

Dialysis Outcomes and Practice Patterns Study (DOPPS) Data

- Between **2/3** and **3/4** of patients on maintenance hemodialysis report pruritus
 - More than **40%** of these patients report **moderate to severe pruritus**



Quote by James Burton, MD

*“The first thing is to **go out and ask** people about whether they feel that itch...”*



Worst Itch Numerical Rating Scale (WI-NRS)

Please rate the worst itch you have felt in the previous 24 hours. Select one option:

0 1 2 3 4 5 6 7 8 9 10

0 = No itching

10 = Worst itch imaginable

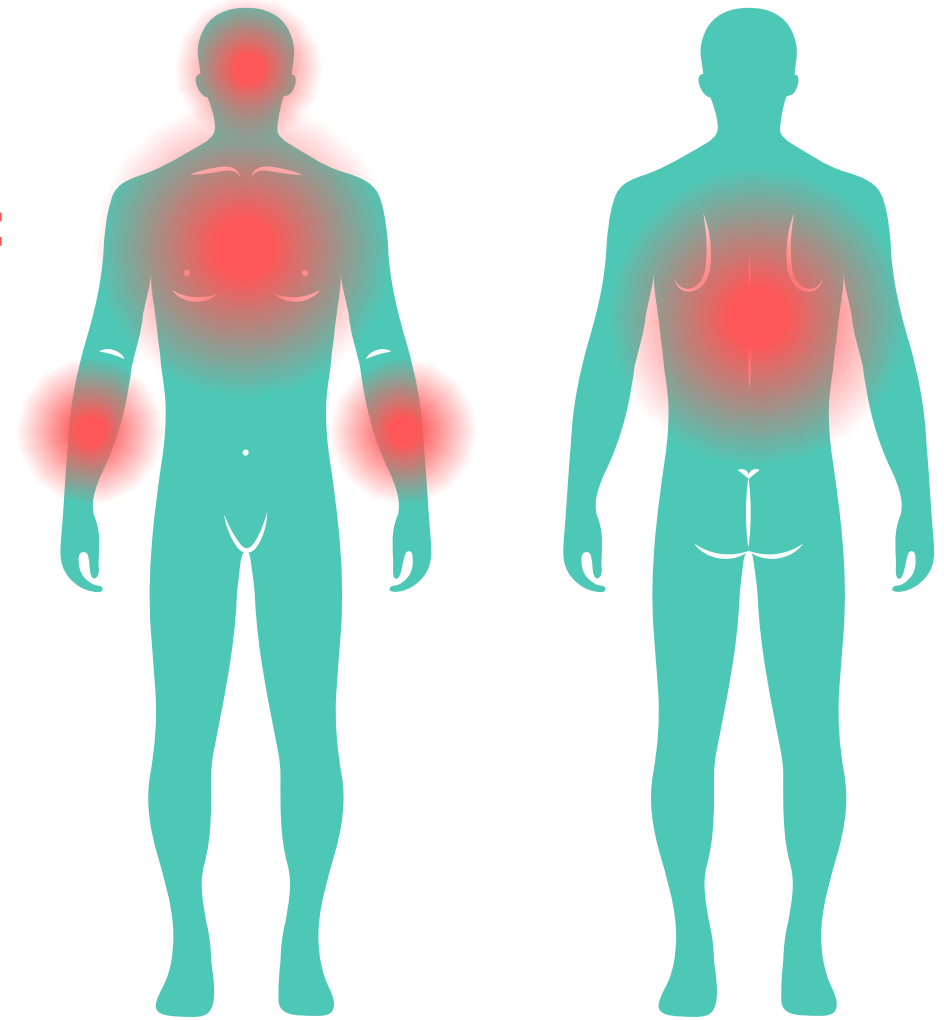


Clinical Presentation of CKD-aP

- Often bilaterally symmetrical and can be localized or generalized

Classic locations:

