

# Worst Itch Numerical Rating Scale (WI-NRS) Itch-Severity Assessment Tool

Please indicate the intensity of the worst itching you experienced over the past 24 hours.

0    1    2    3    4    5    6    7    8    9    10

0 = No itching

10 = Worst itch imaginable

- Measures **patient-reported** itch over a **24-hour** period
- Quick & simple for clinical settings
- Validated in KALM Studies
  - **≥3-point improvement** = clinically meaningful
- Can be used to assess itch trends weekly



# Treatment Selection for CKD-aP

<b>Skin Moisturizers</b>	<ul style="list-style-type: none"><li>• For dry skin</li><li>• Safe</li></ul>
<b>Gabapentinoids</b>	<ul style="list-style-type: none"><li>• Lack of evidence for effectiveness</li><li>• Serious adverse effects (eg, cognitive impairment, ↑ suicidal risk)</li></ul>
<b>Antihistamines</b>	<ul style="list-style-type: none"><li>• Sedative effect</li><li>• Not recommended</li></ul>
<b>UVB</b>	<ul style="list-style-type: none"><li>• Time intensive</li><li>• Requires dermatologist supervision</li><li>• Potential skin harm</li></ul>





# National Institute for Healthcare and Excellence (NICE) Recommends Difelikefalin for Treating Pruritus in Adults with CKD on Hemodialysis

- Enables eligible patients in England, Wales, and Northern Ireland to access difelikefalin, the first licensed treatment for moderate to severe chronic kidney disease (CKD)-associated pruritus in adult patients on hemodialysis



# KALM-1 and KALM-2

## Phase 3 Randomized Clinical Trials

### 12 weeks N = 851

	≥3-point ↓ of WI-NRS at 12 weeks	≥15-point ↓ of Skindex-10 at 12 weeks	≥5-point ↓ of 5-D Itch at 12 weeks
Difelikefalin	<b>51%</b>	<b>55%</b>	<b>52%</b>
	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> < 0.01
Placebo	35%	40%	42%

### Conclusions:

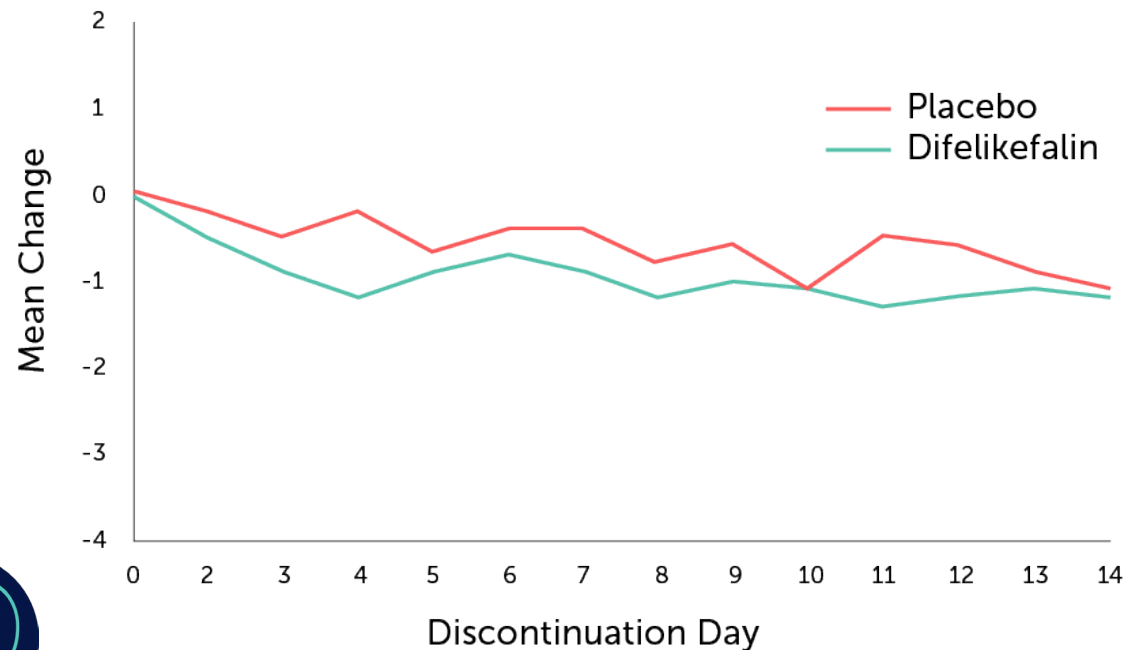
- **Rapid and sustained efficacy** of difelikefalin in patients on hemodialysis
- Well tolerated and acceptable safety profile



