

Live. Learn. Hope.

CKD-associated pruritus & Korsuva

Clinical Directors & Nurse Managers
April 2022



NORTHWEST
Kidney Centers

“The itch is driving me crazy!”



Mr. J was a 70 yo gentleman with ESKD due to DKD, former Marine and self-professed ‘tough guy’ on dialysis for 2 years with worsening itch, that was severe at night and made it hard to tolerate 4 hours of dialysis. His wife said it was so bad that she couldn’t sleep with him. He had tried skin creams, showers with oil, seen skin doctors, and the more he itched, the more he scratched.

‘Doc, is this common? Can’t we do something about this?’





CKD-aP - a.k.a uremic pruritus

- Common
- Distressing
- Under-recognized
- Treatment options limited
 - One FDA-approved in U.S. currently
 - Future options worth understanding
 - How to fold this in to current care system

CKD-aP - a.k.a. uremic pruritus



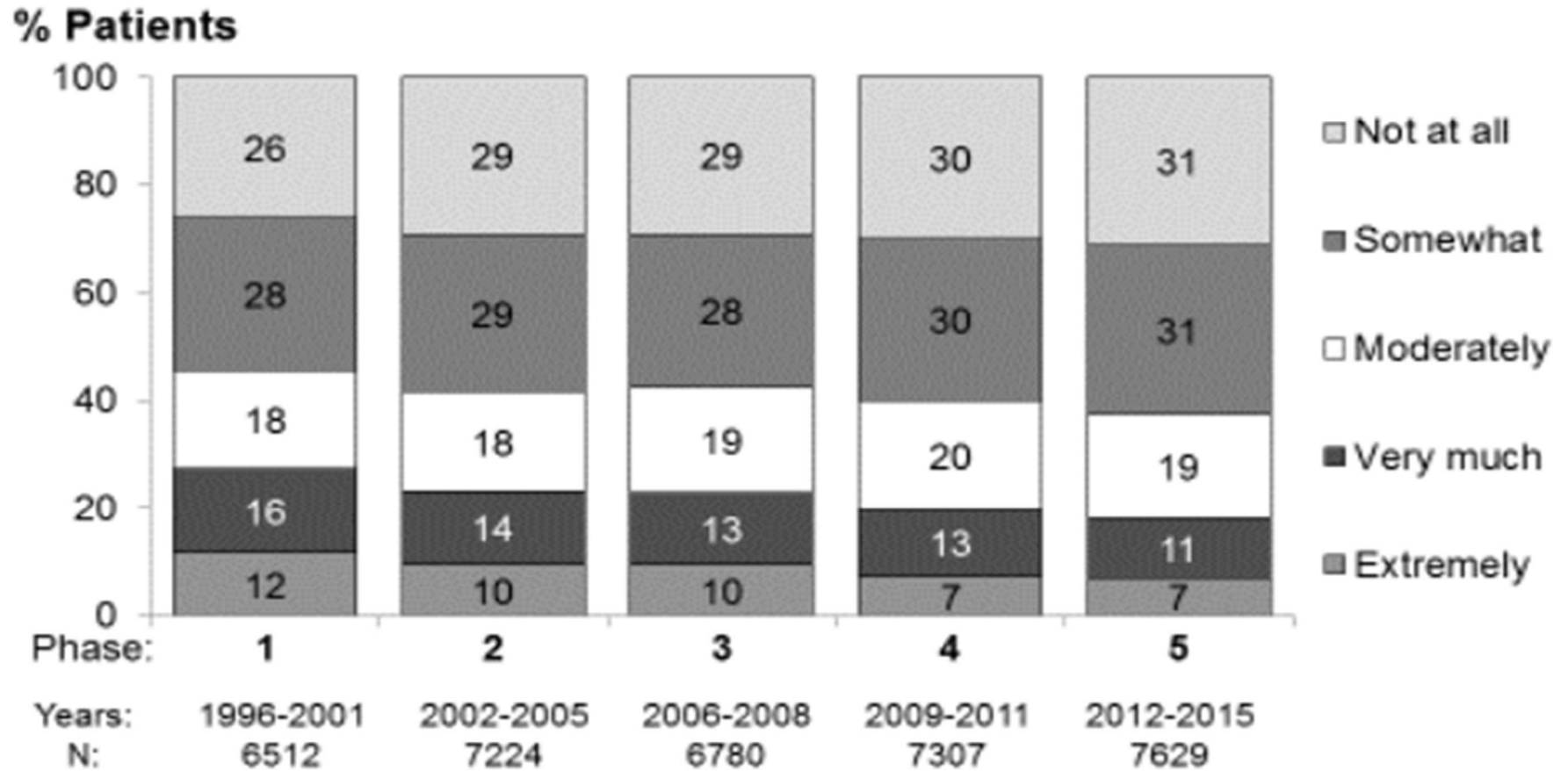
Clinical diagnosis - Itching directly related to kidney disease without another comorbid condition to explain it - However multifactorial. Bilateral and symmetrical, variable in intensity, may not have skin lesions.



