Abstract N°: 6476

**Tapinarof Cream 1% Once Daily: Significant Efficacy in the Treatment of Moderate to Severe Atopic Dermatitis in Two Pivotal Phase 3 Trials in Adults and Children Down to 2 Years of Age**

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**Introduction & Objectives:** Tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated in adults and adolescents with moderate to severe atopic dermatitis (AD) in a previously reported phase 2 trial. Here, we report pivotal phase 3 efficacy and safety results for tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with moderate to severe AD.

**Materials & Methods:** ADORING 1 and 2 were two identical phase 3, randomized, double-blind, vehicle-controlled trials. Eligibility criteria included a Validated Investigator Global Assessment for Atopic DermatitisTM (vIGA-ADTM) score of ≥3, Eczema Area and Severity Index (EASI) score of ≥6, and body surface area (BSA) involvement of 5–35%. Patients were randomized 2:1 to receive tapinarof cream 1% or vehicle cream QD for 8 weeks. The primary efficacy endpoint was vIGA-ADTM response, defined as a score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline at Week 8. Secondary efficacy endpoints included ≥75% improvement in EASI score (EASI75) and proportion of patients (aged ≥12 years) with a baseline Peak Pruritus-Numerical Rating Scale (PP-NRS) score of ≥4 who achieved a ≥4-point reduction at Week 8. Adverse events (AEs) included rates of AEs of special interest (AESIs): contact dermatitis, follicular event, and headache.

**Results:** 407 and 406 patients aged 2–81 years were randomized in ADORING 1 and 2, respectively. At baseline, 84.0–89.9% of patients had a vIGA-ADTM score of 3 (moderate), mean EASI score of 12.5–13.3, and mean BSA affected of 16.7–16.9% across trials. At Week 8, both the primary and all secondary efficacy endpoints were met with statistical significance in the tapinarof groups versus vehicle: vIGA-ADTM response rates were 45.4% vs 13.9% and 46.4% vs 18.0% (both P<0.0001); EASI75 response rates were 55.8% vs 22.9% and 59.1% vs 21.2% (both P<0.0001); and a ≥4-point reduction in PP-NRS was achieved by 55.8% vs 34.2% (P=0.0366) and 52.8% vs 24.1% (P=0.0015), in ADORING 1 and 2, respectively. AEs were mostly mild or moderate; the most frequent (≥5% in any group) were folliculitis, headache, and nasopharyngitis. Trial discontinuation rates due to AEs were lower with tapinarof versus vehicle (ADORING 1: 1.9% vs 3.6%; ADORING 2: 1.5% vs 3.0%, respectively). Rates of AESIs with tapinarof versus vehicle were: contact dermatitis 1.5% vs 2.2% and 1.1% vs 1.5%; follicular events 10.0% vs 0.7% and 8.9% vs 1.5%; and headache 7.0% vs 2.2% and 1.5% vs 0%, in each trial, respectively.

**Conclusion:** Tapinarof cream 1% QD demonstrated statistically significant efficacy compared with vehicle for primary and secondary efficacy endpoints in adults and children down to 2 years of age with moderate to severe AD. Tapinarof was well tolerated, with no new safety or tolerability signals. AEs were mostly mild to moderate and led to low rates of trial discontinuation, demonstrating the predictable safety profile of tapinarof cream 1% QD.