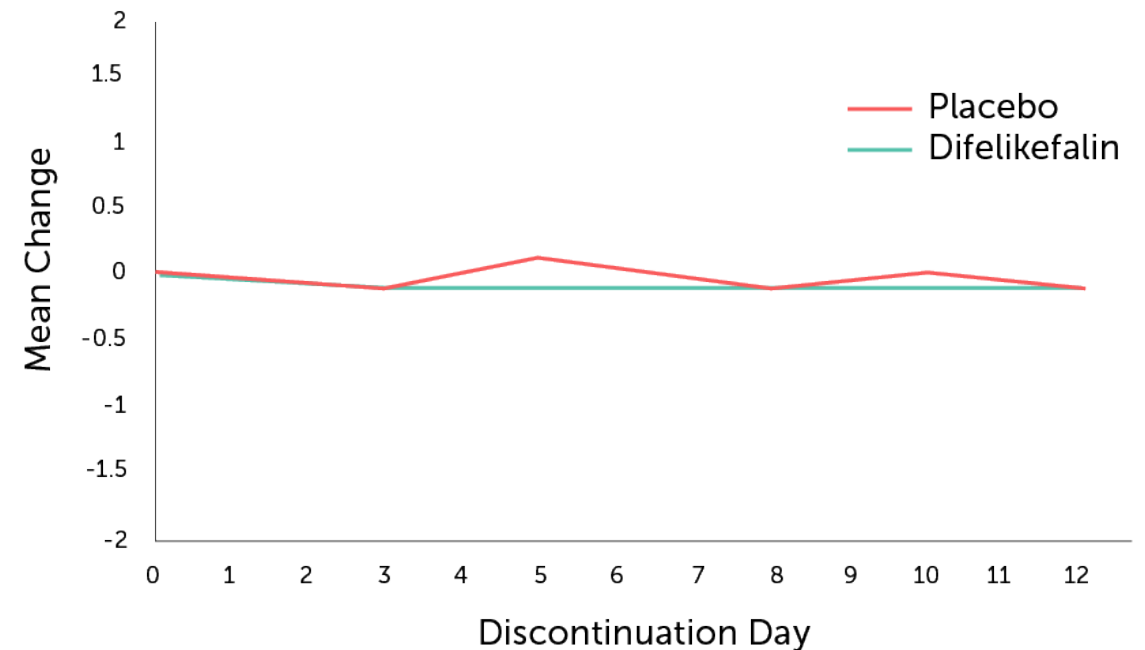
# Difelikefalin: Opioid Dependence? Monitored for 2 Weeks After Last Dose

