Rapid and early onset of itch relief with tapinarof cream 1% once daily in two pivotal phase 3 trials in adults and children down to two years of age with atopic dermatitis

Authors: Eric Simpson¹, Jonathan I. Silverberg², Robert Bissonnette³, Linda Stein Gold⁴, April Armstrong⁵, Adelaide A. Hebert⁶, Rocco T. Serrao⁷, Jeannette R. Jakus⁸, Philip M. Brown⁹, David S. Rubenstein⁹, Stephen C. Piscitelli⁹, Anna M. Tallman⁹, Lawrence F. Eichenfield¹⁰

Affiliations:
¹Oregon Health & Science University, Portland, OR, USA;
²The George Washington University School of Medicine and Health Sciences, Washington, DC, USA;
³Innovaderm Research Inc., Montreal, QC, Canada;
⁴Henry Ford Health System, Detroit, MI, USA;
⁵University of California Los Angeles, Los Angeles, CA, USA;
⁶UTHealth McGovern School of Medicine and Children’s Memorial Hermann Hospital, Houston, TX, USA;
⁷Dermatologists of Southwest Ohio, Mason, OH, USA;
⁸SUNY Downstate Health Sciences University, New York, NY, USA;
⁹Dermavant Sciences, Inc., Morrisville, NC, USA;
¹⁰University of California San Diego and Rady Children’s Hospital, San Diego, CA, USA

Abstract word count (excl. title, authors, author affiliations, references, or disclosures) = 484/600

Introduction: Itch is the most bothersome symptom for patients with atopic dermatitis (AD), with a significant negative impact on health-related quality of life. Rapid onset of pruritus relief
with sustained efficacy is a key outcome for AD therapies. In a phase 2 trial in adults and adolescents with moderate to severe AD, tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated.

**Objective:** Here, we evaluate time to onset of itch relief in the pivotal phase 3 trials with tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with AD.

**Materials and Methods:** In ADORING 1 and 2, two identical, double-blind, vehicle-controlled trials, patients were randomized 2:1 to tapinarof cream 1% or vehicle QD for 8 weeks. Patients with a Validated Investigator Global Assessment for Atopic Dermatitis™ score of ≥3, an Eczema Area and Severity Index score of ≥6, and body surface area involvement of 5–35% were included. Efficacy endpoints that evaluated itch relief were mean changes in Peak Pruritus-Numerical Rating Scale (PP-NRS) score (daily and by visit [Weeks 1, 2, 4, and 8]) from baseline through Week 8. The PP-NRS considers a person’s worst itch over the past 24 hours, assessed on an 11-point scale (0 indicates “no itch” and 10 is “worst imaginable itch”). Daily PP-NRS scores were recorded in diaries. Patients aged ≥12 years self-completed the PP-NRS, while caregivers completed it for children aged <12 years.

**Results:** 407 and 406 patients were randomized in ADORING 1 and 2. At baseline, mean (standard deviation [SD]) PP-NRS scores were 6.7 (2.4) and 6.8 (2.3) in both trials, respectively. For daily evaluations of itch from baseline, greater reductions in PP-NRS scores (mean [SD]) for tapinarof versus vehicle were observed as early as Day 1, 24 hours after initial application, in ADORING 1 (−1.2 [2.2] vs −0.9 [2.0]) and Day 2 in ADORING 2 (−1.6 [2.4] vs −1.4 [2.1]). Improvements in daily PP-NRS scores (mean [SD]) with tapinarof versus vehicle continued through the first 2 weeks (Day 14; −3.0 [2.8] vs −2.0 [2.4] and −2.9 [2.7] vs −1.8 [2.6]), and through Week 8 of both trials. There were statistically significant and clinically meaningful reductions in mean weekly PP-NRS scores as early as Week 1, the first assessment, for patients treated with tapinarof compared with vehicle (−2.0 vs −1.2 [P<0.0001]) and (−2.0 vs −1.3 [P=0.0010]), in ADORING 1 and 2, respectively. Significantly greater reductions in mean
PP-NRS scores with tapinarof versus vehicle were seen for all visits through Week 8 (−4.1 vs −2.6 and −4.1 vs −2.4 [both \( P<0.0001 \)], for both trials.

**Conclusions:** Tapinarof cream 1% QD demonstrated rapid, clinically meaningful, and significant onset of pruritus relief as early as 24 hours after initial application compared with vehicle. Improvements in itch with tapinarof cream increased through Week 8 in both trials in adults and children down to 2 years with AD.

**Keywords (max 5):** tapinarof cream 1% QD, phase 3, pruritus relief, adults and children, Peak Pruritus-Numerical Rating Scale (PP-NRS)

**Funding Support:** Research was funded by Dermavant Sciences, Inc.