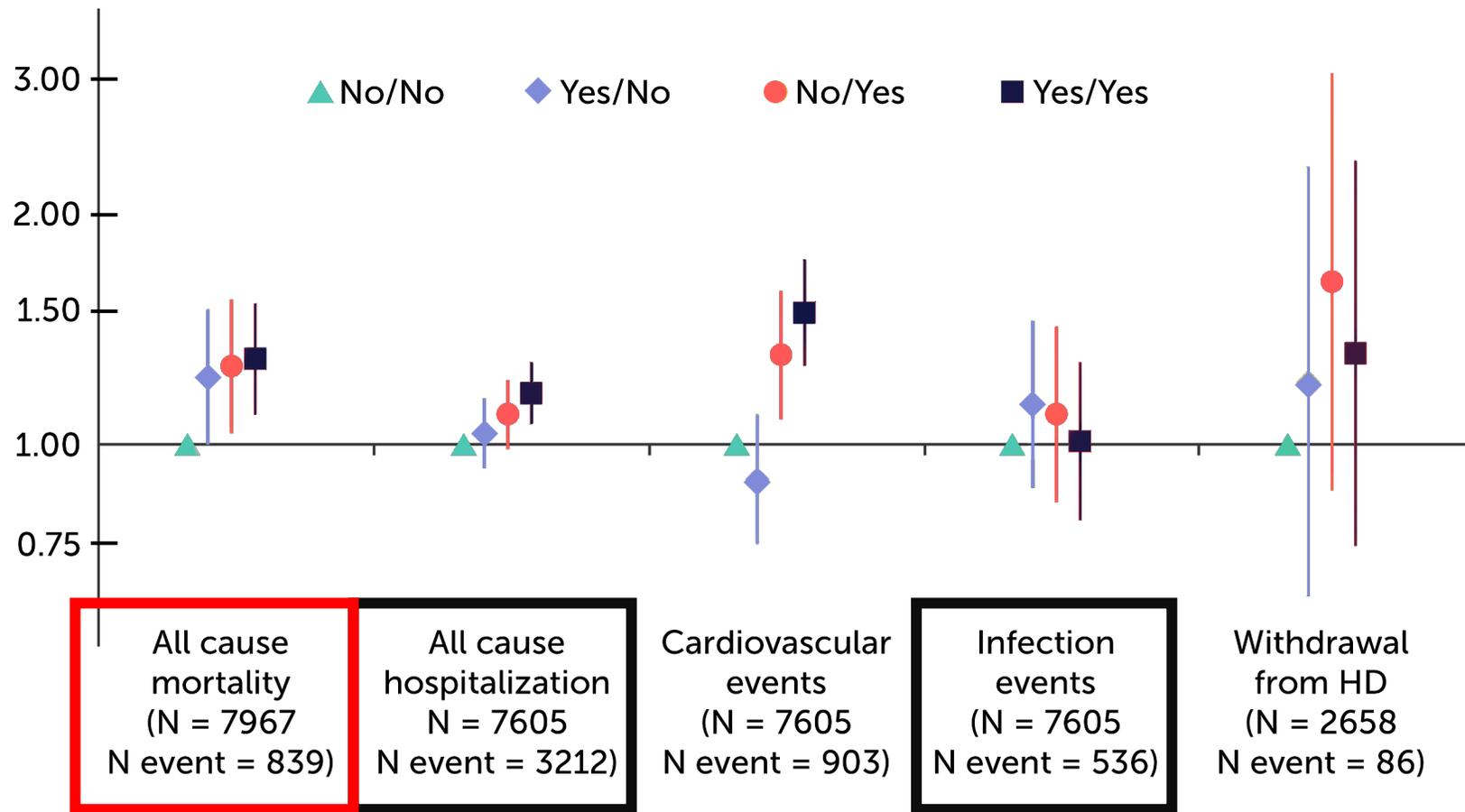


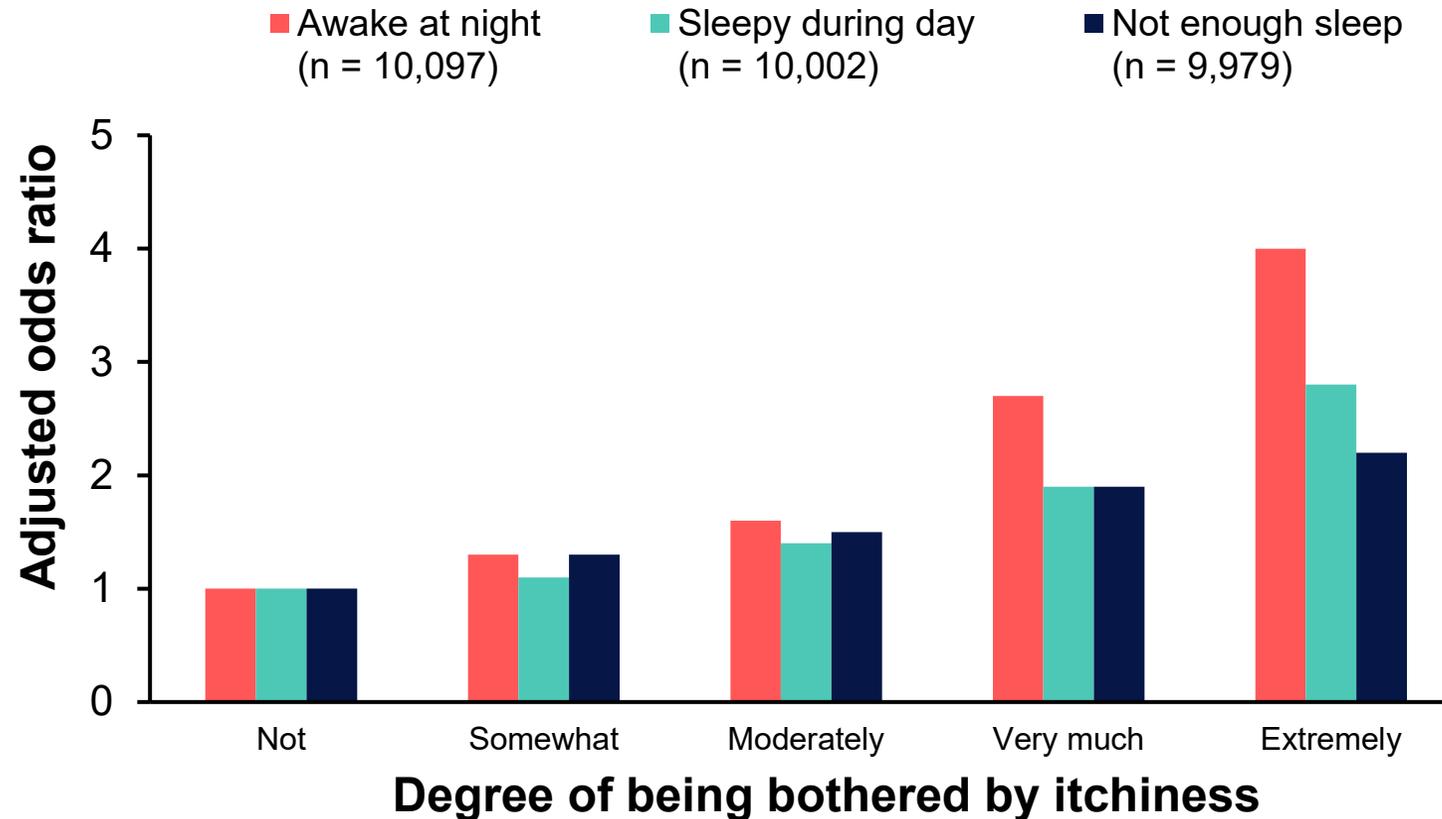
# Association Between Change in Pruritus Symptoms and Subsequent Rates of Clinical Outcomes