KALM-1 Trial

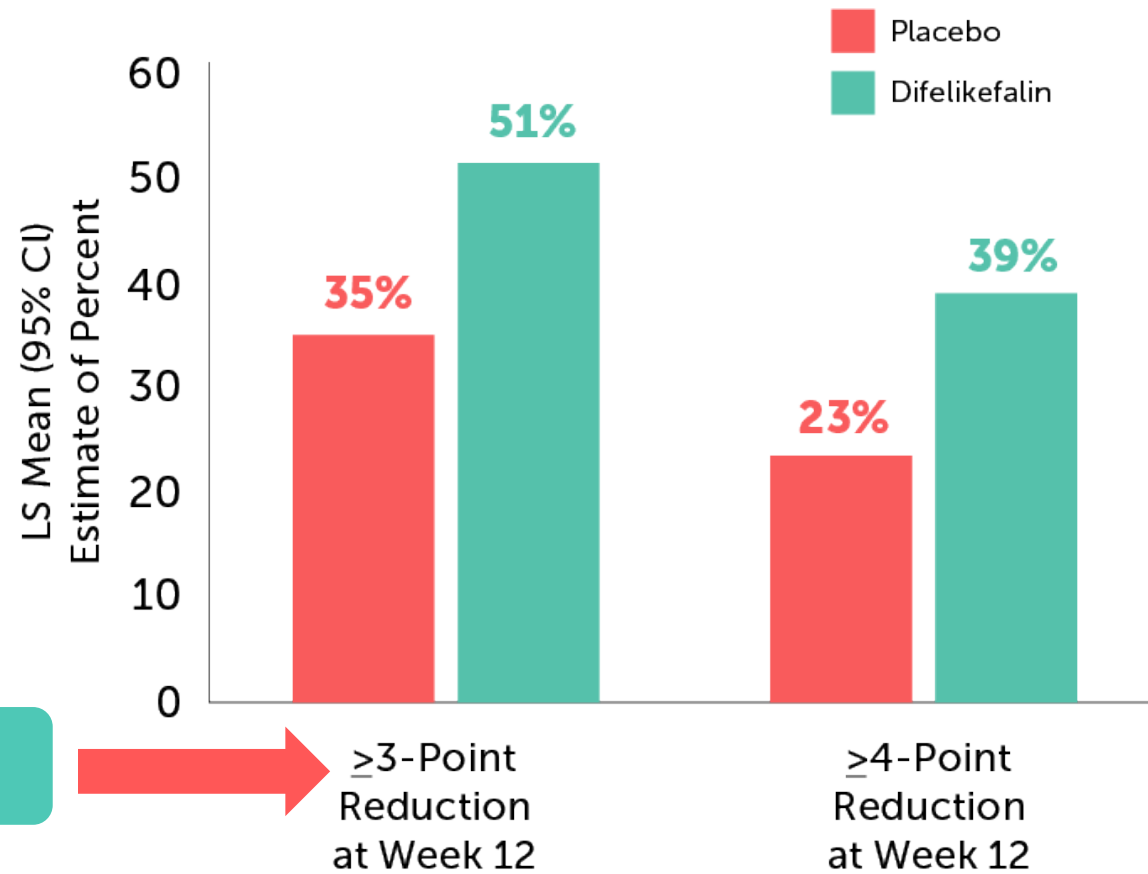
### Short Opioid Withdrawal Scale



### Objective Opioid Withdrawal Scale



# Pooled Analysis: KALM-1 & KALM-2



$P < 0.001$

KALM-1 N = 378

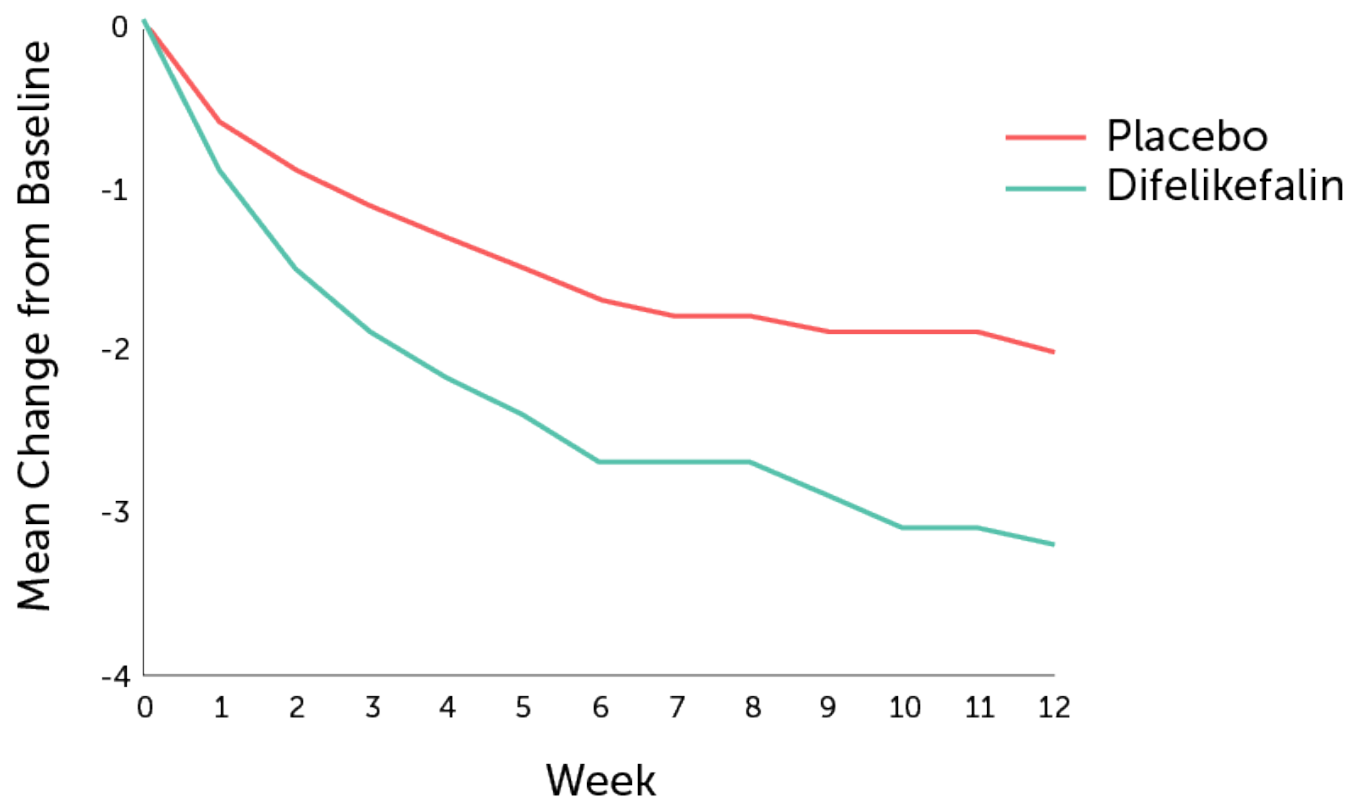
KALM-2 N = 473

Primary outcome



# Difelikefalin: Efficacy

Itch reduction was seen by week 4 and **sustained** by week **12** (WI-NRS)



