Biomarker Evidence of Anti-inflammatory Effects of EDP1815 in a Phase 2 Psoriasis Clinical Trial

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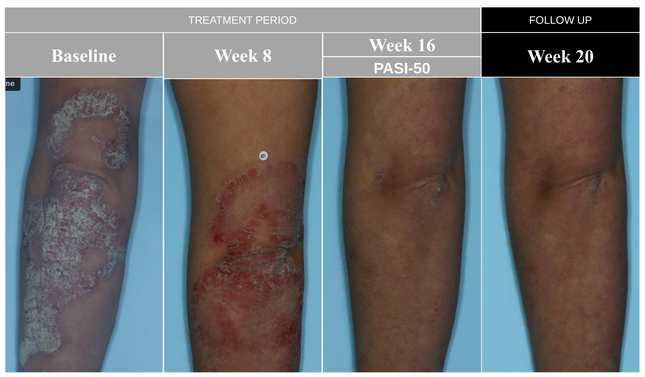
Introduction

EDP1815 is an investigational oral medicine with a novel mechanism of action being developed for the treatment of inflammatory diseases, including psoriasis. It is a non-live pharmaceutical preparation of a single strain of *Prevotella histicola*, a commensal bacterium isolated from a duodenal biopsy. EDP1815 modulates systemic inflammation through its interaction with immune cells in the epithelial lining of the small intestine through the small intestinal axis (SINTAX). It is not absorbed into the systemic circulation, and the microbe does not colonize in the intestine or change the background microbiome. EDP1815 has been shown to have broad inflammation resolving effects across Th1, Th2 and Th17 pathways in preclinical models.

Clinical responses

EDP1815-201 (Eudra CT# 2019-004901-28, ClinicalTrials.gov ID NCT04603027) was a double-blind, placebo-controlled, phase 2 clinical trial evaluating the safety and efficacy of 3 doses of EDP1815 in 249 participants with mild and moderate psoriasis over a 16-week treatment period. Statistically significant differences were observed in the number of EDP1815 responders (29%) using Psoriasis Area and Severity Index (PASI) 50 responses compared to placebo (12%), and also for the number of participants achieving a PGA-0/1 score at week 16. The safety and tolerability observed was comparable to placebo across all doses.

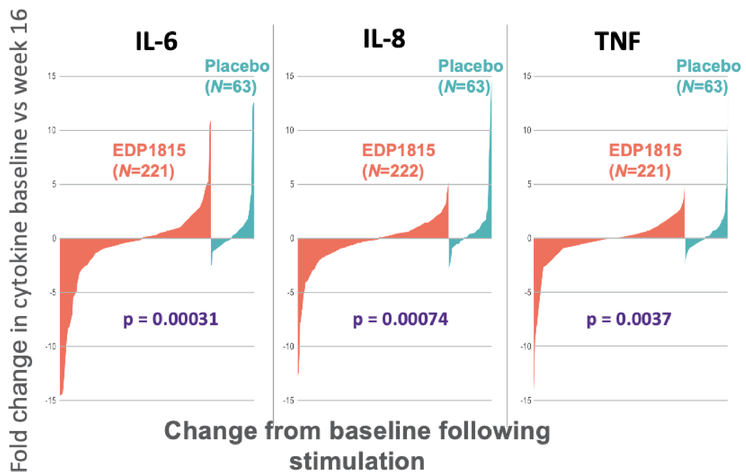
Statistically significant clinical responses were observed in EDP1815-201



Reduction in systemic cytokine production

To test EDP1815's broad inflammation resolving effects in humans, blood samples were taken from participants in this phase 2 study at baseline and after 16 weeks of once daily oral administration of either EDP1815 or placebo. Whole blood was incubated with three stimuli separately: lipopolysaccharide (LPS), antibodies to CD3 and CD28, and staphylococcal enterotoxin B (SEB). Analyses were performed on blood samples from 96 selected participants based on week-16 PASI scores. 44 of these participants achieved PASI-50 improvement, 11 showed worsening PASI scores of ≥1.5x baseline and 41 were drawn at random from those without significant PASI score changes. The differences between ex vivo stimulated cytokine production at baseline and week 16 were calculated for each stimulus. T-test analysis was performed, pooled across the 3 stimuli, to determine significance between EDP1815 and placebo group at week 16.

EDP1815 reduces cytokine release of PBMCs when stimulated ex-vivo

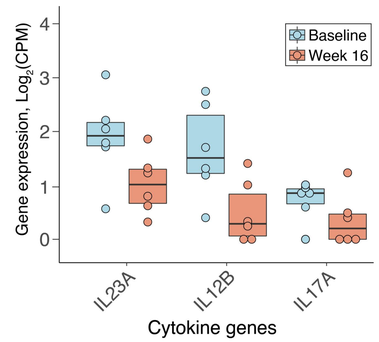


Statistically significant reductions in cytokine release from peripheral blood mononuclear cells, PBMCs, were observed across multiple cytokines using 3 different stimuli following 16 week treatment with EDP1815 compared to placebo. The maximum reduction observed in EDP1815 treated patients was 15 fold compared to 2.5 fold for placebo.

Reduction in skin cytokine gene expression

To test EDP1815's local inflammation resolving effects in psoriatic plaques, RNAseq analysis of paired skin biopsies from 6 participants who received EDP1815 and achieved PASI-50 at week 16 was performed. The same plaque was biopsied at both time points and was prespecified at baseline. The differences in RNA transcript counts for pathologically relevant cytokines at baseline and week 16 were calculated. Down-regulation of multiple psoriasis-relevant cytokine genes: *IL23A*, *IL12B* and *IL17A* at week 16 compared to baseline was observed. These changes were observed in skin biopsies from prespecified sites in subjects with PASI-50 or better responses.

EDP1815 reduces the expression levels of multiple pathological cytokine genes in psoriasis plaques



Conclusions

- EDP1815 is the first SINTAX based medicine that has been tested in humans
- EDP1815 demonstrated clinically meaningful benefit in patients with mild to moderate psoriasis in a phase 2 study, EDP1815-201
- Systemic biomarker analyses from samples taken in the phase 2 study confirmed generalized reduction of systemic immune reactivity consistent with re-establishing immune homeostasis
- Skin biomarker analyses confirmed gene expression reductions in multiple disease relevant cytokine genes suggesting inflammation resolving effects in disease tissues
- The combined clinical and biomarker data confirm that EDP1815 can resolve systemic inflammation without systemic exposure and with a safety and tolerability profile comparable to placebo