Hazard Ratio (95% CI)



# Majority of Patients With CKD-aP Suffer From Sleep Disturbances

## Likelihood of sleep disturbances according to CKD-aP severity



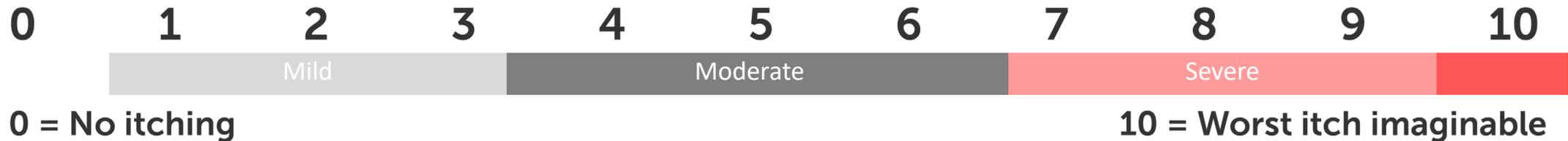
# Quote by Jörg Latus, MD

“We have to start implementing the screening for CKD-aP in our everyday clinical practice.”



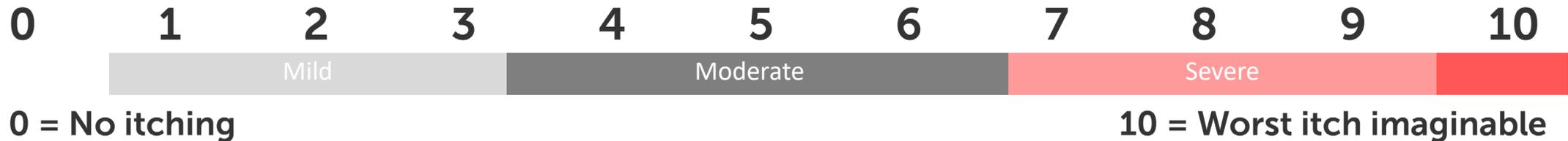
# Worst Itch Numeric Rating Scale (WI-NRS)

