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Impact of Difelikefalin on 5D-Itch Domains in Patients With CKD-Associated Pruritus

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evaluation of different domains and approaches to measure CKD-aP burden, and may further help tailor data capture for future research or clinical care.

Methods: An electronic PRO (ePRO) survey was distributed to HD patients enrolled in the Dialysis Outcomes and Practice Patterns Study (DOPPS) in 2021-2022, and included 4 CKD-aP instruments: (1) a single question from the KDQOL-36 about the extent patients were bothered by itchy skin; (2) the 5-D itch, which assesses five dimensions of itch; and questions about the (3) worst itch [WI-NRS] and (4) average itch [AI-NRS] experienced. We calculated the Spearman correlation between each instrument, and stratified mean 5-D itch and NRS scores by response to the single KDQOL-36 question.

Results: Data collection is ongoing; 250 patients from 24 HD facilities in 4 countries (France, Germany, Spain, UK) have thus far completed the baseline survey. Patients 'not at all' bothered by itchy skin (N=104; 41%) were not asked to complete other CKD-aP instruments. Among the remaining 146 patients, the KDQOL-36 response was correlated with the WI-NRS (0.49), AI-NRS (0.52), and 5-D itch (0.56) – more so with the degree (0.67) and duration (0.55) domains than the distribution (0.42), disability (0.32), and direction (0.21) domains. Across response levels (somewhat, moderately, very much, extremely) of the KDQOL-36 question, the respective mean scores of other CKD-aP instruments were 10.0, 11.7, 14.7, 20.8 for 5-D itch; 2.7, 3.7, 5.6, 8.3 for AI-NRS; and 3.0, 4.1, 6.1, 8.4 for WI-NRS.

Conclusions: Correlation between CKD-aP instruments was relatively high; differences can be partially attributed to the recall period for the KDQOL-36 (4 weeks) vs. the 5-D itch (2 weeks) and NRS (24 hours). Understanding the relationships between CKD-aP instruments will help us interpret and link findings across observational and randomized studies that use different approaches to measure CKD-aP.

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SA-PO286

Improvement of Itch With Difelikefalin in CKD Patients on Dialysis by Baseline Itch Severity

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Background: Difelikefalin (DFK) is a peripherally restricted κ-opioid receptor agonist that reduces itch severity in patients with chronic kidney disease-associated pruritus (CKD-aP) undergoing hemodialysis (HD). The purpose of this analysis was to determine if baseline severity of itch impacts the efficacy of DFK.

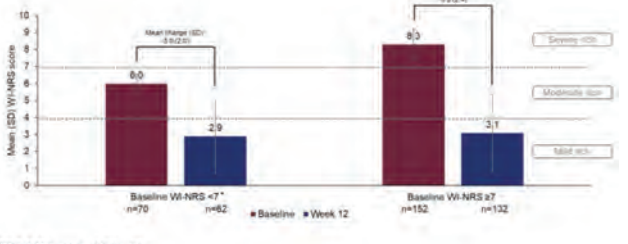
Methods: This was a secondary analysis of a multicenter, open-label study (3105) of intravenous DFK treatment (0.5 μg/kg, 3x per week) in patients on HD with moderate-to-severe CKD-aP (worst itch numerical rating scale [WI-NRS] ≥5). Participants were categorized based on itch severity at baseline as assessed by WI-NRS scores as either moderate (WI-NRS <7) or severe (WI-NRS ≥7). Patients were treated for 12 weeks and mean change in WI-NRS from baseline to the end of week 12 was determined.

Results: Among 222 participants, 70 patients had moderate pruritus (mean ±standard deviation WI-NRS: 6.0 ±0.5) and 152 patients had severe pruritus (8.3 ±0.9) at baseline. Patients with moderate and severe itch at baseline reported on average mild pruritus (WI-NRS <4) at Week 12 (2.9 ±2.2 and 3.1 ±2.3) following an improvement of -3.0 ±2.0 and -5.2 ±2.4 points, respectively, with similar relative improvements in the means from baseline of 51.7% and 62.7%, respectively (**Figure**).

Conclusions: Following 12 weeks' treatment with DFK, itch was on average reduced to mild intensity in patients with both moderate and severe disease at baseline. Together, these data suggest that DFK effectively reduces itch severity in patients with CKD-aP on HD, irrespective of baseline itch severity.

