

**Oral difelikefalin effective in reducing atopic dermatitis- associated pruritus:
Study**

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USA: In a recent study, the researchers observed a rapid, significant anti-pruritic effect of difelikefalin (DFK) in an atopic dermatitis (AD) mouse model and in subjects having mild-to-moderate AD. The results of the study support DFK's role as an anti-pruritic agent for itch-predominant AD patients.

The findings were presented at the AAAAI annual meeting 2022 and subsequently published in the *Journal of Allergy and Clinical Immunology*.

Many AD patients exhibit itch that is disproportionate to rash. In AD, only limited therapies specifically target itch. Difelikefalin is a selective kappa-opioid receptor agonist that is being developed for chronic pruritic conditions.

In the phase 2, randomized, double-blind study, Brian Kim, Washington University School of Medicine, and colleagues enrolled adults with AD and moderate-to-severe pruritus. They received oral placebo (PBO) or DFK (0.25, 0.5, or 1.0 mg) BID for 12 weeks. Also, mice with topical MC903-induced AD were treated with DFK (0.5 mg/kg) intraperitoneally and itch was assessed early (30 minutes).

Change from baseline in mean Itch Numerical Rating Scale (I-NRS) and ≥ 4 -point improvement in I-NRS at week 12 were the primary and key secondary endpoints.

The research led to the following findings:

In mice, DFK promoted rapid, significant itch reduction independently of skin inflammation.

Among 401 subjects randomized, ;64% had mild-to-moderate AD.

In the overall population, treatment difference in mean I-NRS change between the combined DFK group (all doses) and PBO was 20.43 at week 12.

In subjects with mild- to-moderate AD, a significant difference in mean I-NRS was observed at week 12 (20.75) in the DFK group versus PBO (P50.036); a significantly greater proportion of subjects achieved >_4-point improvement in I-NRS with DFK. Itch reduction was observed early (week 1).

Adverse events with DFK were most commonly abdominal pain, nausea, dry mouth, head- ache, dizziness, and hypertension.

"We observed a rapid, significant anti-pruritic effect of DFK in an AD mouse model and in patients with mild-to-moderate AD," wrote the authors. "The findings supports DFK's role as an anti-pruritic agent for patients with itch-predominant AD."

Reference:

The study titled, "Oral Difelikefalin Reduces Atopic Dermatitis–Associated Pruritus," was published in the *Journal of Allergy and Clinical Immunology*.

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