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Results From Dose Escalation From Resolve, an Ongoing Phase 1b/2a Study of EP-104GI (Long-acting Fluticasone Propionate Injectable Suspension) For Eosinophilic Esophagitis

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INTRODUCTION

- Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease characterized by inflammation, influx of eosinophils and esophageal remodeling.
- Therapy for EoE includes swallowed topical corticosteroids, dupilumab, and dietary elimination, but these are not always effective and have potential side-effects.
- EP-104GI is a long-acting fluticasone propionate (FP) injectable suspension being developed as a first-in-class treatment for EoE.
- EP-104GI consists of coated crystals of FP that release at a pre-defined rate via diffusion at the injection site. Steady-state diffusion reduces peak concentrations while prolonging the therapeutic window.
- RESOLVE (NCT05608681) is an ongoing Phase 1b/2a, multicenter, open-label, dose-escalation study to evaluate the safety, tolerability, feasibility, pharmacokinetics, and efficacy of EP-104GI in adults with symptomatic and histologically confirmed active EoE.

METHODS

- EP-104GI is injected once at up to 20 sites in the esophagus, arranged in alternating quadrants at 2 cm intervals.
- Participants are followed for up to 52 weeks.
- Efficacy assessments include histological endpoints and patient-reported symptom outcomes including the Straumann Dysphagia Index (SDI).
- Endoscopies are conducted at baseline, Weeks 4, 12, and at 36 for cohorts 5 and above and assessments include:
  - EoE Endoscopic Reference Score (EREFS)
  - Peak Eosinophil Count (PEC)
  - EoE Histologic Scoring System (EoEHSS)
- Dose escalation cohorts (n=3) explore increasing the dose per injection site and/or number of sites.
- This poster focusses on available data from dose escalation cohorts 3-6:
  - Cohort 3: 2.5 mg × 8 sites, total 20 mg
  - Cohort 4: 2.5 mg × 12 sites, total 30 mg
  - Cohort 5: 4 mg × 12 sites, total 48 mg
  - Cohort 6 : 4 mg × 16 sites, total 64 mg

RESULTS

Previously reported data from cohorts 1-4 (total doses of 4 to 30 mg) showed decreases in SDI for 10/11 patients of 2 to 6 points, the majority maintained to Week 24. Mean PEC declined for 7/12 patients in cohorts 2 to 4 at Week 12 by up to 91%.

Updated data are presented here include Cohort 5 to Week 36 and for Cohort 6 to Week 24. Data for Cohort 6 at Week 36 are pending.

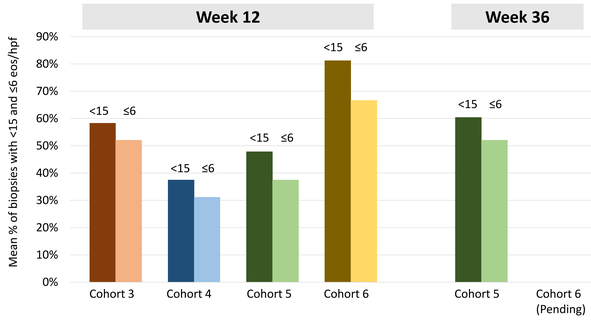


Fig. 1: Percentage of biopsies with PEC counts <15 and ≤6 per hpf by cohort at Week 12 and Week 36
The mean proportion of 16 biopsies taken over the injected area of the esophagus meeting each PEC threshold (<15 in darker shades, ≤6 in lighter shades) for each cohort.
Cohorts 3 and 4 were assessed to Week 12. Cohorts 5+ are assessed to Week 36.

Reduction in PEC to thresholds ≤6 and/or <15 eosinophils per high-power field (hpf) has been observed in the 16 biopsies assessed for each patient (Fig. 1). Notably, one patient in Cohort 5 had zero eosinophils at Week 12 and Week 36.

Decreases in mean EoEHSS grade and stage have improved with increasing EP-104GI dose and further improved from Week 12 to Week 36 for 2/3 patients in Cohort 5 (Fig. 2).

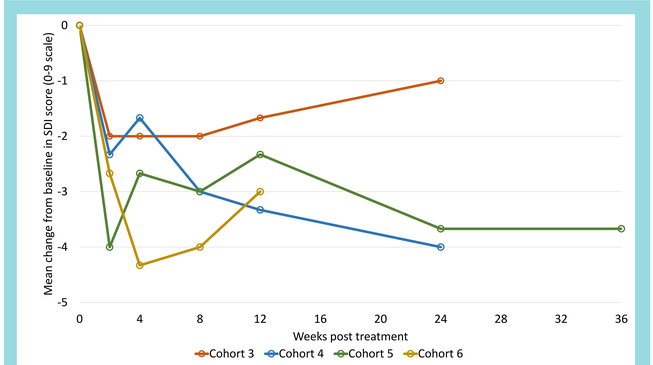


Fig. 3: Mean change from baseline in SDI by cohort at Week 12 and Week 36
Cohorts 3 and 4 were assessed to Week 12. Cohorts 5+ are assessed to Week 36.