Funding: Commercial Support - Vifor Pharma

Figure: Reduction in itch by baseline itch severity following 12 weeks' treatment with difelikefalin



*WI-NRS score of 5 to <7.

WI-NRS, worst itch numerical rating scale; SD, standard deviation.

SA-PO287

Pruritus in Patients With ESKD on Hemodialysis: Initial Results From a Prospective Patient Survey Study

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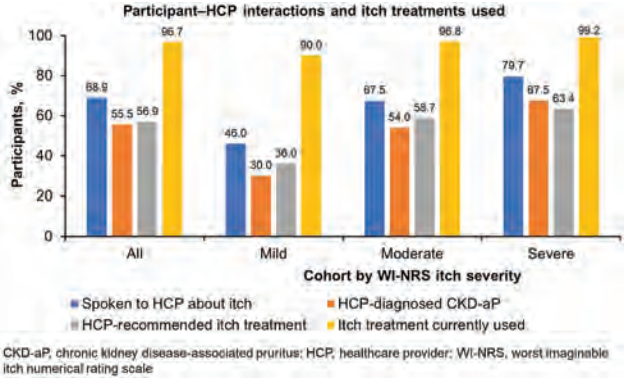
Background: Chronic kidney disease-associated pruritus (CKD-aP) is common in patients on hemodialysis (HD). Real-world assessment of the patient's perspective of pruritis is needed. A US-based patient survey assessed treatment, and the humanistic and economic burden of CKD-aP.

Methods: Eligible participants were ≥18 years old with healthcare provider (HCP) diagnosed ESKD on 3 times/week HD. They self-reported itch assessed on a modified 28-day recall period using the worst itch numerical rating scale (WI-NRS; 0=no itch to 10=worst itch), from which they were stratified into mild (1–3), moderate (4–6), and severe (7–10) cohorts. Sleep quality was assessed on a 0–10 scale (10=itch completely interfered with sleep in the past 24 hours).

Results: Of 299 completed surveys (2/3 planned population) from December 2021 to May 2022: 50, 126, and 123 were stratified into mild, moderate, and severe itch cohorts, respectively. Overall participants were 53% female, 53% white/non-Hispanic, 43% on Medicare plans, and 70% on in-center HD. Proportions of patients who had discussed chronic itch with an HCP, were diagnosed with CKD-aP, received HCP-recommended treatment, or were currently taking itch treatment increased with itch severity (**Figure**). Greater itch severity was associated with high/extremely high self-reported itch burden (mild=4.0%, moderate=26.2%, severe=39.8%), and sleep disruption (mild=2.3, moderate=4.6, and severe=6.4). Topical treatment was ubiquitous in all cohorts (100%) while systemic treatment was limited even in moderate to severe itch cohorts (24–40%).

Conclusions: More severe itch scores were associated with a greater likelihood of patient–HCP engagement about itch and related treatment, and poorer sleep quality. A gap in addressing itch is suggested by a lower rate of HCP-recommended treatment (57%) or HCP-diagnosed CKD-aP (56%) vs patients reporting itch to HCPs (69%), and limited use of systemic treatment in moderate to severe itch cohorts.

Funding: Commercial Support - Vifor Pharma



CKD-aP, chronic kidney disease-associated pruritus; HCP, healthcare provider; WI-NRS, worst imaginable itch numerical rating scale

SA-PO288

Impact of Difelikefalin on 5D-Itch Domains in Patients With CKD-Associated Pruritus

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Background: Chronic kidney disease-associated pruritus (CKD-aP) is common in hemodialysis (HD) patients, impacting quality of life (QoL). In the Phase 3 KALM studies, difelikefalin (DFK), a selective kappa opioid receptor agonist approved in the United States and Europe for the treatment of moderate–severe pruritus in adults undergoing HD, improved itch intensity and QoL. The impact of DFK treatment on the subdomains of the 5D-itch scale (a multidimensional questionnaire validated in patients with chronic pruritus) were explored.

