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Patient-Reported Outcomes in the Randomized, Double Blind Phase 2 Study of ESK-001, an Oral Allosteric TYK2 Inhibitor, in Adults with Moderate-to-Severe Plaque Psoriasis

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Introduction & Objectives: ESK-001 is an oral, highly selective allosteric TYK2 inhibitor being developed for patients with moderate-to-severe plaque psoriasis. The Phase 2 ESK-001 program consists of a completed randomized, placebo-controlled dose ranging study (STRIDE, NCT05600036), and an ongoing open label extension study (OLE, NCT05739435). Here the patient-reported outcomes (PROs) from these studies are reported.

Materials & Methods: STRIDE was a randomized, double-blinded, placebo-controlled study in psoriasis patients with PASI≥12, sPGA≥3 and BSA≥10%. Patients were randomized (1:1:1:1:1:1) to one of five ESK-001 dose arms (10 mg QD, 20mg QD, 20mg BID, 40mg QD, 40mg BID) compared to placebo. The primary endpoint was PASI-75 at Week 12 and PRO secondary endpoints included achievement of DLQI-0/1 and improvement in pruritus numerical rating scale (NRS). Eligible patients from STRIDE were enrolled in the OLE study (currently ongoing) into one of two dose arms (40mg BID or 40mg QD).

Results: The primary and key secondary endpoints were met ($p<0.0001$, top three doses) with a dose-dependent response. At the highest dose (40 mg BID), 64%, 39% and 15% (placebo = 0%) of patients achieved PASI-75, PASI-90 and PASI-100; 59% and 23% (placebo = 8%, 0%) of patients achieved sPGA-0/1 and sPGA-0 at Week 12, respectively. Concordant with these findings, dose-dependent improvements in DLQI and pruritus were observed at Week 12 (**Table**). At the 40mg BID dose, 64% of patients achieved DLQI-0/1 and median % improvement in pruritus for both on-average and at-worst scores were 88%. Improvements for both DLQI-0/1 and pruritus scores were maintained at Week 16 of the OLE study based on 08 Dec, 2023 data date (**Table**). ESK-001 was generally safe and well tolerated in STRIDE with a similar safety profile in the OLE. TEAE severity was similar across dose arms, with the majority of TEAEs mild-to-moderate and self limited. No deaths, treatment related AEs associated with JAK inhibitor class pharmacology, or clinically significant laboratory or ECG trends were observed.

Table: Dose dependent improvement in DLQI and pruritus PROs in STRIDE at Week 12, with maintenance of response at Week 16 in the OLE

STRIDE, Week 12
Placebo (N=38)
40 mg BID (N=39)
40 mg QD (N=39)
20 mg BID (N=39)
20 mg QD (N=36)
10mg QD (N=36)
Open Label Extension, Week 16
40mg BID (N=82)
40mg QD (N=82)

* based on non-responder imputation (NRI)

* Median % change from Baseline in pruritus NRS (scored 0-10: severity of itch, on average or at worst, within the past 24 hours)

Conclusion: In these Phase 2 moderate-to-severe psoriasis studies ESK-001 demonstrated significant improvements in patient reported quality of life (DLQI) and psoriasis-associated pruritus (NRS), with a clear dose-dependent improvement observed. Improvements in PROs were maintained with ongoing treatment in the OLE study. These PRO outcomes highlight the positive impact on the lives of patients with psoriasis, while receiving ESK-001.