Can See:

- Acute excoriations
- Hyperkeratotic nodules
- Deep scars & prurigo nodularis

CKD-aP in maintenance HD



Etiologies of CKD-associated pruritus

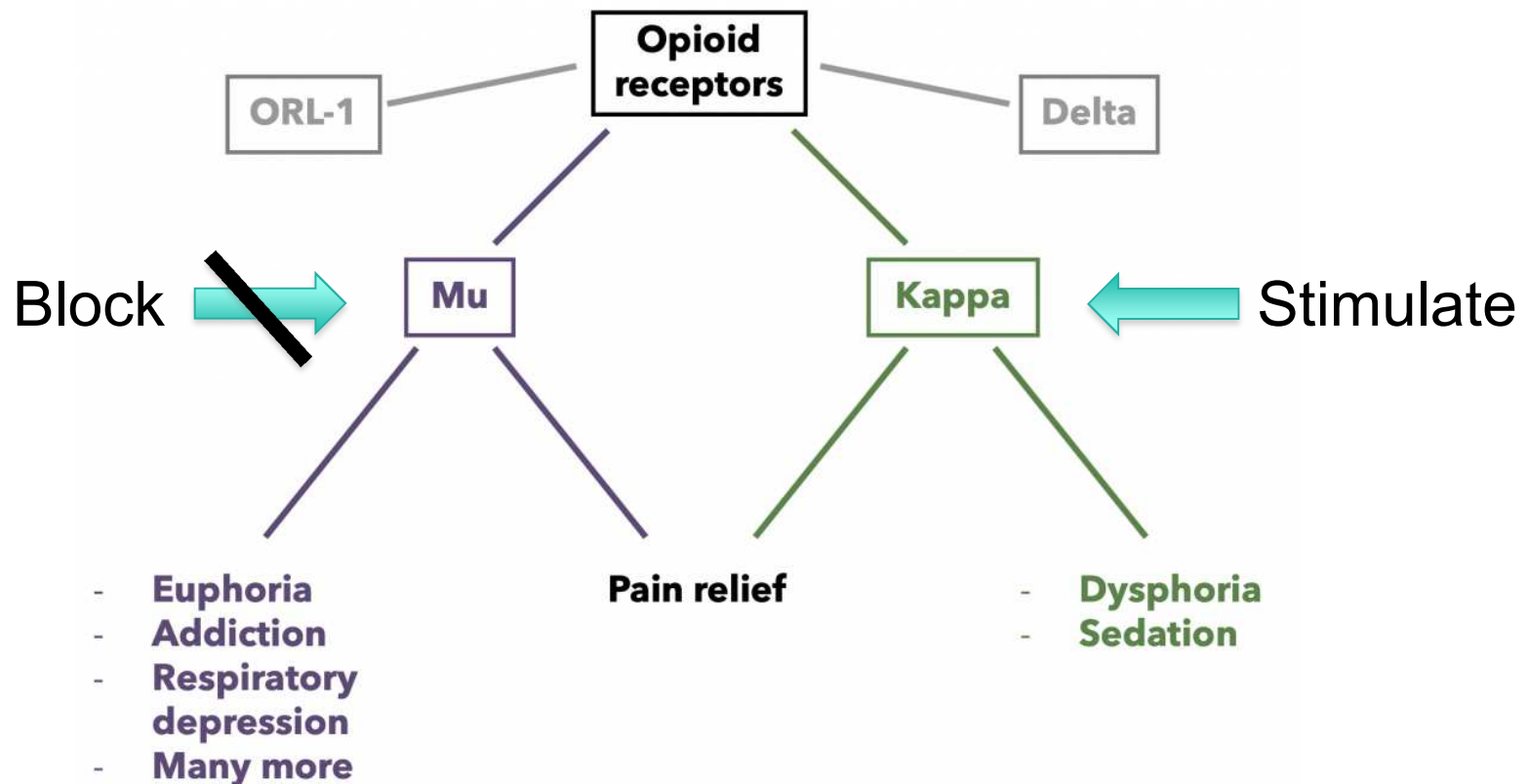


- Metabolic abnormalities
 - CKD-MBD abnormalities (high phosphorus, PTH, Ca++)
 - Inadequate dialysis - Kt/V as marker?
- Histaminergic reactions - but anti-histamines rarely effective
- Structural skin alterations
 - Xerosis (dry skin) – emollients; creams, oils
- Systemic inflammation - Increased markers associated with itch, UV phototherapy downregulates pro-infl. cytokines
- Alterations in nociceptive sensory pathways
 - Symmetric, 'burning, tingling'
 - Some success with gabapentin-oids
- Opioid receptor dysfunction
 - Mu receptor agonists promote itch v kappa suppresses
 - Some prior success in opioid modulation (nalfurafine, nalbuphine)

