



A 57-Year-Old Woman

Current:

- Hemodialysis for 6 months
 - Type 2 diabetes
 - Kidney failure from diabetic nephropathy
-

Past History:

- Peripheral vascular disease
 - Diabetic peripheral neuropathy
 - Hypertension
 - Dyslipidemia
-





A 57-Year-Old Woman

Today:

- **Lives alone**
 - **Cutting back on work due to an inability to concentrate**
 - **Whole body itch present for several months, even prior to starting dialysis**
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- **Despite her biochemistry being excellent on dialysis, her itch persists, and she's finding it difficult to sleep at night due to persistent scratching, and she has difficulty functioning during the day, both from the itching and lack of sleep**



Impact of Itch on Patients' Lives

- Worse health-related quality of life
- **Physical** and **mental** burden
 - Sleep disturbances
 - Daytime sleepiness
 - Unable to work
 - Can't focus on family and friends
 - Concentration difficulties
 - Work difficulties
 - Avoid interacting with people
 - Depression
 - Embarrassment



Shared Decision-Making

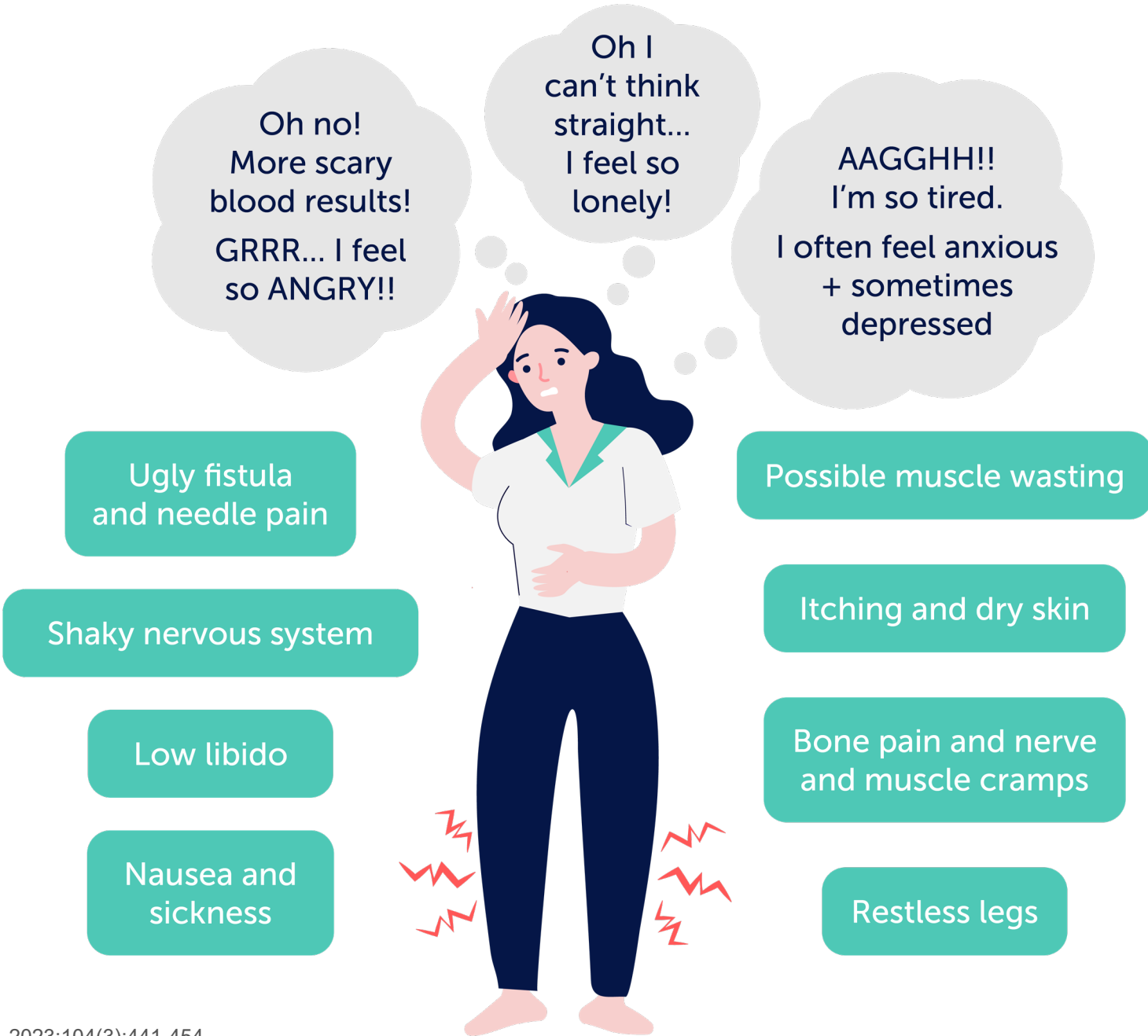


Nursing care

Patient

Patient's family





Oh no!
More scary
blood results!
GRRR... I feel
so ANGRY!!

Oh I
can't think
straight...
I feel so
lonely!

AAGGHH!!
I'm so tired.
I often feel anxious