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



# Worst Itch Numeric Rating Scale (WI-NRS)

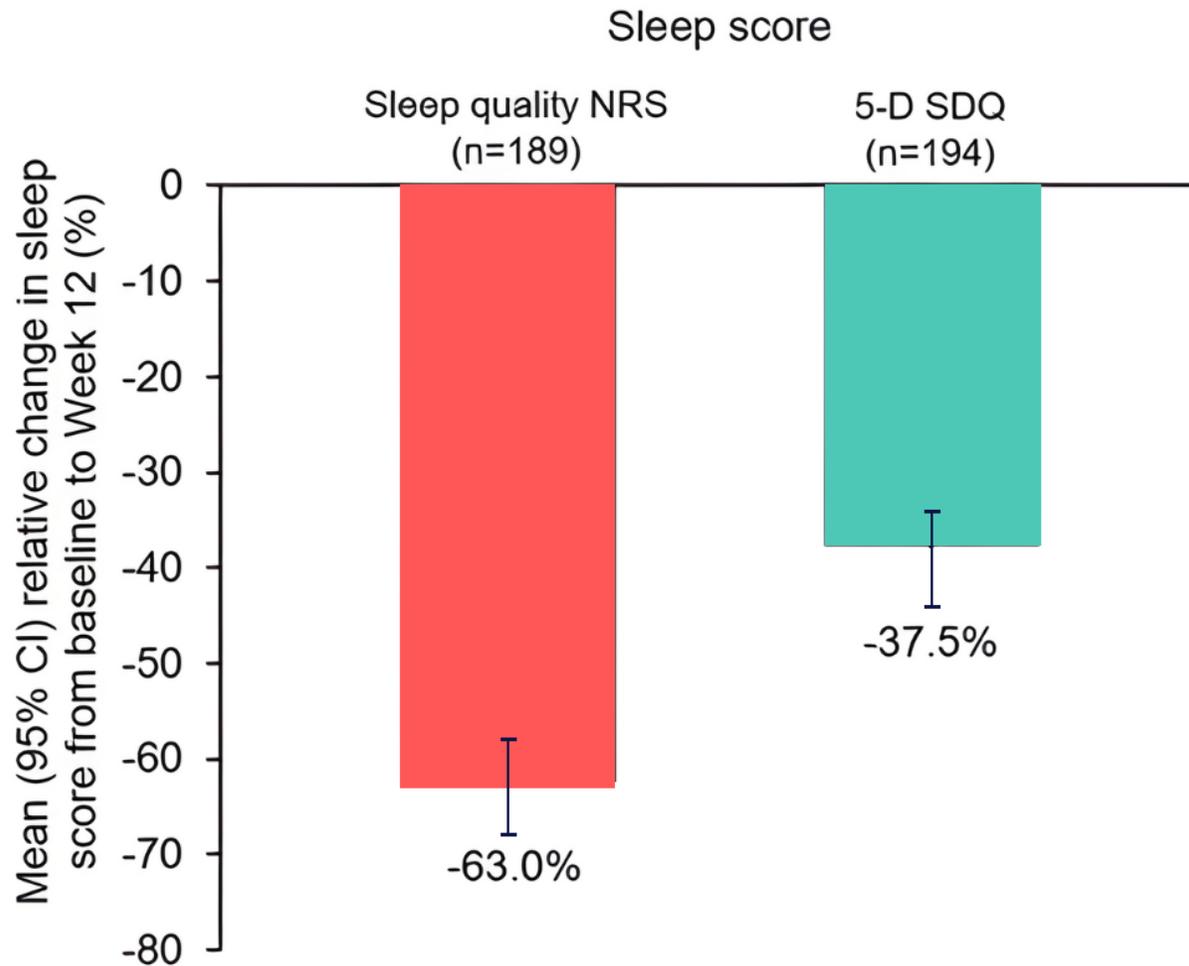
Please rate the worst itch you have felt in the previous 24 hours. Select one option:



National Institute for Health and Care Excellence (NICE)