- Trunk
- Back
- Face
- Arms



Use of Antihistamines in CKD-aP

- Histaminergic pathway is **NOT involved** in CKD-aP
- Patients with histamine-generated itch tend to have a kind of wheal and flare formation
 - Not observed in CKD-aP
- **Sedation** is the main side effect
- Lack of evidence for their effectiveness

Antihistamines are NOT a recommended treatment for CKD-aP



Use of Gabapentinoids in CKD-aP

Gabapentin and Pregabalin (off-label)

- **Narrow** therapeutic index
- Adverse side effects
 - Dizziness
 - Somnolence
 - Weight gain
 - ↑ Suicidal risk
- Excreted by the kidney
 - **Difficult to manage dosing in patients on hemodialysis**



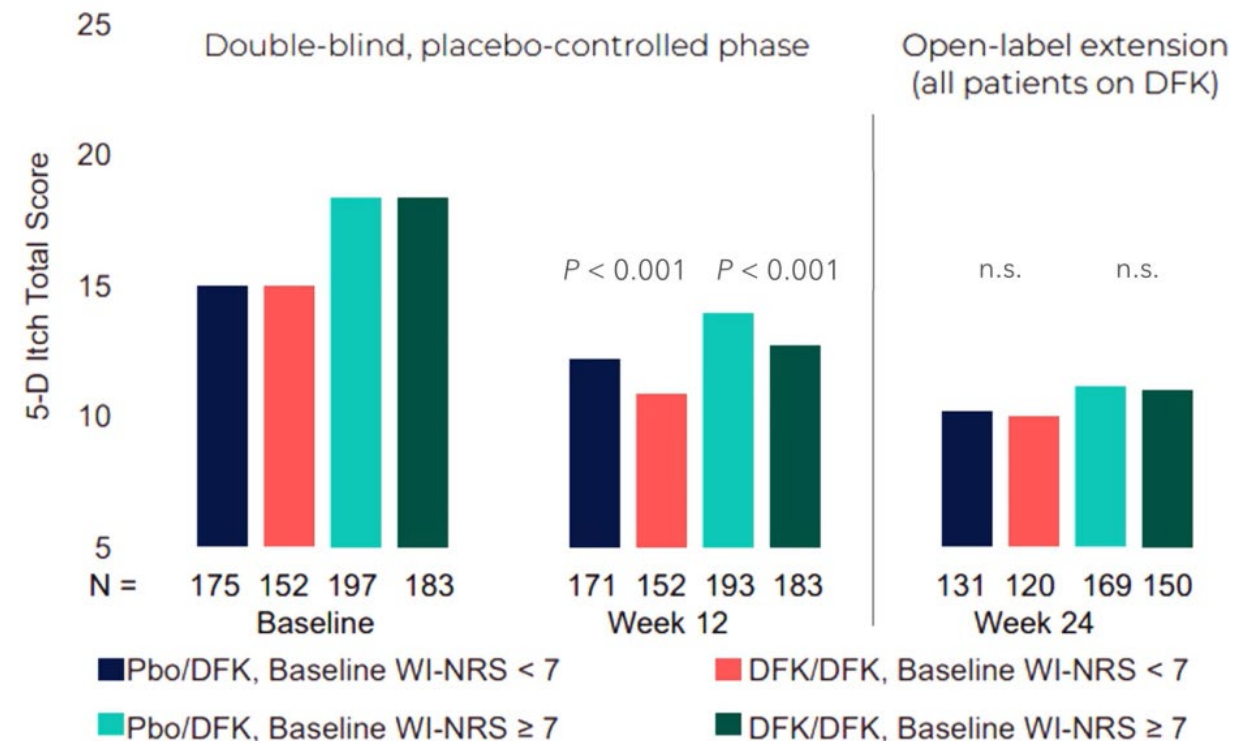
CKD-aP Treatment

Universal Approaches	Itch-Specific Treatment
<ul style="list-style-type: none">• Skin moisturizers 2x daily<ul style="list-style-type: none">▪ Especially after showers/baths• Gabapentinoids	<ul style="list-style-type: none">• Difelikefalin: Selective kappa-opioid receptor agonist<ul style="list-style-type: none">▪ First and only FDA-approved prescription treatment for moderate to severe CKD-aP in adults undergoing hemodialysis▪ Peripherally acting opioid (no dependence liability)