+ sometimes
depressed

Ugly fistula
and needle pain

Shaky nervous system

Low libido

Nausea and
sickness

Possible muscle wasting

Itching and dry skin

Bone pain and nerve
and muscle cramps

Restless legs

CKD-aP Symptom Screening

- Every 3 months
- Dialysis Symptom Index
- IPOS-Renal Symptom Survey
- Edmonton Scale



CKD-aP Symptom Screening

- WI-NRS: evaluate the itch severity
- Self-Assessment Disease Severity (SADS) scale
- 5-D itch scale





A 57-Year-Old Woman

Physical Assessment:

- Cirrhosis
- Evidence of scratching all over arms, legs, trunk
- Few areas of broken skin on upper arms

Counseling on Skin Care:

- Moisturizers 2x/day
- Avoiding hot showers and hard soaps
- No response to antihistamines
- Maximum tolerated dose of pregabalin
- WI-NRS is 9/10



Regular Systemic Symptom Cluster Assessment



Dialysis Outcomes and Practice Patterns Study (DOPPS) Data

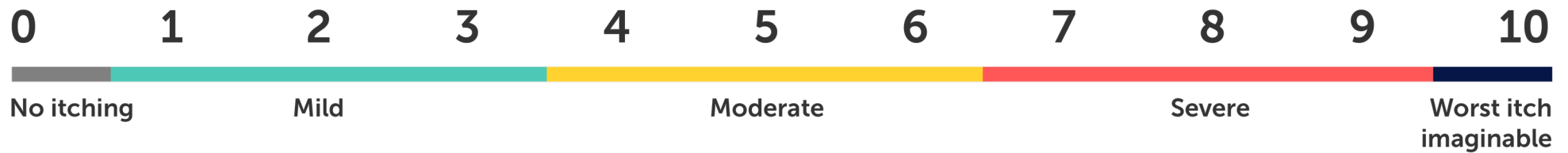
- Between **2/3** and **3/4** of patients on maintenance hemodialysis report pruritus
- More than **40%** of these patients report **moderate to severe pruritus**
- A higher severity of itching correlates to more compromised quality of life



Itch Assessment

- WI-NRS: evaluate the itch severity

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





A 57-Year-Old Woman

Treatment:

