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ATI-501, a novel Janus kinase 1/3 inhibitor, demonstrates hair growth in patients with alopecia areata: Results of a phase 2, randomized, double-blind, placebo-controlled trial

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Background: There is increasing evidence that inflammatory skin diseases, including AA, involve the JAK/STAT signaling pathway. This trial evaluated the efficacy and safety of ATI-501 in AA patients.

Methods: Eligible patients had 30%-100% scalp hair loss as assessed by SALT (Severity of Alopecia Tool); current hair loss episodes ranged from 6 months to 12 years. 87 patients were randomized (1:1:1:1 ratio) and received ATI-501 400 mg, 600 mg, or 800 mg or placebo oral suspension twice daily for 24 weeks.

Results: Patients in each of the 3 ATI-501 dose groups had statistically significant improvements compared with placebo for the primary end point (mean% change from baseline in SALT at week 24): 6% improvement in the placebo group vs 26% ($P = .011$), 30% ($P = .001$), and 26% ($P = .010$) in the 400, 600, and 800 mg groups, respectively. The proportion of patients with ≥50% relative improvement in SALT was analyzed for the subgroup with a baseline SALT of ≥50. No placebo patients achieved this end point versus 18%, 25%, and 31% in the 400, 600, and 800 mg groups, respectively (not statistically significant). Secondary end points demonstrating statistically significant improvements at 24 weeks vs placebo included: absolute change from baseline in SALT ($P < .05$), percent and absolute change from baseline in Alopecia Density and Extent (ALODEX) ($P < .05$ and $P < .01$) for all 3 doses. ATI-501 was generally well tolerated at all doses with no serious adverse events reported.

Conclusions: 24 weeks of ATI-501 treatment resulted in statistically significant hair regrowth in patients with AA, with acceptable safety.

Commercial disclosure: Aclaris was the study sponsor and covered all costs related to the poster development.

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Efficacy of tapinarof cream by body region in subjects with plaque psoriasis in a phase 2b randomized controlled study

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Tapinarof is a therapeutic aryl hydrocarbon receptor modulating agent (TAMA) in development for treatment of psoriasis and atopic dermatitis. In a phase 2b study, Physician Global Assessment (PGA) and Psoriasis Area and Severity Index (PASI) responses at week 12 were significantly higher in all tapinarof groups vs vehicle. Higher responses in tapinarof groups were maintained for 4 weeks after treatment versus vehicle. This post hoc analysis evaluated mean change in PASI from baseline by body region. Overall (n = 175), mean baseline PASI score was 8.8 and most subjects (80%) had a PGA score of 3 (moderate). Mean PASI improvements at week 12 were significantly greater in tapinarof 1% twice-daily (bid), 1% once-daily (qd), 0.5% bid, and 0.5% qd groups vs vehicle bid and qd, overall: −8.70, −6.62, −6.30, and −5.41 vs −2.77 and −1.54, respectively (all $P < .001$); in the upper extremities: −9.65, −9.05, −8.70, and −6.04 vs −4.88 and −1.61 (all $P < .05$); and lower extremities: −8.74, −8.19, −7.16, and −6.33 vs −2.47 and −2.0 (all $P < .001$). In the trunk and head/neck, PASI improvements were significantly greater in all tapinarof groups vs vehicle except the 0.5% bid group: −11.94, −9.13, −9.0, and −8.25 vs −4.08 and −1.85 ($P < .01$); and −9.0, −7.40, −5.0, and −9.0 vs −1.75 and −2.50 ($P < .05$), respectively. Tapinarof cream was generally well tolerated; most adverse events were mild or moderate. Tapinarof cream demonstrated consistent efficacy across body regions as measured by PASI and was generally well tolerated. A phase 3 study of tapinarof cream 1% qd in psoriasis is ongoing (NCT03956355).

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Abrocitinib treatment in patients with moderate to severe atopic dermatitis: Consistency of efficacy responses from randomized, controlled phase 3 and phase 2b clinical trials

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Introduction: Abrocitinib is an oral Janus kinase 1 selective inhibitor under investigation for the treatment of AD. In phase 3 (Ph3) and phase 2b (Ph2b) trials, abrocitinib was effective, with an acceptable safety profile.

Design: Randomized, double-blind, placebo-controlled Ph3 (NCT03349060; JADE MONO-1) and Ph2b (NCT02780167) trials.

Methods: Patients aged ≥12 years (Ph3) or 18-75 years (Ph2b) with moderate to severe AD were randomly assigned to once-daily abrocitinib (Ph3: 200 or 100 mg; Ph2b: 200, 100, 30, or 10 mg) or placebo for 12 weeks. End points assessed in both studies included proportions of patients achieving Investigator's Global Assessment (IGA) response (clear [0] or almost clear [1] with ≥2-grade improvement) at week 12 (primary in both) and proportions achieving Eczema Area and Severity Index (EASI) 75 (≥75% improvement) at week 12 (Ph3: coprimary; Ph2b: additional secondary).

Results: Overall, 387 and 267 patients received study drug in the Ph3 and Ph2b studies, respectively. IGA responses were similar between studies and significantly greater for 200 mg and 100 mg than placebo (Ph3: 43.8% and 23.7% vs 7.9%, $P \leq .01$ for both; Ph2b: 44.5% and 27.8% vs 6.3%, $P \leq .01$ for both). Likewise, EASI-75 responses were similar between studies and significantly greater for 200 mg and 100 mg than placebo (Ph3: 62.7% and 39.7% vs 11.8%, $P < .0001$ for both; Ph2b: 63.7% and 41.6% vs 15.6%, $P < .01$ for both). In both studies, most adverse events were mild and considered unrelated to treatment.

Conclusions: The efficacy of abrocitinib was consistent across Ph3 and Ph2b studies in patients with moderate to severe AD.

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Combination therapy of apremilast and biologic agent as a step-up strategy option of psoriasis and psoriatic arthritis

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The treatment of psoriatic arthritis and psoriasis is complicated by heterogeneity in the presentation of the disease (skin and nail disease, arthritis, enthesitis, dactylitis, and axial involvement) and its course. While monotherapy with biologic agents is effective for many patients, some patients with aggressive disease are not controlled by standard treatment and require combination therapies. Each domain is regulated by a different cytokine. Biologic drugs exclusively block one cytokine while apremilast modulates a wide array of inflammatory mediators. There is barely any data on the safety or efficacy of apremilast treatment combined with biologic therapies. Six patients were treated with biologic drugs but due to the absence of control of activity of one domaine, they required onset of apremilast. These domains were polyarthritis (4), dactylitis (2), and plaque psoriasis (1). The mean of time of treatment was 11 months. Biologic treatments used in combination were adalimumab (2), ixekizumab (1), secukinumab (2) and etanercept (2). The combination controlled the domains. One of the patients required a change of the biologic drug. No relevant adverse effects were observed. Nausea and vomiting were reported by 1 patient (16.6%) and apremilast was stopped. No major side-effects of cancer or severe infection were observed. Apremilast could be safely and effectively combined with biologic agents in patients with psoriasis and psoriatic arthritis non responders to biologic drugs. Apremilast could provide additional control of the activity of each domain without affecting safety. No adverse events and major side-effects such as cancer or infection were reported.

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