ID: 4555

Title: Safety and Biopsy Outcomes of a Topical Treatment (SM04554) for Male Androgenetic Alopecia (AGA): Results from a Phase 2, Multicenter, Randomized, Double-blind, Vehicle-controlled Trial

Description: Introduction: SM04554 is a novel, small molecule modulator of Wnt signaling with potential to treat AGA. Its safety and efficacy were evaluated in a Phase 2 trial.

Methods: Males, aged 18-65 (Norwood-Hamilton 4-6) were treated daily for 90 days with 0.15%, 0.25% SM04554 or vehicle. Safety data (adverse events [AE], labs, vitals, scalp assessments) were collected over 142 days. Scalp biopsies were taken (baseline [BL], Days 91, 135). Biopsies were horizontally-sectioned and hair follicle numbers (vellus [< 30μm], indeterminate [30-60μm], terminal [>60μm]) were counted and categorized by hair-cycle phase. Nuclear expression of β-catenin and Ki-67 were measured in epidermis and follicular infundibula and Ki-67 was assessed in hair bulbs. BL-adjusted Poisson regression was used to estimate differences in absolute follicle counts between groups; BL-adjusted Gamma regression estimated nuclear expression outcomes.

Results: 49 males (0.15% n=16, 0.25% n=14, vehicle n=19), mean age 50 (±11), were randomized. 29 (59%) subjects reported 48 AEs, 6 deemed related to study drug (5 subjects: 1 - 0.15%; 1 - 0.25%; 3 - vehicle). No serious AEs were reported. Labs, vitals and scalp assessments were unremarkable.

Compared to vehicle, the 0.25% group exhibited significantly higher total follicle counts at Days 91 (P< 0.001) and 135 (P< 0.001). This was also seen in the 0.15% group at Day 135 (P< 0.001).

Compared to vehicle, the 0.25% group exhibited significantly higher numbers of vellus (P=0.003), indeterminate (P< 0.001), total anagen (P< 0.001) and terminal anagen (P=0.01) follicles at Day 91. At Day 135, the 0.25% group had significantly higher numbers of vellus (P=0.002), total anagen (P=0.004) and terminal catagen/telogen (P=0.006) follicles. The 0.15% group exhibited significantly higher numbers of vellus (P=0.007), terminal (P=0.01), total anagen (P=0.004) and terminal catagen/telogen (P=0.03) follicles at Day 135.

No significant differences were seen in epidermal β-catenin and Ki-67 between 0.15% or 0.25% and vehicle indicating no significant proliferative signal. Ki-67 was increased in the hair bulb for both SM04554 groups compared to vehicle at Day 91 (0.15% [P=0.07], 0.25% [P=0.25]) suggesting hair growth and/or follicle formation.

Conclusions: SM04554 appeared safe and well-tolerated. Increased follicle counts and hair bulb Ki-67 suggested that treatment with SM04554 may promote follicular neogenesis and
potentially be efficacious for AGA.

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Dermatopathology

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