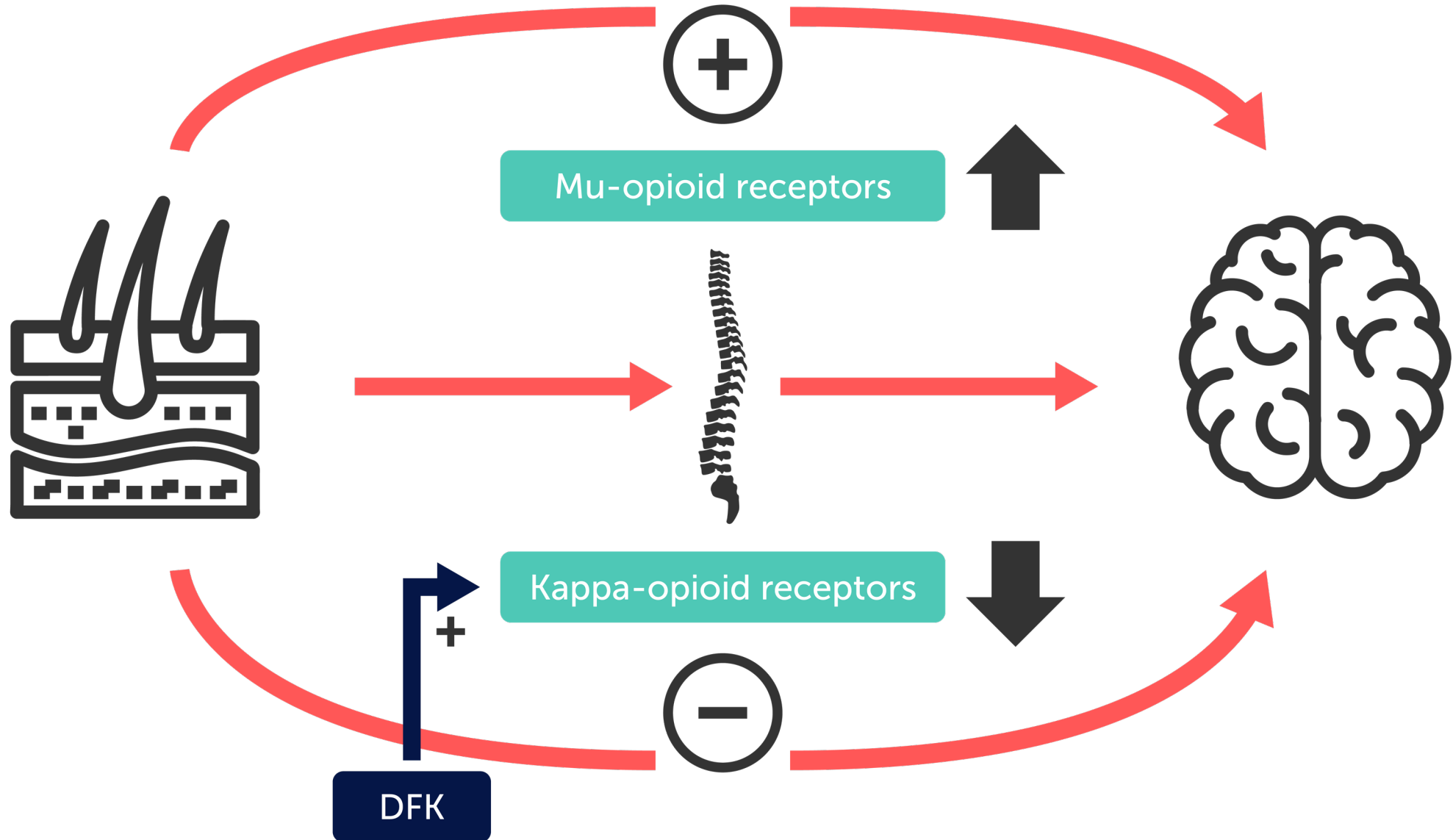
- Started difelikefalin
- After 4 weeks her itch dramatically improved
- WI-NRS 3/10

Treatment after 12 weeks:

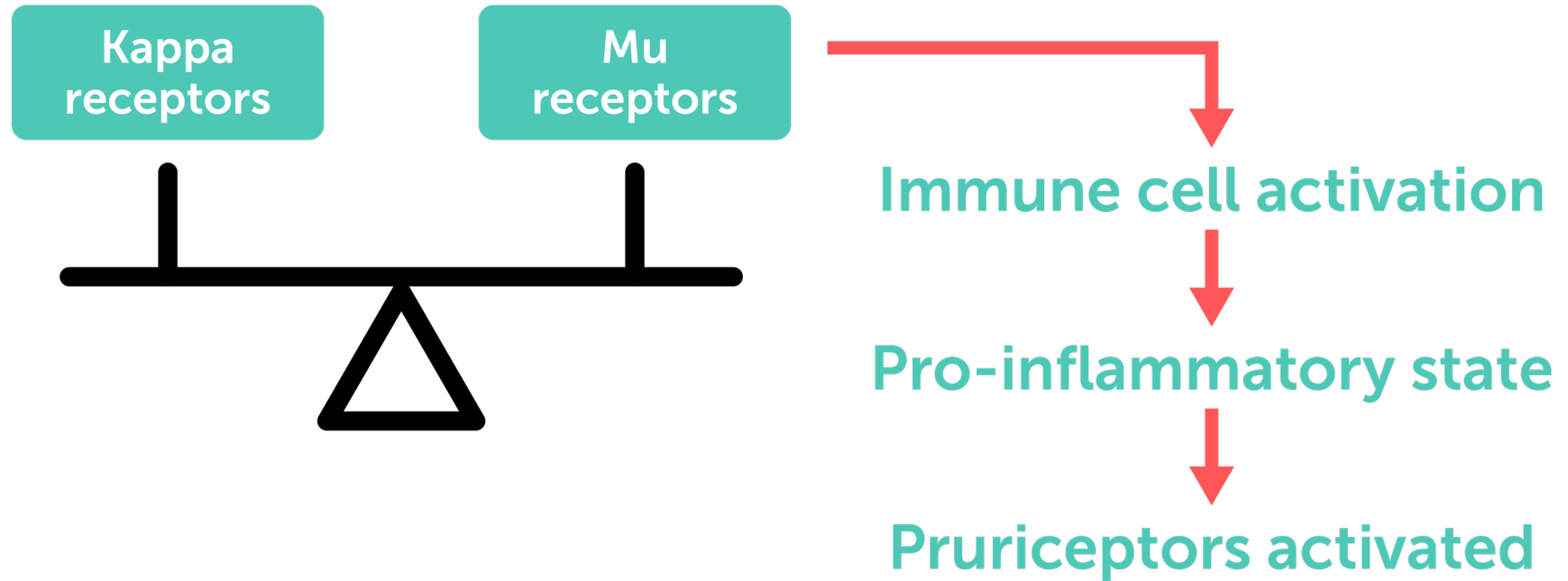
- Sleep quality has improved
- WI-NRS 2/10