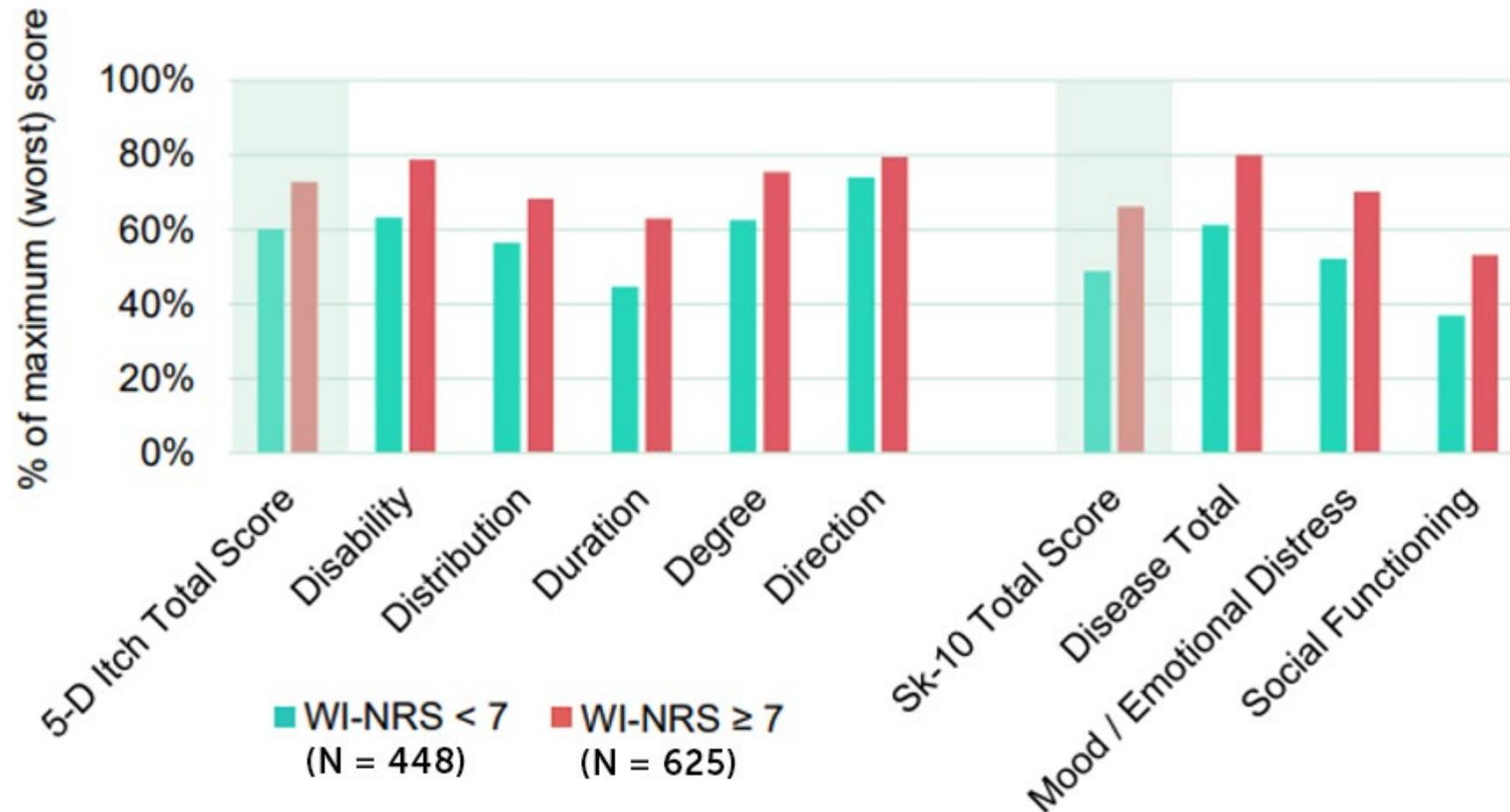
# Difelikefalin Improves Itch-Related Sleep Disruption in Patients Undergoing Hemodialysis



	Sleep Quality NRS (n = 194)	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



# Itch-Related Quality of Life Detriment on 5-D Itch and Skindex-10 Total Scores by Baseline CKD-aP Severity



# 68-Year-Old Man With End-Stage Kidney Disease Due to T2D

- **Hemodialysis:** 4 hours, 3x weekly for 4 years
- **Complaint:** Itchy for several years
- **Tried Treatments:** Antihistamines, moisturizing cream, gabapentin (with no relief)
- **Itching Characteristics:**
  - Worse at night
  - Disrupts sleep
  - Led to him being continuously fatigued