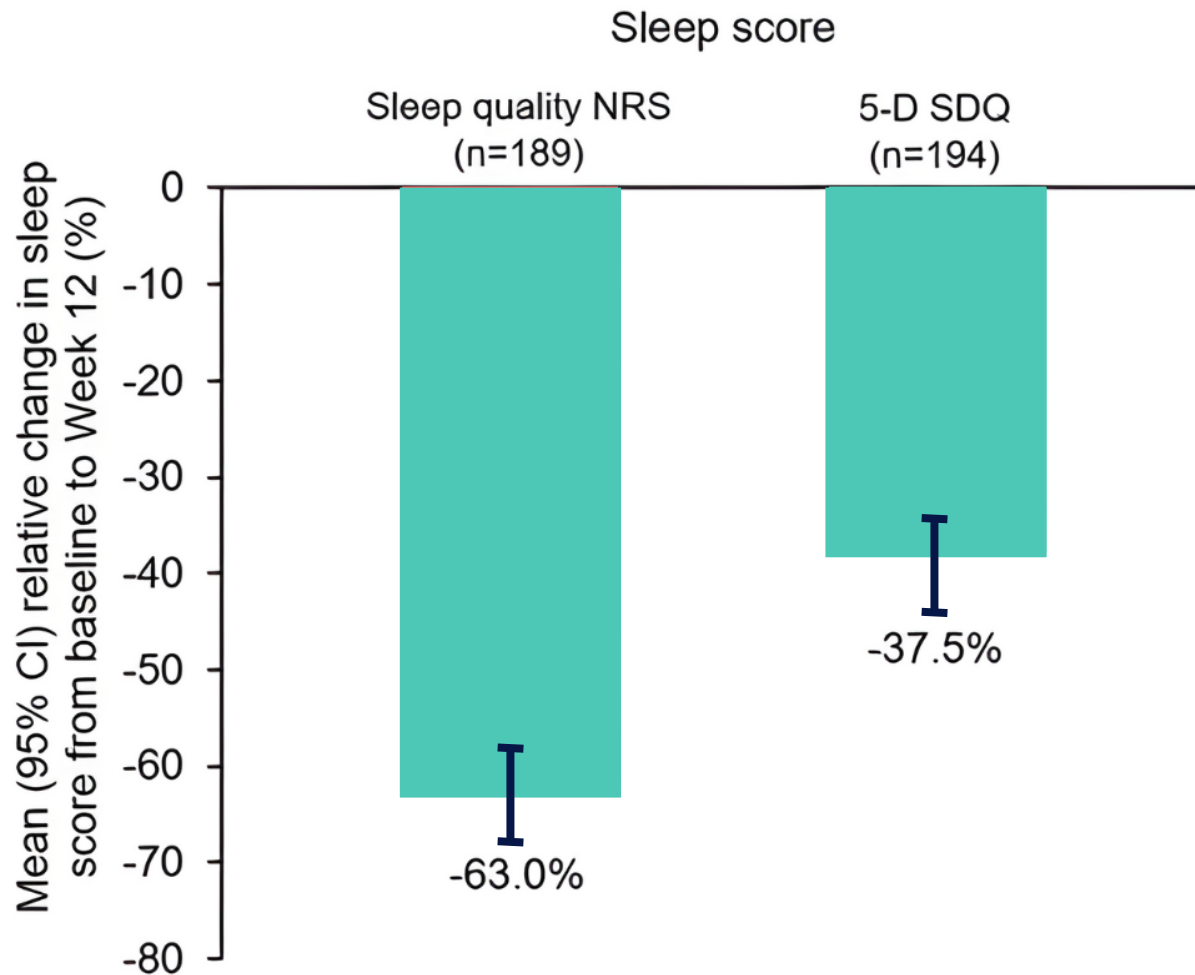


KALM Trials: Continued Improvement of Itch-Related Quality of Life in Patients With CKD-aP Treated With Difelikefalin