Pathobiology of CKD-aP



CKD-aP Pathophysiology



Opioid receptors

- **K (kappa) receptors** – downgraded in pruritus
- **μ (mu) receptors**

Difelikefalin targets the **K (kappa) receptors**

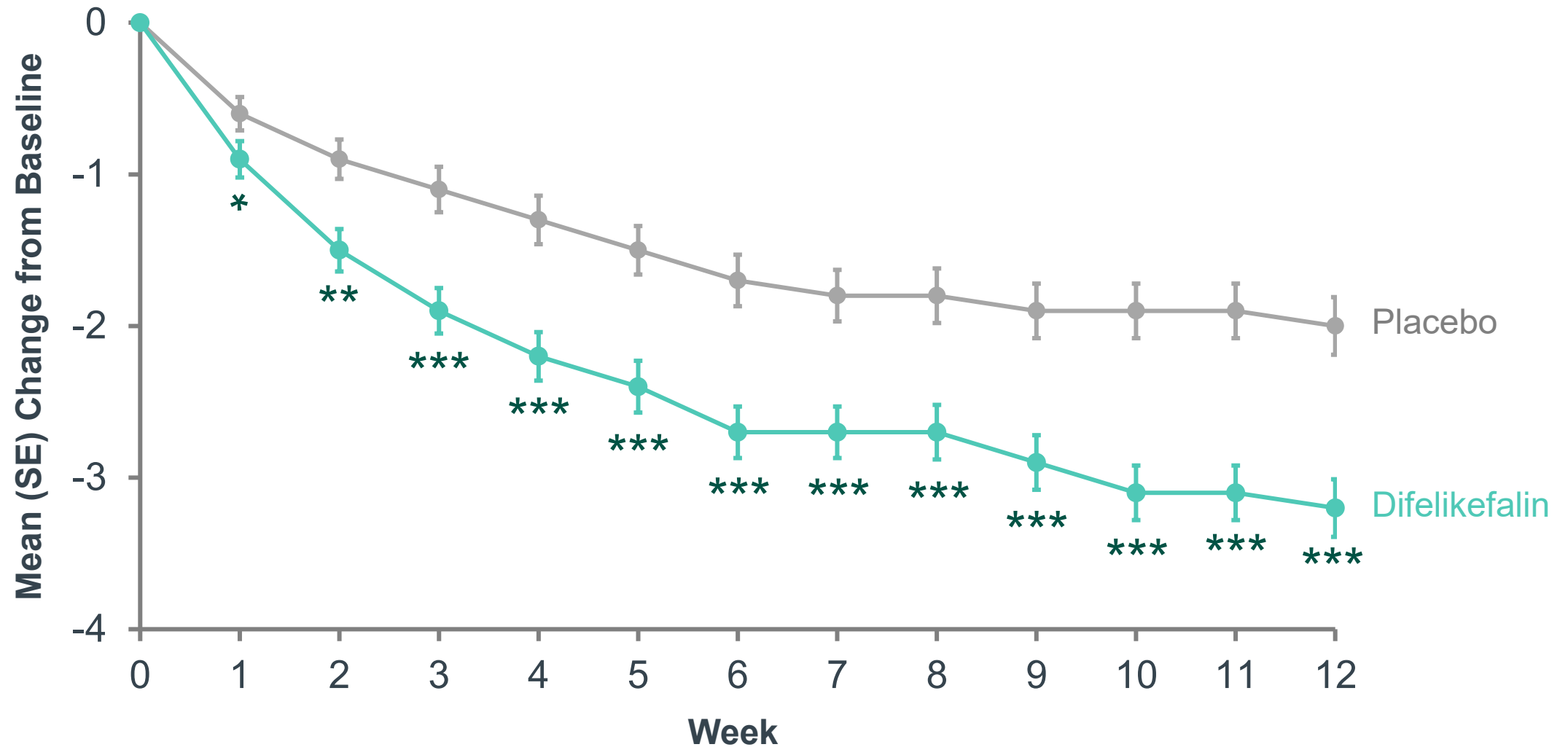


KALM-1 and KALM-2

- Phase 3
- 800 patients
- Difelikefalin vs placebo
- Duration: 12 weeks
- Endpoint: At least 3-point improvement in WI-NRS



