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Clearance of head involvement in plaque psoriasis with tildrakizumab treatment in the phase 3 reSURFACE 1 study

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Background: We present efficacy of tildrakizumab (TIL)—a high-affinity, humanized, anti−interleukin-23p19 monoclonal antibody approved for treatment of moderate to severe plaque psoriasis—for clearing psoriasis on the neck, scalp, and face.

Methods: reSURFACE 1 (NCT01722331) was a 3-part, double-blind, randomized, controlled, 64-week, phase 3 study evaluating TIL administered at week 0, week 4, and every 12 weeks thereafter in adults with moderate to severe plaque psoriasis. This post hoc analysis evaluated Psoriasis Area and Severity Index head component score (PASIh; range, 0.0-7.2; 0.0 defined as clearance) in patients receiving TIL 100 mg through week 28.

Results: At baseline, median (interquartile range [IQR]) PASIh was 1.4 (0.8-2.4); 23/309 patients had baseline PASIh = 0.0. At wk 4, wk 8, wk 12, and wk 28, median (IQR) [median improvement from baseline] PASIh was 0.5 (0.2-1.4) [64.2%], 0.2 (0-0.6) [85.7%], 0 (0-0.5) [100%], and 0 (0-0.4) [100%], respectively. In patients with baseline PASIh ≥1.4 (n = 154), median (IQR) [median improvement] PASIh at baseline, wk 12, and wk 28 was 2.4 (1.8-3.5), 0.3 (0-0.9) [87.5%], and 0.1 (0.1-0.8) [95.8%], respectively; 41.6% had PASIh = 0.0 by wk 28. For patients with baseline PASIh ≥2.4 (highest quartile; n = 94), median (IQR) [median improvement] PASIh at baseline, wk 12, and wk 28 was 2.7 (1.8-3.6), 0.3 (0-0.9) [88.9%], and 0.3 (0-0.75) [88.9%], respectively; 36.2% had PASIh = 0.0 by wk 28.

Conclusions: Treatment with TIL 100 mg through wk 28 resulted in rapid, progressive reduction in PASIh, with complete clearance at wk 28 in 36% of patients with extensive involvement at baseline.

Commercial disclosure: The studies were funded by Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Kenilworth, New Jersey. Analyses were funded by Sun Pharmaceutical Industries, Princeton, New Jersey.

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Topically applied lotions containing fatty acids provide nourishment to the skin through maturation of the lipid matrix

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Background: Lotions containing a mixture of glycerin, petroleum jelly, and fatty acids have been shown to improve skin moisturization, alleviate visual dryness, and result in a healthier skin barrier over time. A fuller understanding of the molecular level changes which occur with such improvements has been lacking, particularly in the understanding of lipids, but would provide insights to allow the development of more efficacious products.

Objective: To better understand the lipidomic changes occurring within the skin with prolonged healing lotion application.

Methods: Healthy female subjects (30-50 years) provided informed consent to participate in an IRB-approved forearm application study. Subjects applied a healing lotion containing glycerin, petroleum jelly and deuterated fatty acids (palmitic acid) twice daily to one arm for 28 days followed by sample collection and lipid composition measurement (deuterated elongated fatty acids, sphingosine and ceramides).

Results: All subjects were found to have abundant deuterated elongated fatty acids (C18-C26) from analyzed samples. In addition, deuterated sphingosine was found present in all subjects suggesting the deuterated palmitic acid was utilized as a substrate in ceramide formation. Further analysis of the ceramide compartment confirmed this pathway.

Conclusions: Application of the test lotion demonstrated the integration and metabolism into lipid species consistent with that expected from the stratum corneum of healthier skin. Thus, healing lotions containing fatty acids along with glycerin and petroleum jelly are addressing not only the superficial symptoms of skin dryness but are also assisting in the production of a better epidermis and a stronger stratum corneum.

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Randomized, double-blind, placebo-controlled, multiple-dose, phase 2b study to demonstrate the safety and efficacy of tildrakizumab, a high-affinity anti−interleukin-23p19 monoclonal antibody, in patients with active psoriatic arthritis

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Background: This randomized, double-blind, placebo-controlled, multiple-dose, phase 2b study (NCT02980692) evaluated the efficacy and safety of tildrakizumab (TIL)—a high-affinity anti−interleukin-23p19 monoclonal antibody—in patients with active psoriatic arthritis (PsA) to week 24.