- Patients with severe CKD-aP continue to accumulate additional treatment benefit after the initial 12 weeks of treatment with difelikefalin
 - Achieve a similar level of benefit as patients with moderate itch at baseline after 24 weeks of treatment



Difelikefalin Improves Itch-Related Sleep Disruption in Patients Undergoing Hemodialysis



	Sleep Quality NRS (n = 189)	5-D SDQ (n = 194)
Mean (95% CI) change from baseline	-4.3 (-4.6, -3.9), <i>P</i> < 0.001	-1.6 (-1.8, -1.4), <i>P</i> < 0.001

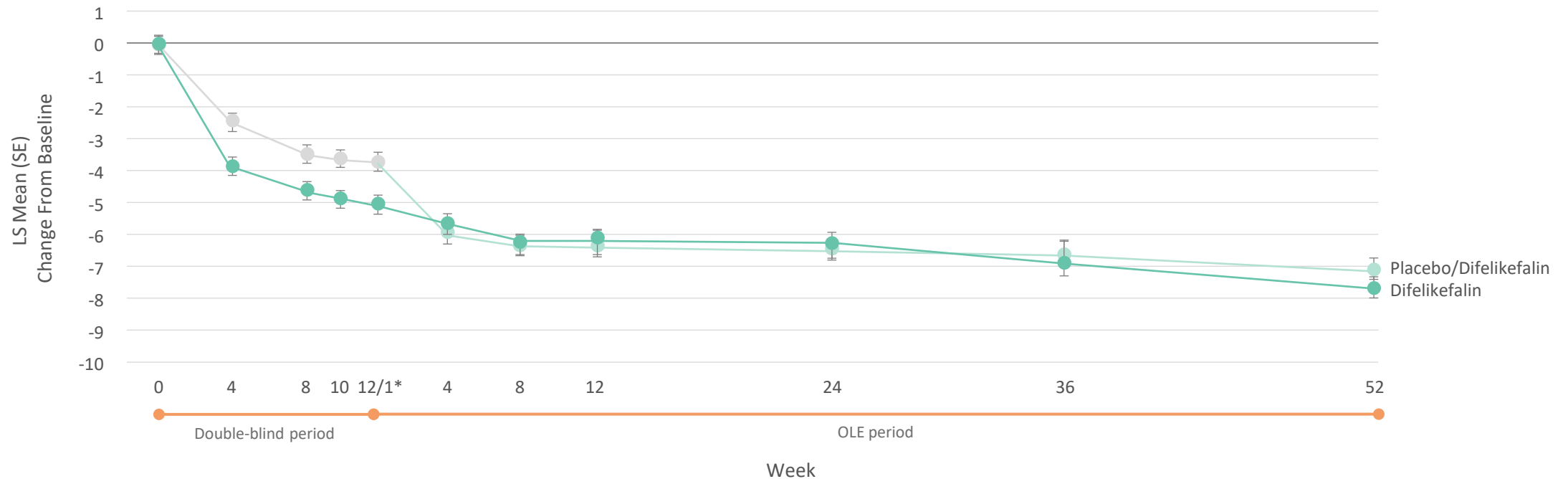


Quote by Joel Topf, MD

*“We had patients on these drugs for weeks, months even, and that we would then stop them, and we did specific surveys and assessments to see if they had any signs of opioid dependence, and we didn’t find any, kind of further backing up that [difelikefalin] just **doesn’t get into the central nervous system.**”*



Mean 5-D Itch Improvement With Difelikefalin Was Maintained Through 52 Weeks



*Week 12 of double-blind period; week 1 of OLE period. In KALM-2, in addition to the patients who discontinued from the OLE, 313/399 (78.4%) patients could not complete the 52-week OLE due to the sponsor's decision to stop the study for reasons unrelated to safety or lack of drug effect. The 2-week discontinuation period in KALM-1 is not pictured in the figure.

LS, least squares; OLE, open-label extension; SE, standard error.