Change in WI-NRS Score From Baseline Over 12 Weeks

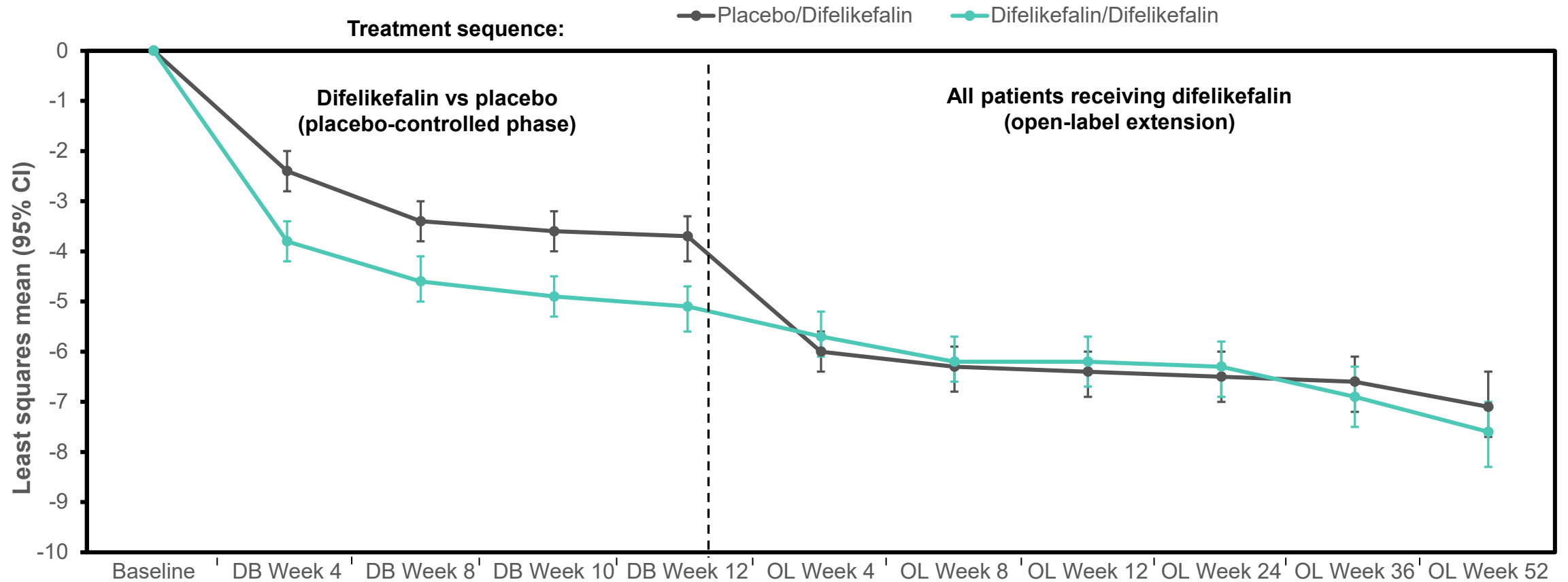


* $P < 0.05$, ** $P = 0.001$, *** $P < 0.001$ vs placebo.
Fishbane S, et al. *N Engl J Med.* 2020;382(3):222-232.



5-D Itch: Itch-Related QoL

52-week open-label extension of POOLED KALM-1 and KALM-2



No. of subjects:

Placebo/Difelikefalin	372	355	363	359	364	352	312	300	206	153	97
Difelikefalin/Difelikefalin	335	325	324	324	331	311	276	265	193	140	92

DB, double-blind; OL, open-label.

Adapted from Fishbane S, et al. NKF 2021 Spring Clinical Meetings. Abstract 87 and poster presentation.

