An investigator-initiated, open-label study evaluating the efficacy and safety of ustekinumab in patients with moderate to severe palmar plantar psoriasis

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Palmar plantar psoriasis (PPP) is a disabling and disfiguring form of psoriasis that is typically chronic and very difficult to treat. It is characterized by the presence of plaques and/or sterile pustules and fissures on the palms and soles, in addition to typical psoriatic plaques. We designed a small, open-label, 24 week study to evaluate the safety and efficacy of ustekinumab, a fully human IL-12/23 monoclonal antibody, in patients with moderate to severe palmar plantar psoriasis. Eligible subjects ≤ 100 kg received 45 mg of ustekinumab subcutaneously, while subjects >100 kg received 90 mg at weeks 0, 4, and 16. Clinical assessments of outcomes included: Physician Global Assessment (PGA), pustule and fissure counts, Dermatology Life Quality Index (DLQI), as well as pruritus and pain visual analogue scale (VAS) assessments. Preliminary results of 14 patients who have completed the primary efficacy endpoint of week 16 of the study indicate that ustekinumab is well tolerated and may be effective at improving PPP. Mean PGA improved from 3.3 to 1.9 ($P < .01$) and DLQI improved from 12.6 to 6.1 ($P = .01$) from week 0 to week 16. Ustekinumab is well tolerated and may be effective at improving clinical outcomes and quality of life in patients with moderate to severe palmar plantar psoriasis.

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Approved adalimumab dosing regimen associated with greater efficacy and lower cost per responder compared with 40 mg every other week dosing without initial 80 mg dose: Analysis of outcomes from adalimumab psoriasis clinical trial database

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Objective: Approved adalimumab dosing for moderate to severe psoriasis is 40 mg every other week (eow), after an initial 80 mg dose. This analysis compared outcomes with the approved dosing regimen vs no initiation dose (ID).

Methods: Patients were pooled from the CHAMPION (Comparative Study of HUMIRA vs Methotrexate vs Placebo In PsOriasis PatieNts), REVEAL (Randomized Controlled Evaluation of Adalimumab Every Other Week Dosing in Moderate to Severe Psoriasis Trial), M02-528/529, and M03-658 trials and stratified into ID (80 mg at week 0; 40 mg eow from week 1) vs no initiation dose (NID) (40 mg eow from week 0) groups. Week 12 and 24 Psoriasis Area and Severity Index (PASI) response rates and Physician's Global Assessment (PGA) scores were compared between groups using descriptive and regression analysis (controlling for baseline scores, REVEAL trial origin, age, sex, and race). Cost per PASI 75 responder was measured.

Results: On an unadjusted basis, ID group (N = 982) vs NID group (N = 258) had significantly ($P < .03$) greater PASI 75 response rates (week 12 71.8% vs 59.7%; week 24 74.5% vs 64.0%) and greater PASI 90 response rates (week 12 40.2% vs 32.4%; week 24 52.2% vs 39.1%). Controlling for baseline covariates, compared with NID group, ID group was significantly ($P \leq .02$) more likely to achieve PGA of "moderate" or better (week 12 odds ratio [OR] = 3.32; week 24 OR = 3.67), PASI 75 response (week 12 OR = 1.73; week 24 OR = 1.70), and PASI 90 response (week 12 OR = 1.42; week 24 OR = 1.77). At wek 24, ID group was projected to have $1275 lower costs per PASI 75 responder than NID group.

Conclusion: Adalimumab treatment with the approved dosing regimen is associated with significantly greater improvement in psoriasis severity symptoms compared with adalimumab treatment of 40 mg eow dosing without initial 80 mg dose.

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Apremilast is effective in the treatment of nail psoriasis: Results from a phase IIb, randomized, controlled study

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Background: Phosphodiesterase-4 (PDE4) is expressed in cells mediating immune response. Apremilast (APR) is a novel, orally available small molecule that specifically targets PDE4, thereby increasing cellular cAMP, which modulates multiple pro- and antiinflammatory mediators. We evaluated the clinical efficacy of APR in the treatment of nail psoriasis.

Methods: In a phase IIb, multicenter, double-blind, placebo (PBO)-controlled, dose-ranging study, subjects with moderate to severe plaque psoriasis (Psoriasis Area and Severity Index [PASI] ≥ 12; body surface area [BSA] $\geq 10\%$) were equally randomized to oral APR 10 mg (APR10), 20 mg (APR20), 30 mg (APR30) BID, or PBO for 16 wks. After the first 16 wks, PBO subjects were re-randomized to APR20 (P/20) or APR30 (P/30); the remaining subjects maintained their dosing through week 24. An exploratory prespecified analysis assessed effects of APR on subjects with nail psoriasis using the Nail Psoriasis Severity Index (NAPSI; 0-8 scale) for a digit nail representing the most severe nail psoriasis involvement; endpoints were percent change from baseline (BL) and proportion of subjects achieving 50% reduction in NAPSI score from BL (NAPSI-50) at weeks 16 and 24. The proportion of subjects achieving NAPSI-50 at week 16 was compared between treatment groups using 2-tailed Chi square test. Missing data were handled using last observation carried forward.