Etiologies of CKD-associated pruritus



- Opioid hypothesis
 - Mu-receptor activation, kappa-receptor blockade → incr pruritus



New treatment options



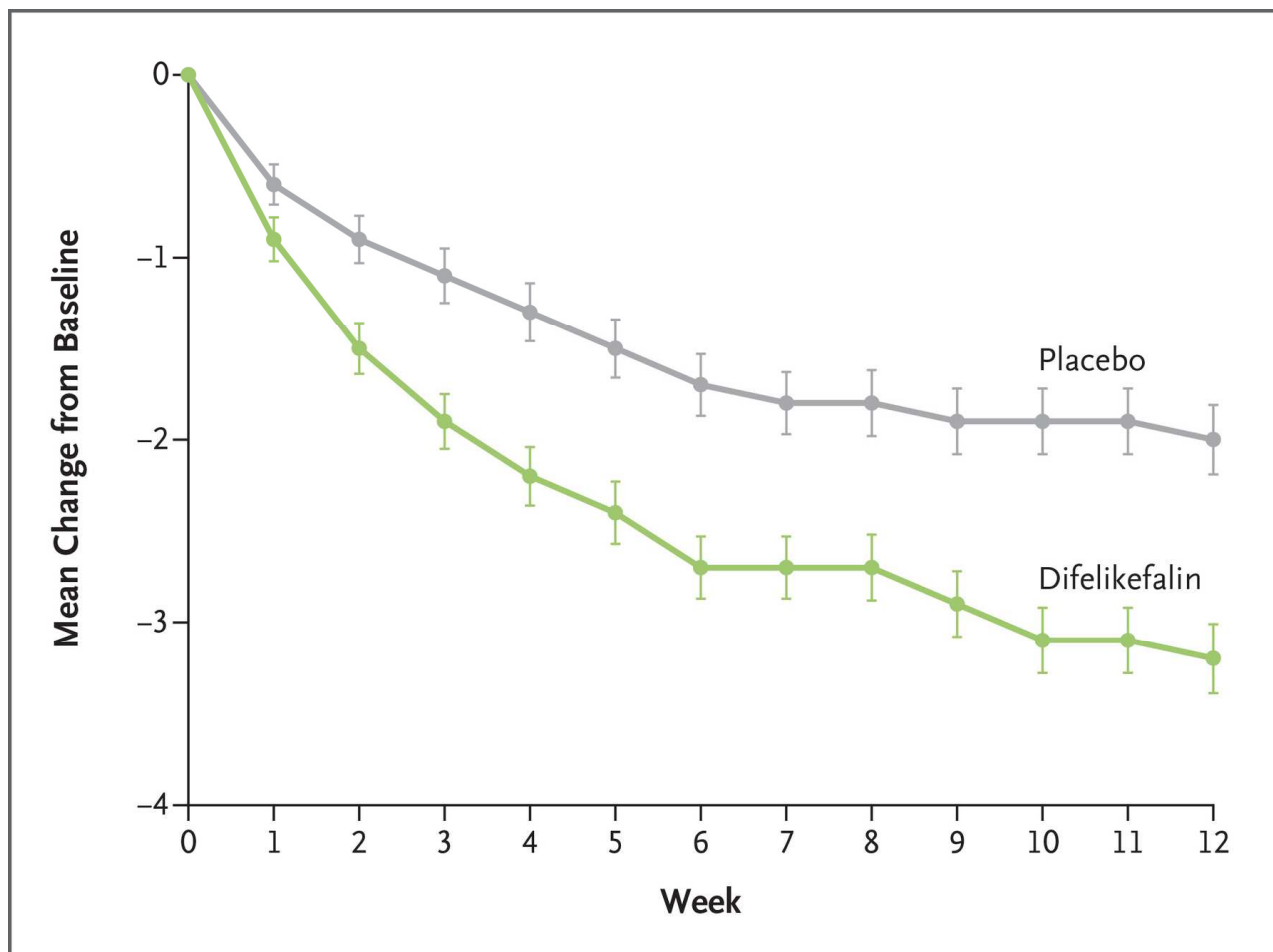
- Difelikefalin (Korsuva - Cara Therapeutics)
 - Initially underwent assessment as modulator of post-op pain, chronic pain, and pruritus
 - Peripherally restricted and selective agonist of kappa opioid receptors
 - Poor penetration of the blood-brain barrier
 - High kappa selectivity over other opioid receptors and no known affinity for non-opioid receptors
 - Modulates pruritus in CKD (possible modulator of pain)
 - Recommended 0.5mcg/kg IV, end of dialysis, venous line of circuit (65mcg/1.3mL)