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



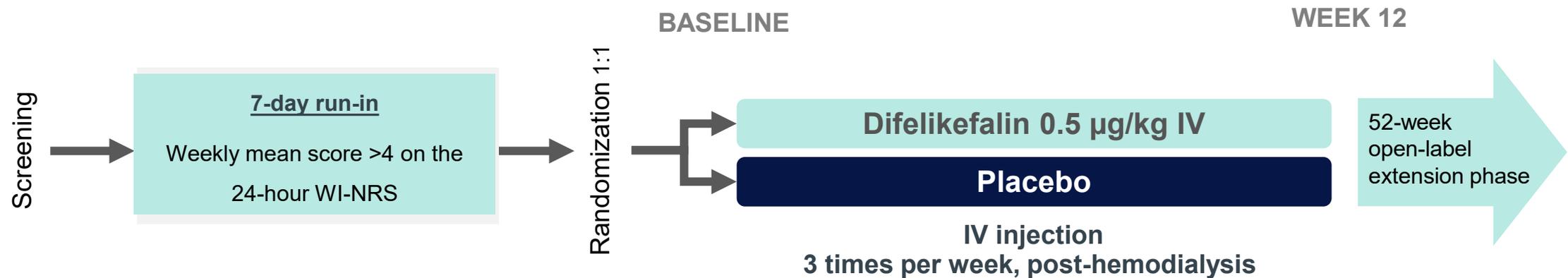
# Gabapentinoids Off-Label Use

- **Lack of evidence** for long-term treatment benefit in CKD-aP
- Potential drug dependency and abuse
- Adverse effects:
  - Neurological events (eg, dizziness, somnolence)
  - Weight gain
  - ↑ suicide risk



# KALM-1 and KALM-2: Pivotal Phase 3 Studies

- Patients  $\geq 18$  years of age with ESRD and moderate to severe pruritus
  - On hemodialysis ( $\geq 3$ x per week) for  $\geq 3$  months



## KALM-1

US multicenter study

Difelikefalin (n = 189) vs placebo (n = 188)

Completion date: April 2020

## KALM-2

Global multicenter study

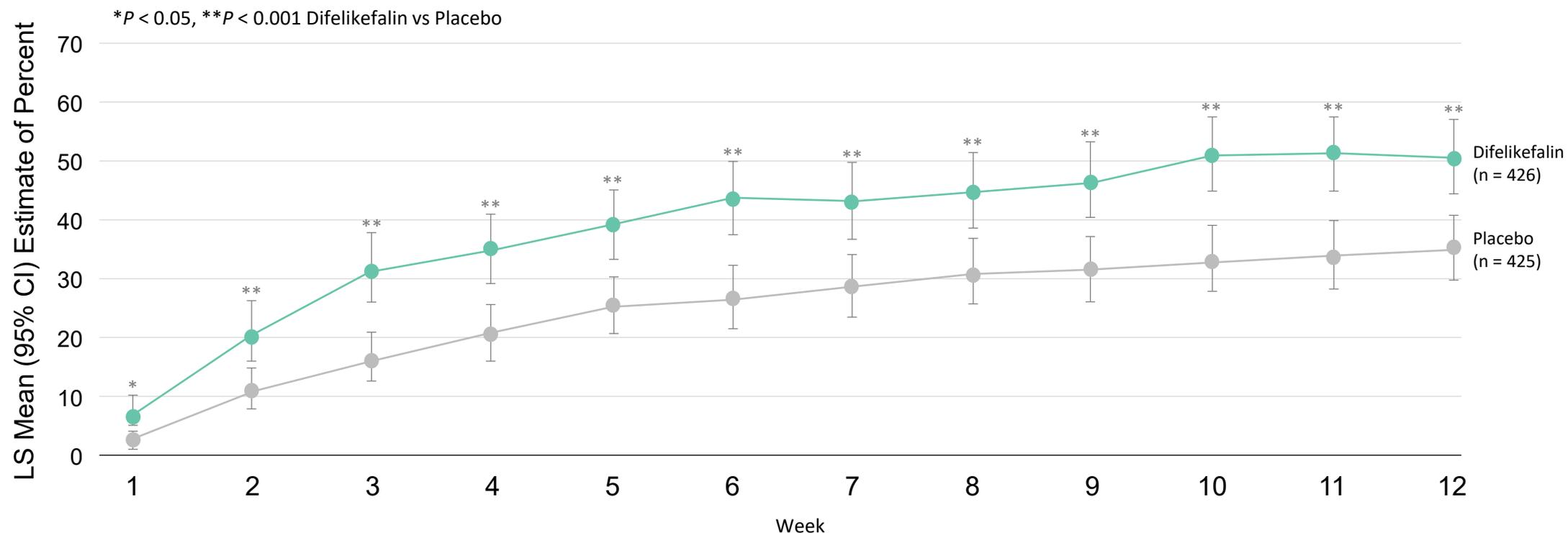
Difelikefalin (n = 235) vs placebo (n = 236)