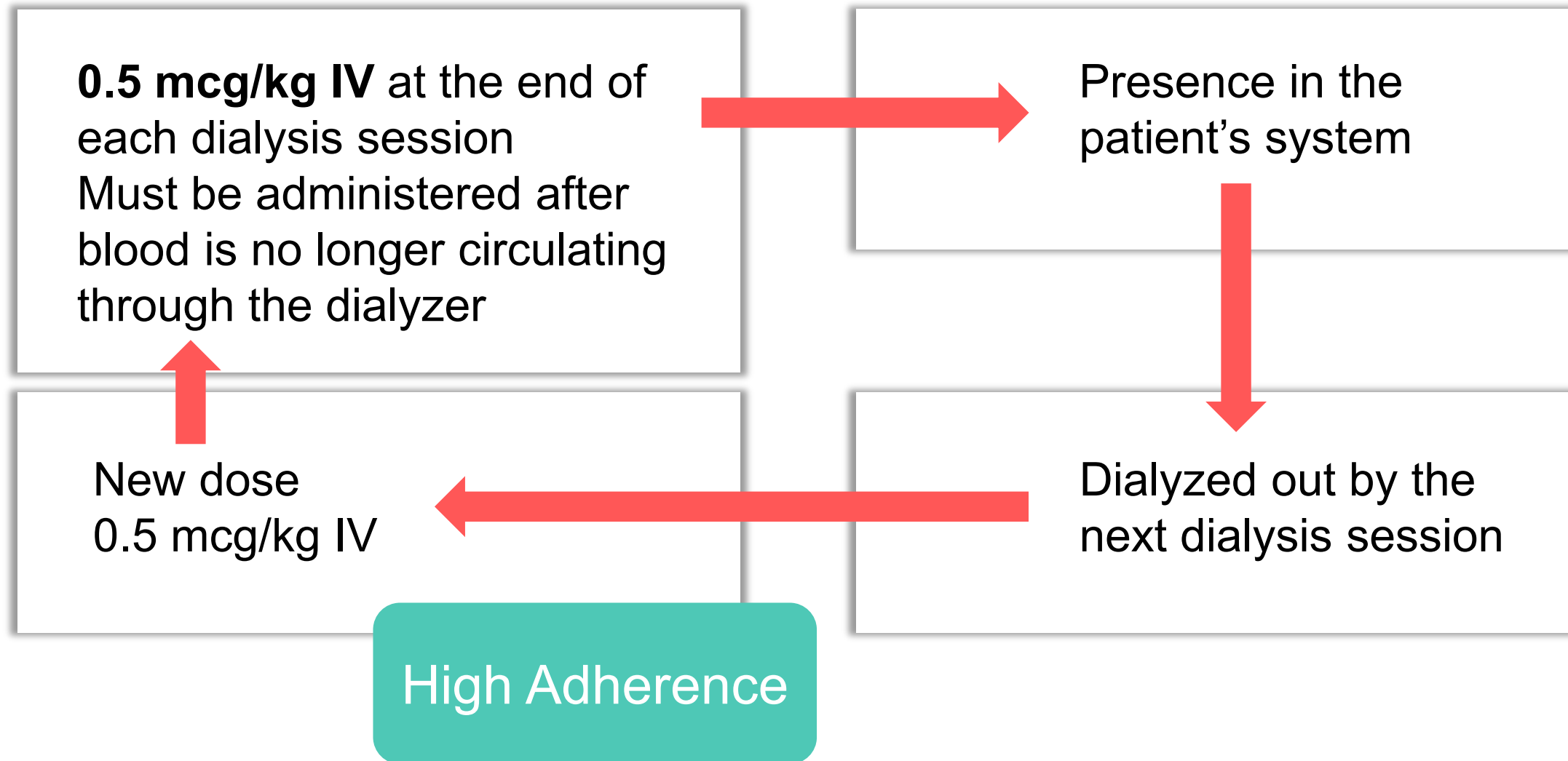
# Difelikefalin: Safety

	Diarrhea	Nausea	Dizziness	Gait Disturbance
Difelikefalin	9%	7%	7%	7%
Placebo	6%	5%	4%	5%





# Difelikefalin: Dosing & Administration



