesterday's WI-NRS was as effective at diagnosing moderate to severe CKD-aP compared to asking patients every day for a week. And we found it was a very good correlation between yesterday's WI-NRS and the weeklong WI-NRS, which we used as one of the inclusion criteria for the KALM study.

And what my take-home from this is that it makes it easier to start and to ask our patients to establish whether or not they've got moderate to severe CKD-aP by simply asking, in the last day, can you tell me how itchy you were? Naught being no itch at all, and 10 being the worst itch imaginable. And that way we can quantify their baseline itch and then also look in a real-world basis about the improvements in itch seen with difelikefalin.

For those of you just tuning in, you're listening to CME on ReachMD. I'm Keiran McCafferty, and here with me today is Mauricio Gallieni, and we're discussing CKD-associated pruritus, the prevalence, the burden, and the new options for treating this disease in our patients.

Dr. Gallieni:
One interesting point regarding this drug is that it does not cross the blood-brain barrier, right? And this can explain the fact that, although it is an opioid receptor agonist, in reality, the side effects are very low.

Can you comment on the comparison between difelikefalin and placebo studies regarding side effects?

Dr. McCafferty:
Yes. So the side effect profile, as you said, the side effect profile was it was well tolerated. Some of the side effects were based around some patient-reported dizziness or somnolence, but there was certainly no significant side effects.

Maurizio, when it comes to the other treatments prescribed for CKD-aP, is there anything that providers need to know?

Dr. Gallieni:
As you know, there are other treatments for CKD-aP. One of them is gabapentin, which has been used in the past, although it is an off-label medication. It can be effective in a number of patients, and it is used also for neuropathic pain. Now, we have data on side effects of this drug. In particular, a poster that was recently presented by a Canadian group, by Dr. Claudio Rigatto and collaborators. They studied a large number of patients, both with neuropathic pain and with CKD-aP, and they found a prevalence of side effects, which is about 38 events for 100 patient-years for altered mental state, 20 for falls, 19 for dizziness, 15 for somnolence, and 9 for fractures, which of course are a consequence of the increased incidence of dizziness. Therefore, this is a drug that should be used with caution by physicians because of the possibility of these side effects.

In addition, the side effect is dose-dependent. The higher the dose of gabapentin, the higher the incidence of side effects. The mean dose is about 400 mg/day for patients with CKD-aP, and therefore, what the study points out is that, at a lower dose, probably also, you have lower side effects. But if you need to increase the dose to control intractable CKD-associated pruritus, then you have to expect a significant number of neurologic side effects.

Dr. McCafferty:
Thank you. I completely agree. With all these things, I would also say that with difelikefalin, that's got the best evidence for reducing CKD-aP, both in two different landmark trials with data out to one year. So as well as the side effect burden of gabapentin, we've also got the lack of proven efficacy in large-scale randomized controlled trials.

Fantastic. So before we close, Maurizio, what would be your final take-home message for our audience?

Dr. Gallieni:
Well, my main take-home message, based on the CENSUS-EU study, is the relevant number of patients that have CKD-associated pruritus. It's about one-third of them with moderate to severe pruritus. And this is quite a huge number of patients, if you consider how many dialysis patients we are treating, and therefore, this was not expected by many doctors, by many nephrologists. And the second point for that study, which I would like to point out as a take-home message is the huge number of patients, 40%, with severe pruritus that did not get any treatment despite a very disabling condition.

Dr. McCafferty:
I would say that CKD is more common than the nephrologists think, and it was more common than I thought before I started doing trials in CKD-aP. I was surprised how many of my patients had CKD-aP. And I guess the other thing I want people to take home is that the burden of CKD-aP is not just itching but the downstream effects of that that have on people's quality of life, on people's sleeping patterns and social functioning, lethargy, tiredness, and their mood, which are all huge problems for patients on dialysis. So I think CKD is underreported and underappreciated by a nephrologists. So that would be my one plea to my nephrology colleagues, is to take CKD-aP more seriously in the future.

So thank you very much. I'd like to thank our audience for listening and thank you, Maurizio, for joining me and sharing all of your really valuable insights and expertise. It was great speaking with you today.

Dr. Gallieni:
It was my pleasure to be with you and having the possibility to discuss this important clinical condition.

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.