Tapinarof cream 1% once daily for the treatment of extensive atopic dermatitis in adolescents and children: outcomes from the 4-week maximal usage trial

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Introduction: Tapinarof is a first-in-class, non-steroidal, topical, ary1 hydrocarbon receptor agonist approved by the Food and Drug Administration for the treatment of plaque psoriasis in adults, and under investigation for the treatment of atopic dermatitis (AD) in adults and children. Tapinarof cream 1% once daily (QD) demonstrated significant efficacy versus vehicle and was well tolerated in adults and adolescents with moderate to severe AD in a previously reported phase 2b trial. The pharmacokinetic (PK) profile of tapinarof across psoriasis and AD trials in adults is characterized by no-to-minimal systemic absorption and decreasing plasma concentrations over the course of treatment.

Objective: Here, we report PK, tolerability, and safety of tapinarof cream 1% QD in adolescents and children down to age 2 years with extensive AD.

Methods: Adolescents and children with a Validated Investigator Global Assessment scale for Atopic Dermatitis™ (vIGA-AD™) score ≥3 (moderate or worse) and body surface area (BSA) involvement ≥25% (ages 12–17 years) or ≥35% (ages 2–11 years) were enrolled into three age cohorts (2–6, 7–11, and 12–17 years) and were treated with tapinarof cream 1% QD for 4 weeks. Primary endpoints included PK parameters, investigator-assessed Local Tolerability
Scale (LTS) scores by visit (overall and for sensitive areas), and treatment-emergent adverse events (TEAEs).

**Results:** Overall, 36 patients (12 per cohort) were enrolled. Patients’ mean age was 8.9 years and 66.7% were male. At baseline, 66.7%, 75%, and 91.7% of patients had a vIGA-AD™ score of 3 for cohorts 2–6, 7–11, and 12–17 years, respectively. Mean BSA (range) affected was 52.4% (36.0–90.0%), 42.0% (35.0–72.0%), and 33.9% (26.0–54.5%) for the three age cohorts, respectively. Mean Eczema Area and Severity Index (EASI) scores were 30.2, 21.0, and 20.3, respectively. No-to-minimal tapinarof systemic exposure was observed, consistent with previous trials in adults. Mean tapinarof maximum plasma concentration ($C_{\text{max}}$) at Day 1 was 2.4 ng/mL and the median time to $C_{\text{max}}$ was approximately 3 hours, for all patients. Approximately 25% of post-treatment plasma samples were below the quantifiable limit of the highly sensitive assay (<50 pg [10$^{-12}$]/mL). There was no correlation between tapinarof exposure ($C_{\text{max}}$ on Day 1) and baseline %BSA affected. Mean overall investigator-assessed LTS score was 0.1 (no irritation) at Weeks 1 and 4. Investigators assessed that the majority of patients had no irritation (LTS score of 0), including on sensitive and intertriginous skin. TEAEs were reported by 8 patients (22%) and were all mild or moderate; one patient discontinued due to two unrelated TEAEs. One case of mild folliculitis and no contact dermatitis occurred. Most patients (87.5%) chose to enroll in the 48-week long-term extension trial.

**Conclusions:** This is the first trial evaluating tapinarof in children down to 2 years of age.

Tapinarof cream 1% QD demonstrated no-to-minimal systemic exposure in children with extensive AD, even when measured with a highly sensitive assay. There was a low incidence of TEAEs in patients with up to 90% BSA affected. Tapinarof cream was well tolerated, including on sensitive and intertriginous skin areas.

**Keywords (max 5):** atopic dermatitis, pediatrics, tapinarof, maximal usage trial

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