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

I Just Need to Sleep! Improving Itch in Patients With CKD-aP

Announcer:
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Dr. McCafferty:
Patients on dialysis often suffer from CKD [chronic kidney disease]-associated pruritus, or CKD-aP, as it's called. This is an intense itch that affects their sleep and overall quality of life. This condition is often underestimated and underdiagnosed. Today, we're focusing on improving outcomes in our patients on hemodialysis who have moderate to severe CKD-aP. This isn't just about treating itch. It's about reclaiming sleep and ultimately allowing our patients to live their life to the fullest, one itch-free moment at a time.

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

Dr. Latus:
And I am Dr. Latus.

Dr. McCafferty:
The diagnosis of CKD-aP is often overlooked in clinical practice. Dr. Latus, how does this oversight impact the quality of life of our patients with CKD-aP, especially those on hemodialysis?

Dr. Latus:
CKD-associated pruritus is completely underreported and under recognized in our CKD patients. Of course, there is an increased risk of infection, hospitalization, and mortality in very severe cases. They had depression; they had anxiety; they had sleep disturbance and reduced health-related qualities. And as we know, almost all of our patients, they have to undergo hemodialysis 3 times a week, so the quality of life is already significantly impaired. So if this is compounded by pruritus, this means, for example, that the patients are not able to go to work and may even become socially isolated. So I believe insomnia is a particular big problem for our patients, and for some patients, the daily sleepiness means that they cannot go to work and many activities are no longer possible. In the past, I have had patients who wanted to stop dialysis because they had no longer any quality of life due to itching.

Dr. McCafferty:
I didn't think that many of my patients had CKD-aP, and yet when I asked them, I was shocked at how many were saying, yeah, yeah, oh, yeah, I've had itching for ages. And I think patients don't necessarily realize that the itching has got to do with their kidney disease. It's important to ask your patients, do they itch?

So, Jörg, what do we need to do to change clinical practice to address this oversight?

Dr. Latus:
We have to start implementing the screening for CKD-aP in our everyday clinical practice.

So there are various tools that we can use easily to ask about itching. I believe the simplest, certainly, the WI-NRS [Worst Itch Numerical Rating Scale], ranging from 0 to 10, but it is always furthermore important to ask about the effects on quality of life.

Dr. McCafferty:
Fantastic. Yeah, I totally agree. As a busy clinical doctor having to get round your dialysis patients so quickly, I think the 5-D itch and the Skindex are great, and they tell us a lot about how the itch affects the patients, but just from the end of the bed, I think the WI-NRS, you know, it almost takes as long to say as to do, asking your patients, how itchy were you on a scale of 0 to 10, 0 being no itch, 10 being the worst itch imaginable. I think that, to me, the WI-NRS is the best one because it gets the heart of the idea. Certainly, from a UK point of view, it's how we, you know, decide whether or not people can, according to NICE [National Institute for Health and Care Excellence], get on the new therapies.

Dr. Latus
Until recently, there were no approved therapies for CKD-aP, that there were off-label treatments for pruritus, such as oral antihistamines followed by gabapentin or pregabalin, which are prescribed for pruritus because we had no other medication. But they have limited clinical evidence to support their long-term use in treating CKD-aP. Now we have new drugs. And coming back to the problems with the sleep and sleep disturbances, often, I believe, a major problem in our patients with CKD-aP. And this year there was a post hoc analysis published that showed that pruritus reduction with difelikefalin [DFK] was associated with improved sleep quality.

This was a post hoc analysis of an open-label, multicenter, single-arm, intervention trial which assessed for pruritus severity and health-related quality of life at baseline and 12 weeks of DFK treatment, and we used a lot of the scales, the WI-NRS, but as well as the Sleep Quality Numeric Rating Scale, the 5-D itch scale, the Skindex-10 scale. About 60% of the patients had at least 3-4 point improvement from baseline to week 12, with respect to sleep quality, NRS [numerical rating scale] scores, and I think that's very important for our patients, and 20% of the patients achieved complete resolution in sleep quality at week 12. There was significant reduction in the mean overall 5-D itch scale from baseline to week 12, and we included all of the 5 domains – disability, distribution, duration, degree and direction – indicating that we can use difelikefalin, and we had significant improvement in pruritus when compared with baseline in regard to several aspects of quality of life.

Kieran, I know that you have a case for us to demonstrate how we can improve the itch-related quality of life and sleep for our patients on hemodialysis with CKD-aP.

Dr. McCafferty:
He's a pretty standard hemodialysis patient. A 68-year-old man with end-stage kidney disease due to type 2 diabetes, as more than half of our patients are. He's been dialyzing for 4 hours, 3 times a week for the last 4 or 5 years. I asked him if he was itchy, given that I'm interested in itch, and he told me he'd been itchy for several years. He's tried antihistamines; he's tried moisturizing creams; he had tried a course of gabapentin. When I asked him if any of these worked, none really worked. He was fed up. He told me that nothing seemed to help him. He particularly noticed itch was particularly bad at night, when he was hot under the bedclothes, making it difficult for him to get to sleep. He'd often wake up at night with itching, and this led to him being tired all the time and fatigued on dialysis, and, you know, that's a really common symptom for our patients on dialysis. I asked him to do a WI-NRS, and he said he was a 9.