Methods: In this pooled KALM-1 and KALM-2 analysis (n=712), HD patients with moderate–severe CKD-aP were randomized 1:1 to receive intravenous DFK 0.5 μg/kg or placebo (PBO) 3 times/week (Wk) for 12 Wks (double-blind [DB], PBO-controlled phase), followed by an up to 52-Wk open-label extension ([OLE] all patients receiving DFK). The change from DB baseline (BL) in 5D-itch scale domains was assessed including duration, degree, direction, and body distribution of itch and disability (sleep and daily activities) with a 2-Wk recall period.

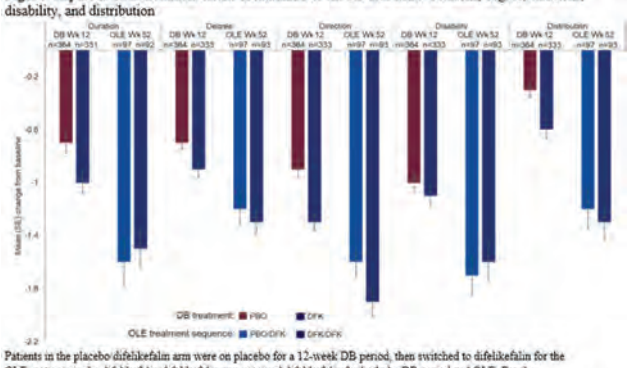
Results: In the DB phase, patients on DFK reported greater improvements than PBO in all domains. Throughout the OLE, patients reported ongoing improvements: Duration of itch (~6 h/day at OLE Wk 52 vs ~12–18 h/day at BL); Degree ("mild-moderate" vs "moderate-severe" at BL); Direction ("a little/much better" vs

"unchanged" at BL); Disability, ("rarely" affected daily activities [including sleep] vs "frequently/occasionally" affected at BL); and Distribution (3–5 body parts affected vs 6-10 at BL).

Conclusions: In the 12-wk DB period patient-reported improvements in 5D-itch scale domains were greater with DFK than PBO. In the OLE, with all patients receiving DFK up to 52 wks, further improvements were observed across all domains.

Funding: Commercial Support - Vifor Pharma

Figure: Impact of DFK treatment on the subdomains of the 5D-itch scale: duration, degree, direction, disability, and distribution



Patients in the placebo difelikefalin arm were on placebo for a 12-week DB period, then switched to difelikefalin for the OLE; patients in the difelikefalin/difelikefalin arm received difelikefalin for both the DB period and OLE. For the distribution domain, the number of affected body parts is tallied (potential sum 0–16) and the sum is sorted into five scoring bins: sum of 0–2 = score of 1, sum of 3–5 = score of 2, sum of 6–10 = score of 3, sum of 11–13 = score of 4, and sum of 14–16 = score of 5. For the disability domain, daily activities include sleep, leisure social, housework/errands, and work/school. DB=double-blind; DFK= difelikefalin; OLE = open-label extension; PBO= placebo; SE = standard error; Wk = week.

SA-PO289

Insights Into Current Practices and Unmet Needs Relating to CKD-Associated Pruritus: Results From a Canadian Nephrologist Survey

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Background: Chronic kidney disease-associated pruritus (CKD-aP) is a common condition in patients with CKD undergoing hemodialysis (HD). In this real-world study, Canadian nephrologists were surveyed to gain insight into current practices and unmet needs related to the treatment of CKD-aP.

Methods: Quantitative data regarding the perception of current treatment practices for CKD-aP were collected in November and December 2021 by a 20-minute survey completed by 62 nephrologists across Canada. Respondents' level of agreement was assessed using a 7-point scale.

Results: In current practice, the mean perceived prevalence of CKD-aP in HD patients was 30.5%. Of these, 33.6% and 18.3%, respectively, experience moderate or severe CKD-aP. CKD-aP was most frequently identified (75.8% of cases) through patients complaining of itch to the multidisciplinary health care team. In clinical practice 63% of respondents currently do not use formal scales to diagnose and assess CKD-aP. Treatments used for severe and moderate CKD-aP are shown in the table. Nephrologists used topical moisturizers / emollients (85%), oral antihistamines (14%), and gabapentinoids (2%) as first-line treatments. Nephrologists reported 42% of patients with severe CKD-aP and 41% with moderate CKD-aP do not respond to treatment. Most nephrologists (94%) agreed there is a need for new treatments specifically designed to address CKD-aP, 68% agreed they do not expect to resolve a patient's CKD-aP with currently available treatments, 89% agreed CKD-aP is challenging to treat, and 69% agreed there is a need for guidelines for the treatment of CKD-aP.