Methods: Patients with active PsA were randomized 1:1:1:1:1 to receive TIL (200 mg every 4 weeks [q4w], 200 mg every 12 weeks [q12w], 100 mg q12w, 20 mg q12w), or placebo q4w. Assessments included proportion of patients who achieved a 20/50/70% reduction from baseline by American College of Rheumatology response criteria (ACR20/50/70), Psoriasis Area and Severity Index (PASI) 75, Leeds Enthesitis Index (LEI), patient pain (0-100 mm visual analog scale), and treatment-emergent adverse event (TEAE) monitoring.

Results: Overall, 391/500 patients met inclusion criteria. At wk 24, 79.5/52.6/28.2%, 77.2/50.6/29.1%, 71.4/45.5/22.1%, 73.1/39.7/16.7%, and 50.6/24.1/10.1% of patients receiving TIL 200 q4w, TIL 200 q12w, TIL 100 q12w, TIL 20 q12w, and placebo, respectively, achieved ACR20/50/70 ($P < .01/0.05/0.05$ vs placebo [except TIL 20 q12w ACR70]); and 64.2%, 79.6%, 55.6%, 46.3%, and 16.7% achieved PASI 75 ($P < .01$ vs placebo). TIL 200 q4w significantly improved LEI by 71.2% ($P < .05$). All TIL arms improved patient pain from baseline (least squares mean reduction 28.9-35.2, $P < .05$ vs placebo except TIL 20 q12w). The most frequent TEAEs for TIL vs placebo included nasopharyngitis (5.4% vs 6.3%) and diarrhea (1.3% vs 0). No candidiasis, inflammatory bowel disease, major adverse cardiac events, or malignancies were reported.

Conclusions: By wk 24, TIL was significantly more efficacious than placebo in treating joint and skin manifestations of PsA, with a low rate of TEAEs.

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Rates of malignancies through 5 years of tildrakizumab exposure in 2 phase 3 clinical trials

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Background: Immunosuppressive medications may increase malignancy rates. We present malignancy rates for up to 5 years in patients receiving tildrakizumab (TIL), a high-affinity anti−interleukin-23p19 monoclonal antibody approved for treatment of moderate to severe plaque psoriasis.

Methods: reSURFACE 1 and 2 (NCT01722331/NCT01729754) were 3-part, double-blind, randomized, controlled studies with optional long-term extensions evaluating TIL monotherapy every 12 weeks in adults with moderate to severe chronic plaque psoriasis. This post hoc analysis reports exposure-adjusted rates of malignancy excluding cervical carcinoma in situ as cumulative incidence per 100 patient years (PY) of exposure to TIL 100 vs 200 mg.

Results: In reSURFACE 1/2, 239/376 and 267/347 patients receiving TIL 100 and 200 mg entered the extension studies for a mean of 154.2/146.8 and 165.7/148.5 weeks, respectively. Total TIL exposure was 1094.6/1513.3 and 1266/1404.7 PY for TIL 100 and 200 mg, respectively, in reSURFACE 1/2. Malignancy rates for reSURFACE 1/2 were 1.6/0.8 vs 0.9/1.0 per 100 PY in patients receiving TIL 100 vs 200 mg, respectively. Melanoma rates were 0.1/0.1 vs 0.1/0.1 per 100 PY and nonmelanoma skin cancer (NMSC) rates were 0.5/0.3 vs 0.4/0.5 per 100 PY in reSURFACE 1/2 patients receiving TIL 100 vs 200 mg, respectively. Excluding NMSC, malignancy rates were 1.1/0.5 vs 0.5/0.5 per 100 PY for reSURFACE 1/2 patients receiving TIL 100 vs 200 mg, respectively.

Conclusions: Malignancy rates in reSURFACE 1/2 were similar between patients receiving TIL 100 vs 200 mg for up to 5 years, suggesting no dose-dependent effect on incidence of malignancy.

Commercial disclosure: The studies were funded by Merck Sharp & Dohme Corp, a subsidiary of Merck & Co, Kenilworth, New Jersey. Analyses were funded by Sun Pharmaceutical Industries, Princeton, New Jersey.