A Phase 3 Study to Investigate the Efficacy and Safety of Abrocitinib and Dupilumab in Comparison With Placebo in Adults With Moderate-to-Severe Atopic Dermatitis

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Background: Systemic therapies with favorable benefit-risk profiles are necessary for long-term disease control in moderate-to-severe atopic dermatitis (AD) unresponsive to topical agents. Not all patients have an adequate response with dupilumab, and some patients develop conjunctivitis or prefer oral therapy.

Objectives: The primary study objective was to evaluate the efficacy of once-daily abrocitinib (200 mg or 100 mg) with that of placebo in patients with AD on background medicated topical therapy. Key secondary objectives were to compare itch response for

abrocitinib and dupilumab at 2 weeks and to estimate the proportion of patients with improved AD signs in the 3 active treatment arms.

Methods: Adults with moderate-to-severe AD (Investigator's Global Assessment [IGA] ≥3, Peak Pruritus Numerical Rating Scale [PP-NRS; used with permission of Regeneron Pharmaceuticals, Inc., and Sanofi] score ≥4, Eczema Area and Severity Index [EASI] score ≥16, and percentage of body surface area affected ≥10) were randomly assigned 2:2:2:1 to receive oral abrocitinib 200 mg or 100 mg once daily, dupilumab 300 mg subcutaneous injection every 2 weeks after a 600-mg loading dose (+ oral placebo once daily or placebo subcutaneous injection every 2 weeks as appropriate), or placebo, along with background medicated topical therapy (low- or medium-potency topical corticosteroids, calcineurin inhibitors, or phosphodiesterase 4 inhibitors) for 16 weeks for active lesions. Coprimary (IGA response [clear (0) or almost clear (1) with ≥2-grade improvement] and ≥75% improvement in EASI [EASI-75] response at week 12) and key secondary endpoints (PP-NRS4 response [≥4-point improvement] at week 2 and IGA and EASI-75 responses at week 16) were analyzed using the Cochran-Mantel-Haenszel test adjusted by baseline disease severity and controlled for multiplicity.

Results: In the abrocitinib 200-mg, 100-mg, dupilumab, and placebo arms, 226, 238, 242, and 131 patients, respectively, were treated, of whom 89.3%-92.1% completed 16 weeks of therapy. Median age was 34.0 years; 51.1% of patients were female, 72.4% were white, and 21.3% were Asian. Median (Q1, Q3) AD duration was 21.8 years (9.5, 32.5) and Dermatology Life Quality Index (DLQI) total score was 15.0 (11.0, 21.0); mean (SD) EASI score was 30.9 (12.8); PP-NRS score was 7.3 (1.7); 35.4% had severe IGA. At week 12, the proportion of patients achieving IGA and EASI-75 response was significantly higher with abrocitinib than with placebo (P<0.0001). IGA response was 48.4% for abrocitinib 200 mg, 36.6% for 100 mg, 36.5% for dupilumab, and 14.0% for placebo; EASI-75 response was 70.3%, 58.7%, 58.1%, and 27.1%, respectively. At week 2, the proportion achieving PP-NRS4 response was significantly higher with abrocitinib 200 mg than with dupilumab (P<0.0001): 49.1% for abrocitinib 200 mg, 31.8% for 100 mg, 26.4% for dupilumab, and

13.8% for placebo. At week 16, the proportion achieving IGA and EASI-75 response was significantly higher with abrocitinib than with placebo (*P*<0.0001). IGA response was 47.5% for abrocitinib 200 mg, 34.8% for 100 mg, 38.8% for dupilumab, and 12.9% for placebo; EASI-75 response was 71.0%, 60.3%, 65.5%, and 30.6%, respectively. For abrocitinib 200 mg, 100 mg, dupilumab, and placebo, median time to PP-NRS4 response was 13 days, 29 days, 31 days, and “not evaluable,” respectively. At week 12, the proportion of patients achieving PP-NRS4 response (abrocitinib 200 mg, 100 mg, dupilumab, and placebo) was 63.1%, 47.5%, 54.5%, and 28.9%, respectively; PP-NRS <2 response was 36.9%, 21.1%, 24.9%, and 7.4%, respectively; DLQI <2 response was 29.7%, 21.9%, 22.5%, and 8.6%, respectively; ≥90% improvement in EASI was 46.1%, 36.6%, 34.9%, and 10.1%, respectively. More patients in the 200-mg arm experienced adverse events (AEs); in the abrocitinib 200 mg, 100 mg, dupilumab, and placebo groups, the proportion was 61.9%, 50.8%, 50.0%, and 53.4%, respectively. The proportion of patients with serious or severe AEs or AEs leading to discontinuation across treatment arms were similar (all <5%).

Conclusion: This study shows the efficacy and safety of both abrocitinib doses through 16 weeks combined with background medicated topical therapy in adults with moderate-to-severe AD. Abrocitinib 200 mg provided significantly faster itch relief than dupilumab. Through 12 weeks, the rate of improvement in AD signs was similar between dupilumab and abrocitinib 100 mg and was higher with abrocitinib 200 mg. By week 16, the responder rate was highest for abrocitinib 200 mg, followed by dupilumab and abrocitinib 100 mg. Both drugs were well tolerated.