So, you know, it was obviously severe itch. And so then I discussed with him trying difelikefalin on dialysis. I think this is a fairly indicative case of people having itch for a long time, trying different treatments, none of which – I have to say, the evidence for these treatments are not as good as for difelikefalin. I mean, you know, proven in multiple randomized controlled trials. I think, often, patients go through a series of therapies, and this is perhaps in the era before difelikefalin. I think, certainly, giving moisturizing cream is a good first step. We know that dry skin, seen commonly in our dialysis patients, can make skin more itchy, and obviously moisturizing cream is safe and very inexpensive. I think, obviously, gabapentinoids are used off-license for itch, and some studies find that they help. They've got significant side effects for patients due to their central nervous system effects in terms of drowsiness, muzzy headedness.

KALM-1 and KALM-2 studies looking at the effectiveness of difelikefalin in adult patients on dialysis with moderate to severe pruritus. So these patients had more than 4 or more than 5 on the WI-NRS scale. They were randomized to difelikefalin 0.5 µg/kg, given at the end of dialysis. And so the good thing about difelikefalin is it hangs around. So we give it at the end of dialysis, it hangs on to the next dialysis session, and then they give it at the end of dialysis again. The primary endpoint was week 12, so a change in the WI-NRS at week 12 from baseline.

There was also an open-label part of this so that after week 12, patients felt the benefits of difelikefalin out to 1 year, so the results show that the itch remains reduced out to a year. There is a placebo effect as with many trials involving itch. But when they were moved from placebo, which they didn't know they were on, to open-label difelikefalin, they saw an additional significant improvement on their itch. So I think we're in a time now that we've had very, very little in the way of treatment for CKD-associated pruritus, and now in the era of

difelikefalin, I think we've got a real opportunity to, as we said already, help our patients improve their symptoms of itch across multiple domains of quality of life.

It's a peripherally restricted kappa-opioid receptor agonist, so the importance about it being peripherally restricted is it doesn't cross the blood-brain barrier that other, perhaps, opioid agonists may do, so that's reassuring in terms of abuse or central side effects of difelikefalin. In the UK, our National Institute of Clinical Excellence has produced a brief guideline on who should be offered difelikefalin.

So it's those patients established on hemodialysis who have moderate to severe itch based on the WI-NRS questionnaire. These patients should be prescribed difelikefalin in line with the KALM-1 and KALM-2 studies.

From my, kind of, busy nephrologist, the less work I can do with my patients, the better. So I do a WI-NRS at baseline and then a WI-NRS at week 12, and for those patients who have a 3 points or more fall in their WI-NRS scale, I continue on with difelikefalin if the patients remain well and are happy to continue.

Dr. Latus:
It's the same in Germany. We have a guideline from our dermatology colleagues, and they recommend difelikefalin as the first choice of treatment in patients with CKD-aP, and that's how I do it, how we do it in Germany. I think some colleagues, they wait too long to start the therapy. We know from studies that moderate or, let's say, less severe itching can also be treated very well. And I have to say it again: We have to discuss the patient's quality of life together with the patient. And we recently published real-world data from patients on hemodialysis with moderate pruritus from Europe. The vast majority of these patients we included in the study are always on therapy with DFK, and the patients who responded are free of itching.

Dr. McCafferty:
In the trials, there were very few treatment-emergent adverse events that led to discontinuation, so I think in the overall cohort, around 9% of patients in the difelikefalin group versus 4% of patients in the placebo group stopped the therapy due to a presumed or a guessed-at treatment-emergent adverse event. I think, looking at the overall side effect profile of difelikefalin, it's a lot of what kind of common side effects we see in patients on dialysis. So things like diarrhea, again, this was commonly seen in both placebo and difelikefalin group. Some dizziness, some nausea some gait disturbances, although, again, this was seen commonly in the placebo group. There wasn't something that jumped out at me, certainly from in our patients in the trial, that we need to be looking out for.

Dr. Latus:
It's noteworthy that the dizziness, diarrhea, and the nausea occurred mostly during the first month of therapy. The duration was, in the poster that we showed at the Kidney Week in Philadelphia, was less than 3 days, suggesting they typically resolved while the difelikefalin treatment was ongoing. So I think that it's important for the practical aspects while treating patients with difelikefalin.

Dr. McCafferty:
That's a great point, yes. So just tell the patients, just, you know, persevere with it for a couple of weeks, and it will get better.

As part of the wrap-up, what's your one take-home message for our audience?

Dr. Latus:
For many years, there were no good treatment options, so it didn't used to be so bad, if you didn't ask about pruritus. But now we have a new treatment with DFK, and that works and has a good safety profile, as you showed us, and times have gone much better for patients with pruritus. That's why we have to ask for pruritus.

Dr. McCafferty:
You've kind of stolen my thunder, because I completely agree with all of your take-home messages. We need to ask our patients do they itch, because we've got this opportunity now to give them a treatment which has been shown in multiple landmark clinical trials to improve their itch but also, more importantly, their quality of life.

I think that's all the time we have today. I want to thank our audience for listening. Thank you, Dr. Jörg for joining me and for sharing all of your valuable insights.

Dr. Latus:
Thank you. It was a pleasure for me.

Announcer:
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