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### ReachMD

[www.reachmd.com](http://www.reachmd.com)

[info@reachmd.com](mailto:info@reachmd.com)

(866) 423-7849

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### Difelikefalin: Managing CKD-aP for Improved Quality of Life

#### Announcer:

You're listening to ReachMD. This activity, titled "Difelikefalin: Managing CKD-aP for Improved Quality of Life" is provided by Medtelligence.

#### Dr. Latus:

This is ReachMD, and I'm Dr. Jörg Latus. Chronic kidney disease-associated pruritus is a chronic disease. It's a common and distressing symptom experienced by up to 60% to 70% of patients receiving hemodialysis. Although we know this problem in our patients, the high prevalence of CKD-aP is often underdiagnosed and undertreated, yet it has a profound impact on a patients' life. The pathophysiology is complex and involves dysregulation of opioid receptor pathways, inflammation, and neural sensitization.

It's very important. You have to screen your patients for CKD-aP because there's no typical pruritus patient. And when you have a diagnosis of CKD-aP, treat in the early stages of the disease and do not wait until the patient develops severe symptoms of CKD-aP.

When we go back several years ago, there was no treatment option available for our patients with severe pruritus. The patient had depression, they were unable to live their lives, so there was a high unmet medical need to have a new drug available to treat our patients with CKD-aP. Nowadays, I am very happy that we have a new treatment option. And when we go to the data and to the real-world evidence, we see there's a rapid onset of treatment response in a high proportion of patients, often within 1 to 2 weeks.

When we look into the pathophysiology of CKD-aP, it makes no sense to treat your patient with antihistamines. You need to target directed therapy to treat patients with CKD-aP, and therefore, difelikefalin is the best treatment option you have for your patients.

It's a peripherally restricted kappa-opioid receptor agonist and it selectively activates kappa-opioid receptors located on the peripheral sensory neurons and immune cells.

So when we look, we talk about efficacy, now we talk about the safety of our data. So we have data from RCTs and we have the real-world data. They're very promising.

So in 2023 we published real-world evidence using the European managed access program. This was the first global real-world experience in patients with severely affected CKD-aP. And what we could find in our study was a rapid onset of itch relief, often within 1 to 2 weeks, sustained efficacy over a long time.

Now, I presented the safety data of our patients in the managed access program for more than 400 patients. They are treated with difelikefalin for up to 3 years. And it's noteworthy that no new signal in regard to safety was detected during our managed access program compared to the RCTs.

So yes, there were adverse events in our patient population, but 88% of them resolved during the treatment period so the patient was

still on DFK. And of course there were some nonserious adverse events in 85 patients, but overall, we could not detect any new signal in regard to safety.

So again, the majority of adverse events and severe adverse events were consistent with typical comorbidities and clinical events in patients with CKD on hemodialysis or were expected based on the known safety profile of difelikefalin.

So together, these data provide strong reassurance that difelikefalin is generally well tolerated with no new safety signals and provide consistent with prior RCTs.

What's coming up in the future? The PARADIGM registry, a large multinational, prospective, observational study aiming to assess real-world safety and long-term effectiveness of DFK and evaluate—and I think that this is very important—patient-related outcomes, including itch severity—and not only severity of itch, including sleep quality and health-related quality of life.

I think we have new options now to treat CKD-aP, so it's very important to make the diagnosis, to send a patient to a dermatologist to exclude other differential diagnoses of pruritus in a hemodialysis patient, then you have now a really good new treatment option to treat your patient with a very good safety profile.

So to summarize, chronic CKD-aP, it's a chronic disease in dialysis patients. It's a severe, underappreciated burden that urgently requires effective and well-tolerated treatment options. Now we have a new treatment option. Difelikefalin offers a novel peripherally acting mechanism with robust evidence from RCTs and real-world studies confirming its efficacy, rapid onset, and now a favorable safety profile.

That's all the time we have today. So I want to thank the audience for listening and keeping up with the changing landscape of CKD-aP.

**Announcer:**

This activity is provided by Medtelligence. Thank you for listening to ReachMD.