Results: Of 352 subjects enrolled (63% male; mean age 44 yrs; mean BMI 31 kg/m^2; mean affected BSA 22%; mean PASI 18.5), 221 (62.8%) had nail psoriasis at BL and qualified for the analysis (n = 54-57/treatment group). Mean NAPSI scores at BL were 4.1-4.3. At week 16, median reductions in NAPSI from BL were 0% (PBO), 16.7% (APR10), 33.3% (APR20), and 42.9% (APR30). NAPSI-50 was achieved by significantly more subjects treated with APR20 (42.1%; $P = .006$) and APR30 (45.5%; $P = .002$) vs PBO (18.2% [APR10, 31.5%; NS]). At week 24, median reductions in NAPSI from BL were 33.3% (APR10), 50.0% (APR20 and APR30), 8.3% (P/20 [n = 15]), and 0% (P/30 [n = 22]). NAPSI-50 was achieved by 44.4% (APR10), 52.6% (APR20), 52.7% (APR30), 52.9% (P/20), and 34.8% (P/30) of subjects.

Conclusion: APR was previously shown to be effective in the treatment of plaque psoriasis. The current analysis demonstrates APR activity in difficult-to-treat nail psoriasis after 16 weeks of therapy, which appeared to continue through week 24. Phase III studies are under way and will further explore APR efficacy for treatment of nail psoriasis.

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Apremilast is effective in the treatment of scalp and palmoplantar psoriasis: Results from a phase II2b randomized, controlled study

(Poster reference number 5532)

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Background: Phosphodiesterase-4 (PDE4) is expressed in cells mediating immune response. Apremilast (APR) is a novel, orally available small molecule that specifically targets PDE4, thereby increasing cellular cAMP, which modulates multiple pro- and antiinflammatory mediators. We evaluated the clinical efficacy of APR in the treatment of scalp and palmoplantar (PP) psoriasis.

Methods: In a phase IIb, multicenter, double-blind, placebo (PBO)-controlled, dose-ranging study, subjects with moderate to severe plaque psoriasis (PASI ≥ 12; BSA $\geq 10\%$) were equally randomized to APR 10 mg (APR10), 20 mg (APR20), 30 mg (APR30) BID, or PBO. At week 16, PBO subjects were rerandomized to APR20 or APR30; the remaining subjects maintained their dosing through week 24. The efficacy of APR was evaluated using the Physician Global Assessment for lesions on the scalp (ScPGA; 0-5 scale) and palms/soles (PPPGA; 0-4 scale); exploratory efficacy endpoints were the proportion of subjects with baseline scores ≥ 3 achieving PGA scores of "clear" or "almost clear" (0-1) and "clear," "almost clear," or "mild" (0-2) at wks 16 and 24.

Results: Of the 352 subjects enrolled, 231 with moderate to very severe scalp psoriasis (PBO, n = 53; APR10, n = 62; APR20, n = 57; APR30, n = 59) qualified for the prespecified analysis. At week 16, more APR-treated subjects achieved ScPGA 0-1 (APR10 [22.6%], APR20 [45.6%], APR30 [44.1%]) vs PBO (15.1%). Improvements were still seen at week 24: 21.0% (APR10), 38.6% (APR20), and 40.7% (APR30). Of PBO subjects rerandomized to APR20 or APR30 at week 16, 43.4% achieved PGA 0-1 at week 24. At week 16, ScPGA 0-2 was achieved by 30.2% (PBO), 38.7% (APR10), 59.6% (APR20), and 59.3% (APR30) of subjects. At week 24, ScPGA 0-2 was achieved by 38.7% (APR10), 52.6% (APR20), and 52.5% (APR30) of subjects. A trend for efficacy was noted in 32 subjects with moderate or severe PP psoriasis (PBO, n = 10; APR10, n = 5; APR20, n = 8; APR30, n = 9). At weeks 16 and 24, 66.7% and 77.8% of APR30-treated subjects achieved PPPGA 0-1 (PBO, 20.0% and 30.0%) and 88.9% and 77.8% achieved PPPGA 0-2 (PBO, 50.0% for both).

Conclusion: APR was previously shown to be effective in the treatment of plaque psoriasis. The current analysis focuses on difficult-to-treat psoriasis lesions. APR has demonstrated activity in treating psoriasis lesions on the scalp. Results also suggest activity in treating PP psoriasis lesions. Phase III studies are under way and will further explore APR efficacy for treatment of scalp and PP psoriasis.

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