Completion date: March 2020

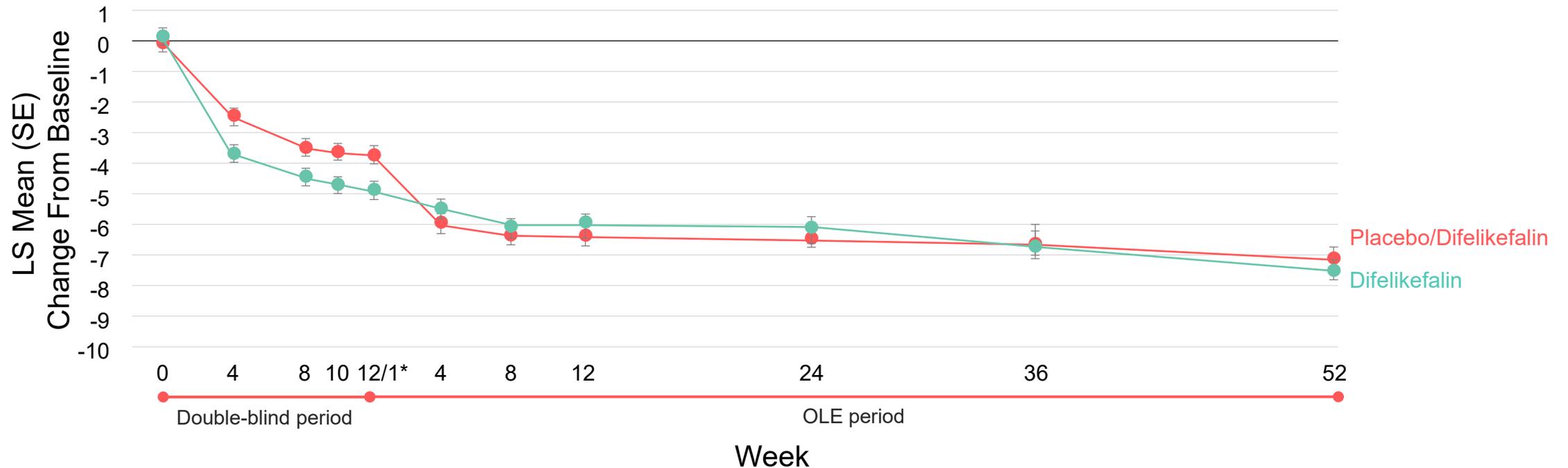


# KALM-1 and KALM-2: Pivotal Phase 3 Studies

Difelikefalin resulted in significantly greater achievement of  $\geq 3$ -point improvement in WI-NRS



# 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.

# Difelikefalin:

- First and only approved therapy for adult patients with moderate to severe CKD-aP
- Peripherally restricted kappa-opioid agonist
  - **Does not** cross blood-brain barrier





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# Difelikefalin for treating pruritus in people having haemodialysis

Technology appraisal guidance [TA890] Published: 17 May 2023 [Register as a stakeholder](#)



WI-NRS  $\geq 4$  at Baseline

Moderate to severe pruritus



Initiate Difelikefalin Treatment



WI-NRS at 12 Weeks

$\geq 3$  points improvement



Continue Difelikefalin

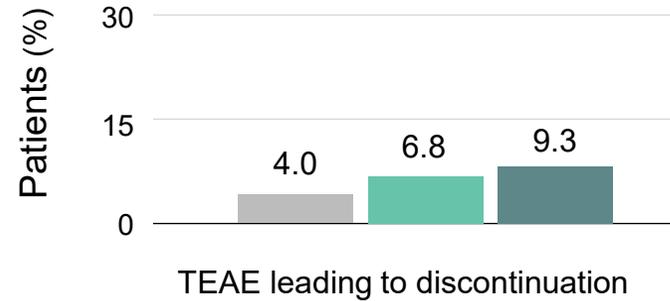


# S2k Guideline

<b>Recommendation</b>	Difelikefalin is recommended for adults with moderate to severe nephrogenic pruritus and hemodialysis.
<b>Strength</b>	↑↑
<b>Agreement</b>	Consensus (90%)