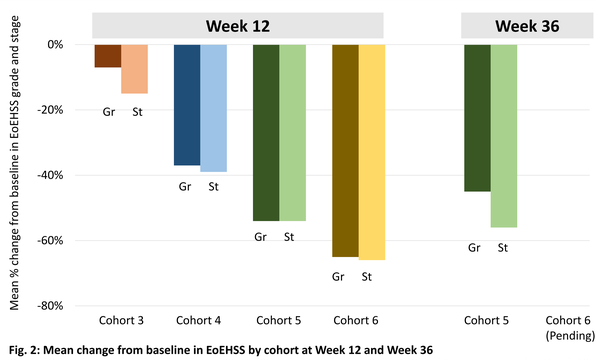


Fig. 2: Mean change from baseline in EoEHSS by cohort at Week 12 and Week 36
Grade (Gr) is shown in darker shades and Stage (St) in lighter shades. Cohorts 3 and 4 were assessed to Week 12. Cohorts 5+ are assessed to Week 36.

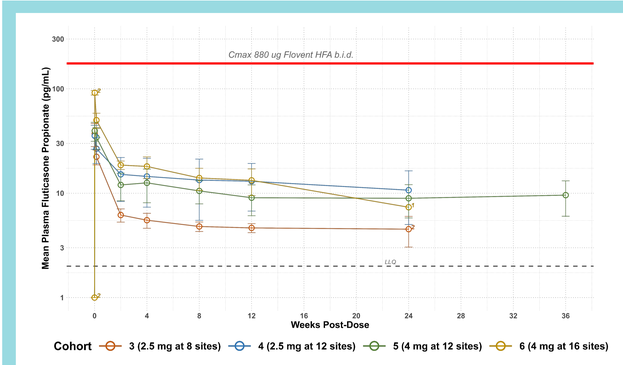


Fig. 4: Mean plasma FP concentration for cohorts 3-6
Note: Points tagged with a number indicate incomplete data, showing how many patient's data are available.

Mean reduction in SDI symptom score (Fig. 3) has been maintained to Week 36 (Cohort 5), with peak reduction in SDI of 3 to 6 points in all patients in Cohort 6.

Reduction in EREFS to zero was noted for 1/3 patients in Cohort 5 at Week 36 with the remaining 2 patients having a stable score and an increase of 1 point respectively.

Safety and Pharmacokinetics:

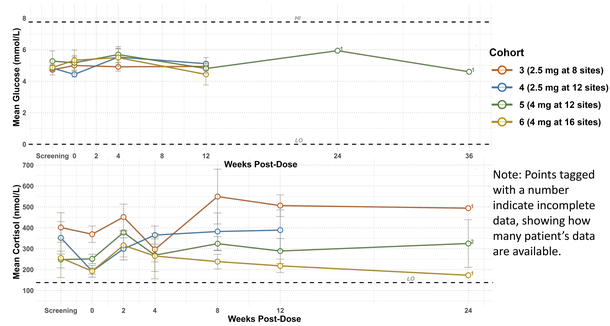
Plasma FP levels increased with dose and continued to be stable at <20 pg/mL after the initial peak (Fig. 4).

Treatment-emergent adverse events (TEAEs) in cohorts 3-6 have been mild to moderate, most not likely related to EP-104GI (Table 1).

Serum glucose and cortisol were stable post-dose (Fig. 5) with no adverse events such as oral candidiasis or adrenal suppression.

Cohort	Treatment-emergent Adverse Event at least possibly related to EP-104GI	Relationship to EP-104GI	Severity
3	None	Not applicable	Not applicable
4	None	Not applicable	Not applicable
5	Sensation of pressure in esophagus Esophageal sensitivity	Possible Definite	Mild Mild
6	None	Not applicable	Not applicable

Table 1: Treatment-related TEAEs occurring in cohorts 3-6



Note: Points tagged with a number indicate incomplete data, showing how many patient's data are available.

Fig. 5: Mean serum glucose and cortisol for cohorts 3-6

CONCLUSIONS

These data support that the ongoing study of local delivery of FP via EP-104GI is feasible and safe. Higher doses yield improved patient responses such as histological remission, enhanced patient-reported symptom scores, and favorable histology results, without occurrence of corticosteroids-related side-effects.

DISCLOSURE AND CONTACT INFORMATION

AM, JH, MMK, CD & VP: employees of Eupraxia Pharmaceuticals. **AJB:** Research funding: Nutricia, Thelial, Sanofi/Regeneron, SST, and Dr. Falk Pharma and received speaker and/or consulting fees from Laborie, Medtronic, BMS, Dr. Falk Pharma, Calypso Biotech, Eupraxia, Aqilion, Alimentiv, Sanofi/Regeneron, Reckitt and AstraZeneca. **NN:** None to declare. **HHK:** Advisory board and speaker's bureau for Sanofi. **ESD:** Research funding: Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Sanfoi, Shire/Takeda, Uniquity; Consultant: Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, Apogee, Apollo, Aqilion, Arena/Pfizer, Aslan, AstraZeneca, Avir, Biorasi, Calypso, Celgene/Receptos/BMS, Celldex, Eli Lilly, EsoCap, Eupraxia, Dr. Falk Pharma, Ferring, GSK, Gossamer Bio, Holoclara, Invea, Knightpoint, Landos, LucidDx, Morphic, Nexstone Immunology/Uniquity, Nutricia, Parexel/Calyx, Phathom, Regeneron, Revolo, Robarts/Alimentiv, Salix, Sanofi, Shire/Takeda, Target RWE, Third Harmonic Bio, Upstream Bio Educational grant: Allakos, Aqilion, Holoclara, Invea.

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