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Absolute PASI response up to 52 weeks with brodalumab in patients with moderate to severe plaque psoriasis

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Background: Skin clearance measured by absolute Psoriasis Area and Severity Index (PASI) may provide more clinically relevant information on disease severity than relative PASI improvement. Brodalumab is a fully human anti−interleukin-17 receptor A monoclonal antibody efficacious for the treatment of adults with moderate to severe psoriasis. In this post hoc analysis, absolute PASI was evaluated through 52 weeks of treatment with brodalumab in a randomized phase 3 trial (AMAGINE-1).

Methods: Patients were initially randomized to brodalumab 210 mg every 2 weeks (q2w) or placebo in a 12-week induction phase. After 12 weeks, a subset of patients with a robust response continued to receive brodalumab 210 mg q2w through 52 weeks. Skin clearance was assessed as absolute PASI from baseline up to 52 weeks. Efficacy data were reported using multiple imputation (induction phase) and last observation carried forward (re-randomization phase) analyses.

Results: In the induction phase, patients received brodalumab 210 mg q2w (n = 222) or placebo (n = 220). Baseline mean (SD) absolute PASI was similar between groups (brodalumab: 19.41 [6.61]; placebo: 19.72 [7.71]). At week 12, absolute PASI was significantly lower in patients who received brodalumab (2.52 [5.74]) than that in patients receiving placebo (19.99 [10.49]; least squares mean treatment difference vs placebo, −17.21; $P < .001$). Following rerandomization at week 12, 83 patients remained on brodalumab 210 mg q2w. Absolute PASI in these patients was 0.63 (1.23) at week 52.

Conclusions: Treatment with continuous brodalumab over 52 weeks resulted in significantly decreased absolute PASI in patients with moderate to severe plaque psoriasis.

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Inaccuracy of self-reported family history of melanoma in high-risk patients

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Family history of melanoma is a known major risk factor for melanoma. However, self-reported family histories for numerous cancers, including melanoma, are commonly inaccurate. Three large melanoma studies have explored this with positive predictive values (PPVs), 28%-83%. Given these wide variations, we explored this question in individuals at high-risk of melanoma, and thus, more likely to be aware of their family history of melanoma. We queried the Utah Population Database (UPDB), a unique, extensive family history database linking >11,000,000 individuals with public records (driver's license, marriage/divorce records), medical records and death records. This offers a more complete multi-generational dataset for a much larger cohort than would be feasible through manual chart review and is the largest cohort study to date. Charts from 1780 high-risk patients (having at least one melanoma risk factor) were reviewed to quantify self-reported family history of melanoma. These data were combined with UPDB and Utah Cancer Registry data serving as the "gold standard." Self-reported family history of melanoma in first- and second-degree relatives had an overall sensitivity of 62%, specificity of 67%, PPV of 31%, and NPV of 89%, with increased accuracy for first-degree relatives. A personal history of melanoma was the only factor associated with increased accuracy in self-reported family history of melanoma. Age, sex, number of nevi, and number of prior personal melanomas were not significant. Dermatologists should educate patients on the differences between melanoma, nonmelanoma skin cancer and pre-cancers. Confirming self-reported family history of melanoma will limit over-screening of otherwise low-risk patients.

Commercial disclosure: None identified.

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Tildrakizumab efficacy by metabolic syndrome status in psoriasis: Post hoc analysis of 3-year data from the phase 3 reSURFACE 2 study

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Background: Metabolic syndrome (MetS) may reduce response to treatment for psoriasis. We present efficacy of tildrakizumab (TIL)—a high-affinity, humanized, immunoglobulin G1κ, anti−interleukin-23p19 monoclonal antibody approved for treatment of moderate to severe plaque psoriasis—in patients with psoriasis with versus without MetS after follow-up for 3 years.

Methods: This post hoc analysis of a phase 3, double-blind, randomized controlled study (reSURFACE 2 [NCT01729754]) included adults with moderate to severe chronic plaque psoriasis continously receiving the same TIL dose (TIL 100 or 200 mg) at week 0, week 4, and every 12 weeks thereafter. We evaluated TIL efficacy (proportion of patients with ≥75% Psoriasis Activity and Severity Index score improvement from baseline [PASI 75] and absolute PASI change from baseline) stratified by MetS status to wk 148.

Results: Of patients continuously receiving TIL 100/200 mg (n = 214/160), 44/30 (21%/19%), respectively, had MetS at baseline. Baseline demographic and disease characteristics were similar except for higher median baseline weight, body mass index, and prevalence of cardiovascular disease and diabetes mellitus in patients with vs without MetS. Proportions of patients receiving TIL 100/200 mg who achieved PASI 75 were comparable between those with vs without MetS at wk 52 (86%/87% vs 94%/87%), wk 100 (77%/73% vs 88%/85%), and wk 148 (73%/63% vs 79%/81%). At wk 148, overall PASI scores decreased from baseline by 93%/84% vs 96%/94% in patients receiving TIL 100/200 mg with vs without MetS.

Conclusions: TIL efficacy was maintained over 148 weeks and comparable between patients with versus without MetS.

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Network meta-analysis to analyze alopecia areata treatment

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Background: Alopecia areata (AA) is an autoimmune disease which results in hair loss. Hair loss can be mild and patchy or severe, affecting greater than 50% of the scalp. There are no approved treatments for AA, thus many off-label strategies have been investigated.

Objective: Compare the efficacies of available AA therapy, including both traditional and emergent.

Methods: A network meta-analysis was used to investigate treatments for both mild (50% scalp hair loss) AA. Efficacy was defined as response to treatment including greater than 75% regrowth and cosmetic acceptability. Trials describing mild disease were analyzed separately from those describing moderate to severe disease.

Results: For mild disease, intralesional corticosteroids were ranked the most likely to produce a response at 78.9% according to SUCRA (surface under the cumulative ranking curve) followed by topical corticosteroids (67.9%), prostaglandin analogs (67.1%), diphenylcyclopropenone (DPCP, 63.4%), topical minoxidil (61.2%), and squaric acid dibutylester (SADBE, 35.0%). In contrast, for moderate to severe disease (>50% scalp hair loss), DPCP was the top-ranked treatment (87.9%), followed by laser (77.9%), topical minoxidil (55.5%), topical corticosteroids (50.1%), SADBE (49.7%) and topical tofacitinib (47.6%). There were insufficient eligible trials to include oral tofacitinib in the network.

Conclusions: Based on the data, intralesional corticosteroids and topical corticosteroids could be recommended in cases of mild disease. In cases of more severe disease, options include DPCP, SADBE, topical minoxidil, topical corticosteroids, and laser. Additional studies are required to further analyze emerging treatments such as tofacitinib and platelet-rich plasma.

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