# Difelikefalin: Overview of TEAEs in Pooled KALM-1 and KALM-2 Safety Population



- Placebo, Placebo-Controlled phase, Weeks 0 to 12 (n = 424)
- Difelikefalin, Placebo-Controlled phase, Weeks 0 to 12 (n = 424)
- Difelikefalin, All Difelikefalin-exposure cohort including OLE (n = 1,306)

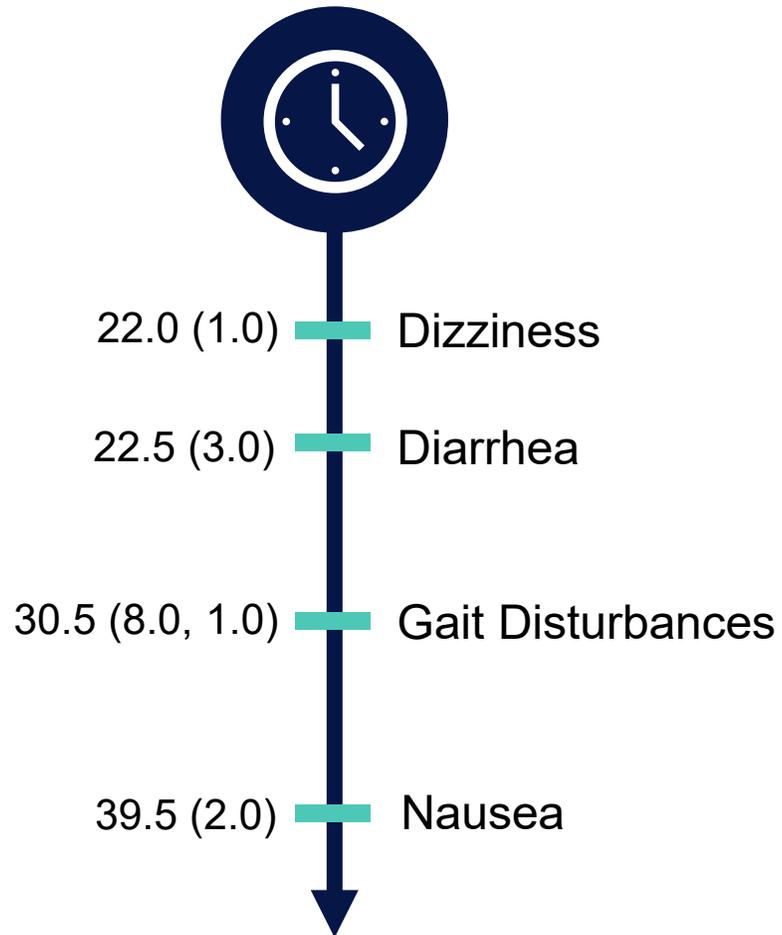


<b>Adverse Event</b>	<b>Difelikefalin</b>	<b>Placebo</b>
<b>Diarrhea</b>	9.0%	5.7%
<b>Dizziness</b>	6.8%	3.8%
<b>Nausea</b>	6.6%	4.5%
<b>Gait disturbance</b>	6.6%	5.4%

Fishbane S, et al. *Kidney Med.* 2022;4(8):100513.



# Median Time to Onset (Median Duration), Days



Reddy J, et al. Presented at: ASN Kidney Week;  
Philadelphia, PA; November 3, 2023. FR-PO426.



## Quote by Jörg Latus, MD

“Now we have a new treatment with DFK, and that works and has a good safety profile...and times have gone much better for patients with pruritus. That’s **why we have to ask for pruritus.**”

