Efficacy of Difelikefalin in Subjects With Moderate to Severe Chronic Kidney Disease–Associated Pruritus: Pooled Subgroup Analysis of KALM-1 and KALM-2

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SYNOPSIS

Moderate-to-severe pruritus can substantially impair quality of life (QoL) in subjects with chronic kidney disease (CKD). Difelikefalin (DFK) is a novel, selective kappa-opioid receptor agonist with minimal central nervous system (CNS) effects. In August 2021, intravenous (IV) DFK received approval from the US Food and Drug Administration for the treatment of moderate-to-severe pruritus associated with chronic kidney disease (CKD) and undergoing hemodialysis (HD).

METHODS

KALM-1 and KALM-2 were randomized, phase 3, multicenter, placebo-controlled studies (Figure 1). KALM-1 was conducted in the United States, and KALM-2 was conducted in the United States, Canada, Europe, Asia, Australia, and New Zealand. Subjects with moderate-to-severe CKD-associated pruritus (CKD-AAP) undergoing HD were randomized to IV DFK 0.5 mg/kg or placebo 3 times/week for 12 weeks.

OBJECTIVE

To further the understanding of the efficacy profile of DFK, we report efficacy and QoL outcomes in the pooled KALM-1 (NCT03452260) and KALM-2 (NCT03636269) study population, including a subgroup analysis based on baseline characteristics.

RESULTS

5-D itch scale

• Other endpoints included achievement of complete response (i.e., ≥80% of weekly WI-NRS scores equal to 0 or 1 for the preceding week); achievement of 15-point improvement from baseline in Skindex-10 total score, and achievement of 15-point improvement from baseline in 5-D itch total score.

• Worst itching intensity numerical rating scale.

• The WI-NRS is a validated 11-point scale ranging from 0 to 10. (Figure 2)

• Statistical analyses

• Skindex-10 scale

• Skindex-10 scale

• Table 1: Demographics and Baseline Disease and Itch Characteristics

• Subgroup % of Responders

• Table 2: Post-hoc Analysis of the Primary Endpoint

• The primary endpoint, proportion of subjects achieving ≥50% improvement in WI-NRS score at Week 12 in KALM-1 and KALM-2.

• Achievement of ≥50% improvement in weekly WI-NRS score was evaluated in subgroups based on baseline characteristics using pooled KALM-1 and KALM-2 data.

• CONCLUSIONS

• In this pooled analysis of the US KALM-1 and global KALM-2 studies, the efficacy of DFK 0.5 mg/kg was maintained across multiple demographic and baseline characteristics compared with moderate-to-severe CKD-AAP undergoing HD.

• Subjects who received IV DFK achieved statistically meaningful improvements in itch intensity regardless of prior anti-itch medication use.

• Rates of complete response in WI-NRS were significantly greater with DFK versus placebo as early as week 3 in the pooled population and maintained through week 12.

• These pooled efficacy findings suggest IV DFK may play an important role in the care of CKD patients undergoing HD by reducing itch and improving QoL.

REFERENCES


CORRESPONDENCE

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