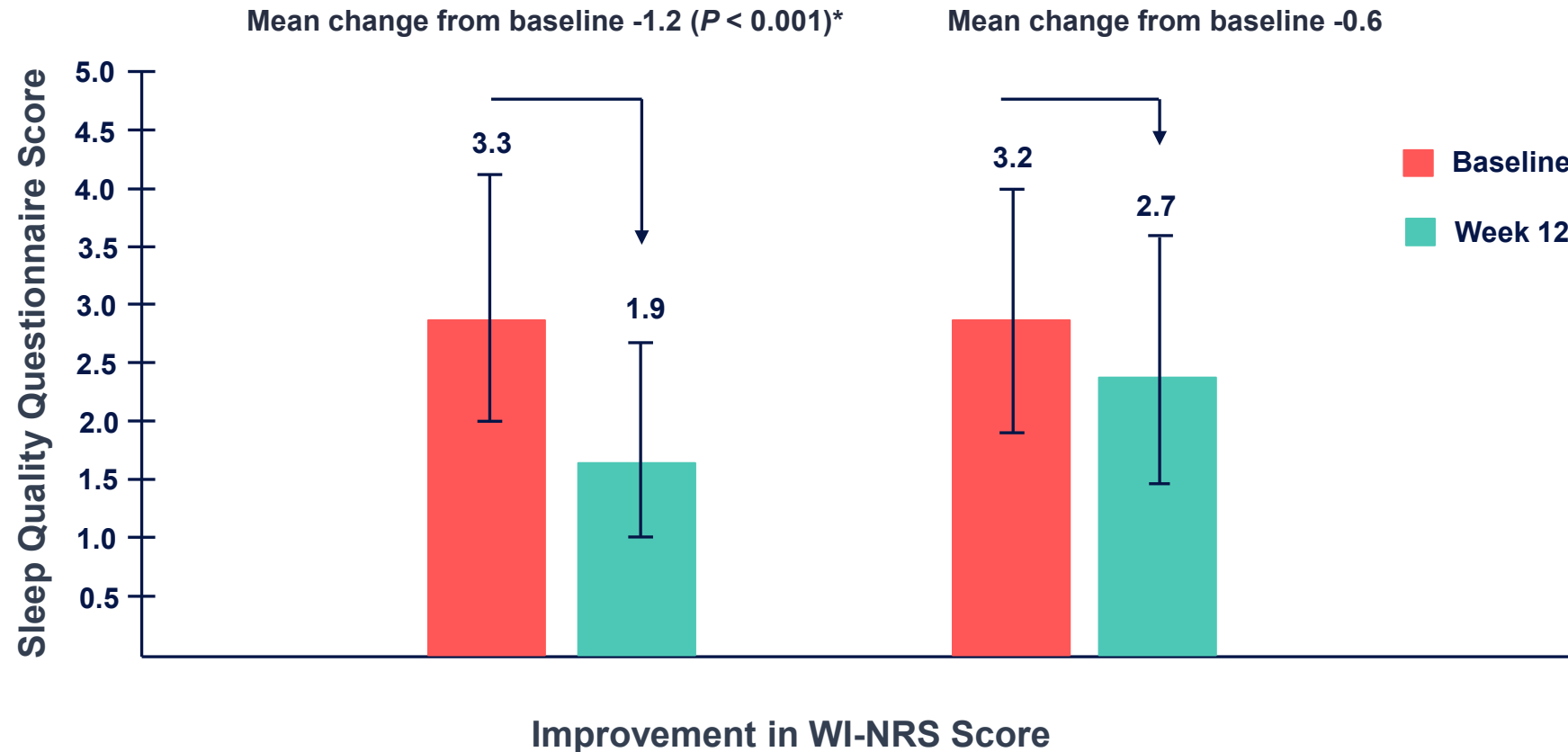


Other Treatments in CKD-aP

- Histaminergic pathway is **NOT involved** in CKD-aP
 - **Sedation** is the main side effect
 - Lack of evidence for their effectiveness
- 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**



Improvements in 5-D Itch Sleep Disability Question Score in Patients With vs Without a Clinically Meaningful Reduction in WI-NRS Score



*Improvements in mean 5-D itch sleep disability question score for patients with ≥ 3 -point WI-NRS score reduction vs < 3 -point reduction. WI-NRS, worse itch intensity numerical rating score. Ahdoot R, et al. *Kidney Int Rep.* 2022;7(2 suppl):S258.

KALM-1 & KALM-2

Randomized Phase 3 Clinical Trials (N = 851)

Clinically meaningful improvement at 12 weeks in adults on hemodialysis with moderate to severe CKD-aP	≥ 15-point ↓ of Skindex-10 (Itch-related QoL)	≥ 3-point ↓ of WI-NRS (Itch intensity)	≥ 5-point ↓ of 5-D Itch (Itch-related QoL)
Difelikefalin 0.5 mcg/kg IV 3x/week	55%	51%	52%
	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> < 0.01
Placebo	40%	35%	42%



Quote by Thilo Krueger, MD

“This drug [difelikefalin] is now the only one that is officially approved in the treatment of CKD-associated pruritus.”



Quote by Paul Bennett, PhD

“DFK, or difelikefalin, is one drug that we can use and we can add to our toolbox.”



Ongoing assessment every 3 months



Key Takeaway

- Difelikefalin is a treatment option for CKD-aP symptom clusters
- Providers need to ask patients about sleep disturbances, as well as itch



Key Takeaway

- Difelikefalin
 - Very well tolerated
 - Very effective



Key Takeaway

- Nurses are patient advocates