Conclusions: This real-world Canadian study of nephrologists showed that CKD-aP is challenging to treat and many patients do not respond to currently-available treatments. There is an urgent unmet need for new, more effective treatments and for guidelines to aid nephrologists in selecting therapy for their patients with CKD-aP.

Funding: Commercial Support - Otsuka

Treatment Choices

Treatment	Reported use in severe CKD-aP (%)	Reported use in moderate CKD-aP (%)
Topical moisturizers / emollients	78	69
Oral antihistamines	58	37
Gabapentinoids	51	31
Topical corticosteroids	35	20
UVB therapy	22	8
Antidepressants / anxiolytics / sedatives	14	5

SA-PO290

Quantifying Physical Activity Behavior Among Adults Undergoing Hemodialysis Using a Gait Assistive Device: A Prospective Observational Study

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Background: People undergoing Hemodialysis (HD) have a higher burden of frailty and physical inactivity. This study aimed to quantify physical activity, strength, depression, and fall risk in people undergoing HD using gait assistive devices (GADs).

Methods: Participants undergoing routine HD were grouped based on the use of any GADs. Physical activity was measured over two consecutive days using a validated pendant sensor. Grip strength, concerns for falling and depression were assessed on FES-I and Center for Epidemiological Studies-Depression Scales.

Results: 136 participants were grouped into those prescribed GADs (n = 39, age = 55.7 ± 1.3 years, female = 40.6%) and no NGAD (n = 97, age = 68.6 ± 1.4 years, female = 61.5%). The proportion with cognitive impairment (40% vs. 23%), depression (51% vs. 16%), and concern of falling (84% vs. 38%) were greater in the GAD vs. NGAD group. Furthermore, number of postural transitions was negatively correlated with FES-I ($\rho = -0.33$, $p < 0.01$) and CES-D ($\rho = -0.22$, $p = 0.025$) scores.

Conclusions: People undergoing routine HD and using GADs showed high fear of falling, depression, and cognitive decline. Furthermore, reduced postural transition was associated with heightened fear of falling and depression level.

Funding: Government Support - Non-U.S.

Table 1. Demographic, clinical, patient reported outcomes of the subject using and not using GAD. Continuous parameters are reported as mean ± standard error and categorical outcomes are reported as Number of subjects with the condition/Total subject (percentage).

	NGAD (n= 97)	GAD (n = 39)	p-value	Effect Size
Demographics				
Age, *years*	55.7 ± 1.3	68.6 ± 1.4	**< 0.01**	**1.10**
Gender (Female), %	40.6	61.5	**0.027**	**0.19**
Body Mass Index, *kg/m²*	30.3 ± 0.7	32.0 ± 1.1	0.19	0.25
Clinical characteristics				
History of falls in past year, %	16.5	31.6	0.052	0.17
History foot ulcer, %	13.4	7.7	0.35	0.08
HbA1c, %	7.1 ± 0.2	6.7 ± 0.2	0.17	0.27
Duration of Diabetes, years	18.7 ± 0.8	17.6 ± 0.6	0.40	0.16
VPT, volts	26.5 ± 1.4	31.8 ± 2.9	0.07	0.35
Presence of Neuropathy, %	43.3	56.4	0.09	0.19
Grip Strength, kg	19.0 ± 0.8	15.7 ± 1.6	**0.05**	**0.38**
Patient-Reported Outcomes				
MoCA, score	25.9 ± 0.5	24.7 ± 0.7	0.09	0.30
Cognitive impairment ≤ 25, %	23	39.5	0.06	0.17
CES-D, score	10.2 ± 0.7	17.3 ± 1.7	**< 0.01**	**0.82**
Depression ≥ 16, %	16	51	**< 0.01**	**0.36**
Short FES-I, score	9.5 ± 0.4	15.9 ± 1.0	**< 0.01**	**1.50**
High concern for falling > 10, %	38	84	**<0.01**	**0.41**
Frailty				
Robust, %	22	5	**0.02**	**0.21**
Pre-frailty, %	45	44.7	0.96	<0.01
Frailty, %	32	50	0.06	0.17