Rapid Reduction and Free or Almost Free of Itch Response With Oral Difelikefalin in Subjects With Notalgia Paresthetica and Moderate-to-Severe Pruritus

Mark Lebwohl, MD[1]; Brian S. Kim, MD, MTR[1]; Javier Alonso-Llamazares, MD[2]; Zoe Diana Draelos, MD[3]; Kristine Nograles, MD[4]; Joana Goncalves, MD[4]; Joshua Cirulli, PharmD[4]; Jennifer A. Mohawk, PhD[4]; Catherine Munera, PhD[4]; Tom Xue, PhD[4]; Robert H. Bissonnette, MD, FRCPC[5]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Coral Gables Dermatology & Aesthetics, Coral Gables, FL, USA; [3]Dermatology Consulting Services, PLLC, High Point, NC, USA; [4]Cara Therapeutics, Stamford, CT, USA; [5]Innovaderm Research, Montreal, QC, Canada

SYNOPSIS

- Notalgia paresthetica (NP) is a common neuropathic itch characterized by pruritus of the upper back[1]
- This phase 2, multicenter, randomized, double-blind study was conducted in subjects with NP and moderate-to-severe pruritus who were randomized to oral difelikefalin (DFK, 2 mg), a kappa-opioid receptor agonist, or placebo twice daily for 8 weeks
- Of the 126 subjects included in this analysis, strict complete response rates (100% of daily Worst Itch Numeric Rating Scale [WI-NRS] scores equal to 0 or 1 during the week) were significantly greater in subjects treated with DFK (14%) versus placebo (1%) as early as week 3 (*P*=0.045) and were maintained through week 8 (25% vs 4%; *P*=0.006)
- Individual WI-NRS scores demonstrated rapid onset of DFK efficacy, which was maintained through week 8
- In subjects with NP, 8 weeks of treatment with DFK led to rapid improvement in itch intensity
- These findings support the role of kappa-opioid receptor activation to control neuropathic itch

OBJECTIVES

- To evaluate free or almost free of itch response rates with oral DFK for the treatment of moderate-to-severe pruritus in subjects with NP in the KOMFORT study
- To examine itch response over time with oral DFK in individual subjects with moderate-to-severe pruritus associated with NP in the KOMFORT study

METHODS

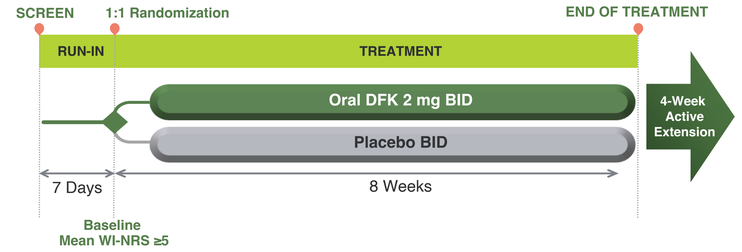
Study Design

- Phase 2, multicenter, randomized, double-blind study conducted in subjects with NP and moderate-to-severe pruritus who were randomized to oral DFK 2 mg or placebo twice daily for 8 weeks (**Figure 1**)
  - Study design[2] and primary results[3] were previously reported

Assessments

- Proportion of subjects who were free or almost free of itch
- Itch severity over time, as measured by weekly mean WI-NRS scores
  - Free or almost free of itch: WI-NRS 0 or 1
  - Mild: WI-NRS >1 to <4
  - Moderate: WI-NRS 4 to <7
  - Severe: WI-NRS 7 to 10

Figure 1. KOMFORT: Phase 2 Study Design

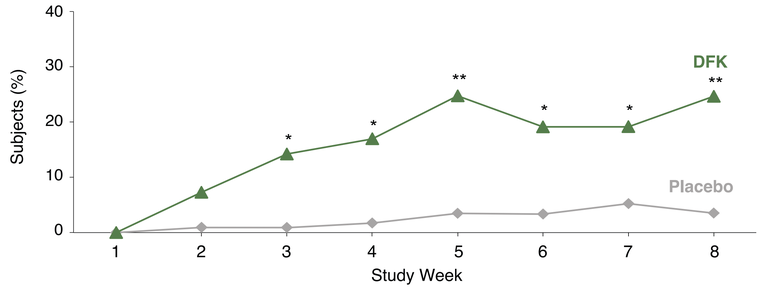


ClinicalTrials.gov: NCT04706975.
BID, twice daily.

RESULTS

- In total, 126 subjects were randomized to treatment with oral DFK (n=63) or placebo (n=63)
- Free or almost free of itch response rates were significantly greater in subjects treated with DFK (14%) versus placebo (1%) as early as week 3 (*P*=0.045; **Figure 2**)
- Statistically significant differences in the proportion of subjects who were free or almost free of itch were maintained through week 8 (DFK [25%] vs placebo [4%], *P*=0.006; **Figure 2**)

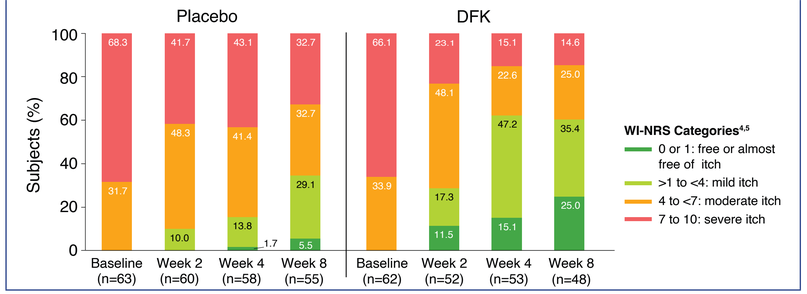
Figure 2. Free or Almost Free of Itch Response Rates Through Week 8



*P<0.05; **P<0.01.

- At baseline, two-thirds of subjects in each treatment group had severe pruritus, and the rest had moderate pruritus (**Figure 3**)
- At week 8, 60% of subjects randomized to DFK had experienced an improvement in itch
  - 25% of subjects treated with DFK were free or almost free of itch compared with 6% in the placebo group
  - 35% of subjects treated with DFK had mild itch compared with 29% in the placebo group

Figure 3. Subject Response Based on Weekly WI-NRS Scores From Baseline to Week 8



CONCLUSIONS

- One in four subjects were free or almost free of itch after 8 weeks of treatment with DFK
  - A statistically significant difference in the proportion of subjects who were free or almost free of itch was observed as early as week 3 with DFK versus placebo
  - More than 4 times as many subjects were free or almost free of itch at week 8 with DFK versus placebo
- Individual subject responses support the rapid onset and robust, durable efficacy of DFK versus placebo in improving itch
- These findings support the role of kappa-opioid receptor activation in controlling neuropathic itch

REFERENCES

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CORRESPONDENCE

Mark Lebwohl – lebwohl@aol.com

DISCLOSURES

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