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Efficacy, Safety, and Tolerability of GSK1070806, an Anti-IL-18 Monoclonal Antibody, in Patients with Moderate to Severe Atopic Dermatitis: A Phase 1b, Randomised, Double-Blind, Parallel Group, Placebo Controlled Study

John B Kelly*[1], Joanne Ellis[2], Lea Fortunato[2], Núria Buil-Bruna[2], Joanna Barnard[2], Jenny Lowe[3], Parima Ghafoori[1], Simon Safa-Leathers[2], Scott Dinehart[4], Gabriel Wong[2], Iain Uings[2]

[1]GSK, Collegeville, United States, [2]GSK, Stevenage, United Kingdom, [3]GSK, London, United Kingdom, [4]Arkansas Dermatology, Little Rock, United States

Introduction & Objectives:

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease characterised by eczematous lesions and intense pruritus, and is associated with skin barrier dysfunction and immune dysregulation. AD heterogeneity is likely a result of the varying contributions from both T-helper cell (TH)2/TH22-skewing and TH1/TH17.

Interleukin-18 (IL-18), a pleiotropic cytokine, may play a role in the pathophysiology of AD. This study compared the clinical effect and patient reported outcomes (PROs) of a single IV infusion of GSK1070806, a novel, first-in-class, highly potent anti-IL-18 monoclonal IgG1 antibody, versus placebo in patients with AD.

Materials & Methods:

This was a multicentre, randomised, double-blind, parallel-group study to investigate the efficacy, safety, and tolerability of GSK1070806 in participants with moderate-to-severe AD.

Eligible patients were adults (≥18 years) with a confirmed diagnosis (≥6 months) of moderate-to-severe AD (Eczema Area and Severity Index [EASI] ≥16; Investigator's Global Assessment [IGA] score ≥3), for whom topical therapies were ineffective or not recommended. Two groups were recruited: patients naïve to biologic treatment and Janus kinase [JAK] inhibitors (BN group), and patients who were inadequate responders (after ≥16 weeks treatment), or intolerant, to dupilumab (Dupi-IR group). Participants were randomised 2:1 (BN group) or 5:1 (Dupi-IR group) to receive a single, one-hour IV infusion of 2mg/kg GSK1070806 or placebo.

The primary endpoint was the percent change from baseline in the EASI score in the BN group at Week 12. PRO measures included worst itch (Peak Pruritis Numerical Rating Scale [PP-NRS]) and quality of life (QoL; Dermatology Life Quality Index [DLQI]). Endpoints were assessed at Week 12 using a Bayesian repeated measures model. Safety assessments included anti-drug antibodies.

Results:

Overall, 34 participants were randomised: 30 in the BN group (GSK1070806 n=20, placebo n=10) and 4 in the Dupi-IR group (GSK1070806 n=3, placebo n=1). Demographics were balanced across subgroups and treatment arms (mean age 44.8 years, 53% female). At baseline, 22 participants (65%) had moderate disease and 12 (35%) had severe disease as assessed using the EASI.

In the BN group, the percent reduction in EASI score was greater in participants treated with GSK1070806 than in those administered placebo (posterior median of difference −33.2% [95% credible interval 51.0, −14.8]) (**Table**). Participants who received GSK1070806 had clinically meaningful improvements in itch (PP-NRS) and QoL (DLQI) until at least Week 12 compared with those who received placebo (posterior median of difference [95% CrI]: PP-NRS −4.10 [−5.63, −2.55]; DLQI −6.13 [−11.41, −0.90]) (**Table**). Outcomes in the Dupi-IR group are not shown due to

low participant numbers.

Across the combined groups, 10 participants (43%) receiving GSK1070806 and 6 (55%) receiving placebo experienced ≥1 adverse event; most were mild in intensity, none were serious, and none resulted in withdrawal from the study. There was no safety signal of concern. No anti-drug antibodies were observed.

Conclusion:

A single 2mg/kg IV infusion of GSK1070806 demonstrated a positive treatment effect on the EASI score and PRO measures of itch and QoL, which was sustained for at least 12 weeks. There were no safety concerns. GSK1070806 may be a promising future treatment option for patients with AD for whom topical therapies are not effective or appropriate.

Table. Primary and exploratory PRO endpoints in the BN group

Week 12 outcome	**GSK1070806 2mg/kg**	**Placebo**
PCFB in EASI (primary endpoint)	n=19	n=9
Posterior median (95% CrI)	–66.1% (–78.7, –53.5)	–32.8% (–46.6, –20.3)
Difference (95% CrI)	**–33.2%** (–51.0, –14.8)	
CFB in PP-NRS score (itch)	n=12	n=7
Posterior median (95% CrI)	–4.61 (–5.58, –3.65)	–0.52 (–1.73, 0.67)
Difference (95% CrI)	**–4.10** (–5.63, –2.55)	
CFB in DLQI score (QoL)	n=8	n=4
Posterior median (95% CrI)	–6.06 (–8.86, –3.29)	0.05 (–4.08, 4.22)
Difference (95% CrI)	**–6.13** (–11.41, –0.90)	

CFB, change from baseline; CrI, credible interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; PCFB, percent change from baseline; PP-NRS, Peak Pruritis Numerical Rating Scale; PRO, patient reported outcome; QoL, quality of life.