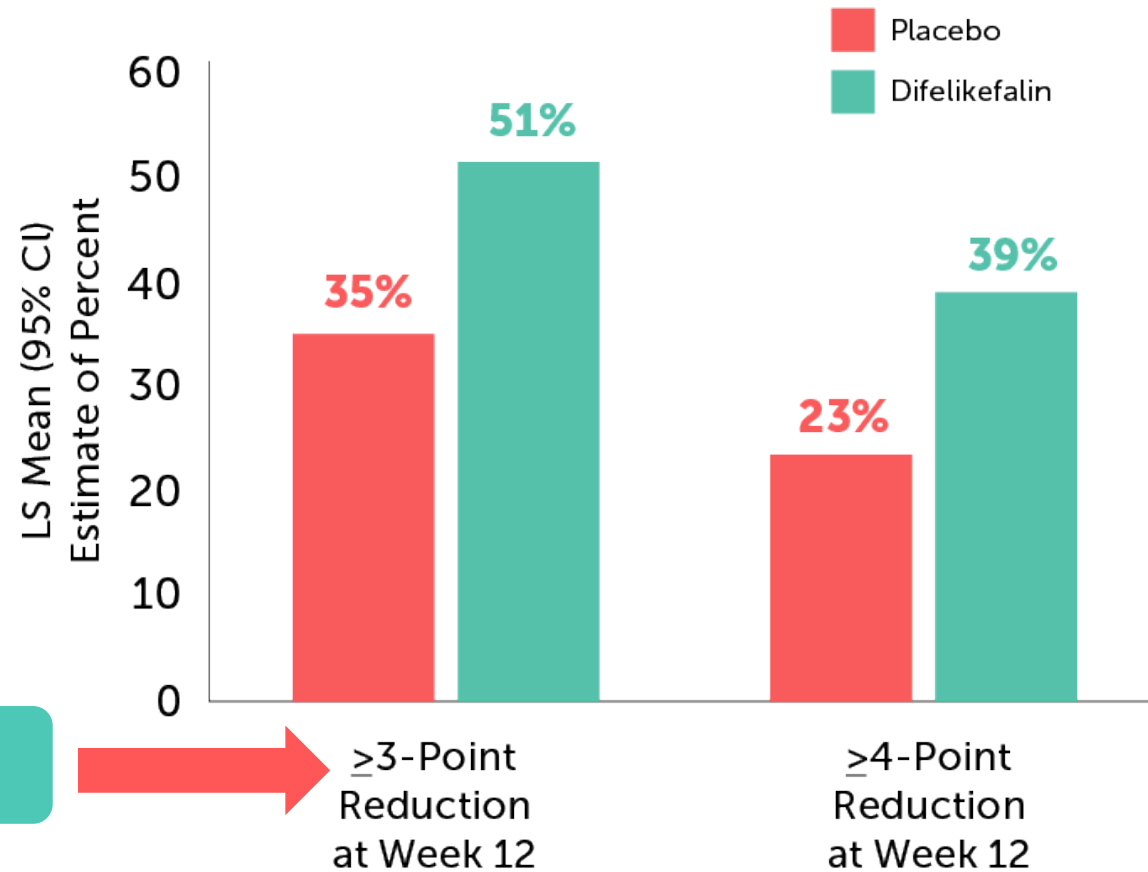
# Pooled Analysis: KALM-1 & KALM-2

Follow up weekly  
up to 3 months



Continue or modify

Primary outcome



$P < 0.001$

KALM-1 N = 378

KALM-2 N = 473

