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Improvements in Itch-Related Quality of Life with Difelikefalin for Moderate-to-Severe Chronic Kidney Disease-Associated Pruritus: Pooled Analysis of KALM-1 and KALM-2 Phase 3 Studies in Hemodialysis Patients

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Background: Chronic kidney disease–associated pruritus (CKD-aP) is common in patients (pts) undergoing hemodialysis (HD) with a negative impact on quality of life (QoL). Difelikefalin, a selective kappa opioid receptor agonist in development for CKD-aP, significantly reduced itch intensity based on the Worst Itching Intensity Numerical Rating Scale (WI-NRS) and was generally well tolerated in pts with moderate-to-severe CKD-aP on HD in US (KALM-1) and global (KALM-2) phase 3 studies. Here we report itch-related QoL outcomes in a pooled analysis of KALM-1 and KALM-2.

Methods: HD pts with moderate-to-severe CKD-aP were randomized to intravenous difelikefalin 0.5 mcg/kg (DFK) or placebo (PBO) 3 times/week (wk) for 12 wks. QoL was assessed with multidimensional itch-related questionnaires (5-D Itch and Skindex-10 scales) validated in this pt population. Pooled data were analyzed based on mixed model for repeated measures.

Results: There were 851 pts in the pooled studies (DFK: 426; PBO: 425). Mean (SD) baseline WI-NRS scores were 7.2 (1.4; DFK) and 7.2 (1.5; PBO), confirming moderate-to-severe itch. The primary endpoint (≥3-point WI-NRS reduction at wk 12) was met in each study; estimates for the pooled population were 51.1% with DFK vs 35.2% with PBO ($P<0.001$). DFK showed overall greater and clinically meaningful improvements in 5-D Itch and Skindex-10 total scores vs PBO. At wk 12, improvements in most individual 5-D Itch and Skindex-10 domains were greater with DFK vs PBO.

Conclusion: DFK administered for 12 wks to pts with moderate-to-severe CKD-aP undergoing HD resulted in significant relief of their itching accompanied by meaningful improvements in itch-related QoL.

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