Treatment options



- Difelikefalin (Korsuva - Cara Therapeutics)
 - Double-blind placebo-controlled phase 3 RCT
 - 378 in-center HD 3x/wk patients
 - Primary outcome - improvement of ≥ 3 pts WI-NRS in 12 wk
 - ‘Worst-Itch numeric rating scale’ 0 to 10,
 - Baseline WI-NRS > 4 (moderate to severe) – 4-5% of pts eligible
 - 37% v 18% reduction in pruritus score for difelikefalin versus placebo group

Primary Outcome



Fishbane NEJM 2020

Adverse Events



Event	Placebo	Difelikefalin
Any (%)	117 (62.2)	130 (68.8)
Diarrhea	7 (3.7)	18 (9.5)
Dizziness	2 (1.1)	13 (6.9)
Vomiting	6 (3.2)	10 (5.3)
SAE	41 (21.8)	49 (25.9)
Death	2	2
Fall (2wk later)	4 (2.2)	0

Drug Approval



- Evaluation by FDA August 23, 2021
 - +
 - This may substantially benefit patients +
 - +
- Eligible for payment outside the bundle? (TDAPA - tbd)
- On everyone's radar
 - LDOs have teams at the ready for this
 - Discussed with CMS
 - Will it require oversight similar to other opioids?
 - Who will be eligible to receive? (4%? 30-40% moderate-severe? all 55%? What process? Very few qualified for study. Do we use similar characteristics? How will this be priced?)



Patient Need vs. Payment Policy

- Shouldn't patient need drive drug use?
- Would value-based programs help?
 - Kidney Care Voluntary Models
 - Get medication to appropriate patients to decrease worse outcomes (e.g. prevent hospitalization)
- What are appropriate drug pricing practices?
 - Preliminary payment projection is **\$150.15** per vial
 - \$1951.95 cost per month (13 HD treatments)

Summary



- Pruritis is common among dialysis patients.
- Associated with inadequate dialysis, dry skin, and Mineral Bone Disorders
- First line treatments:
 - Optimize dialysis
 - Control phosphorus and PTH
 - Emollients
 - Avoid scratching!
- Second line treatments
 - Oral antihistamines
 - Gabapentin and Pregabalin (anti-convulsant)
 - ?Sertraline (anti-depressant)
 - Opioid receptor blockers – including difelikefalin.
- **HOW SHOULD NKC CONSIDER ROLLOUT of this new medication?**

Pruritus Assessment - Difelikefalin Request



Patient Name: _____ DOB: _____

Does your patient have a diagnosis of Uremic Pruritus? (ensure this is documented in NKC EMR) YES NO

Has your patient received therapy for uremic pruritus? YES NO

If YES, list therapies tried or currently taking (e.g. emollients, gabapentinoids, UV Rx, other anti-pruritics)

Emollients Improved Symptoms YES NO

Gabapentinoids Improved Symptoms YES NO

UV therapy Improved Symptoms YES NO

Other _____ Improved Symptoms YES NO

Itch – Description: location, time (e.g. only at dialysis), rash associated

Adequate dialysis for last 2 months: YES NO

| Worst Itching Over the Past 24 Hours | | | | | | | | | | |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Please indicate the worst itching you experienced over the past 24 hours | | | | | | | | | | |
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
| <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| No itching | | | | | | | | | Worst itching | |
| Mild | | | | Moderate | | | Severe | | | |

Score for your patient at minimum on 2 different occasions, optimally more than 24 hours apart. Document dates.

#1 Score: _____ Date: _____

#2 Score: _____ Date: _____

Current opioid use: YES NO; if YES, what is Rx? _____

Does patient have allergy to opioids? YES NO

Process



- **Medication still not available**
- MEC reviewed in February and March.
 - asked to see how medication is tolerated nationally
 - Re-address in 1-3 months
- Requesting medical staff will fill out request
- Process to be finalized
 - Pharmacy in communication with company
 - Pricing not finalized on Pharmaceutical side
 - Administration protocol & education rollout in process
- Please contact me for additional questions
- After rollout, will refine and update process
 - E.G. THIS IS NOT A FINAL PROTOCOL – INPUT WELCOME!

Administration



- 65 mcg vial
- Up to 65mcg (also get paid for what is discarded)
- IV at end of dialysis, every HD in center treatment.
- Side Effects noted – GI (N/D)

“The itch is driving me crazy!”



Mr. J was diagnosed with uremic pruritus by me and his new dermatologist.

- Prescribed specific emollients
- Began gabapention 100mg 3x/d
- Started UV phototherapy
- Tried not to scratch his itch

Pruritus improved mildly



THANK YOU!



- QUESTIONS?
- COMMENTS?