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Abstract # 4031521

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

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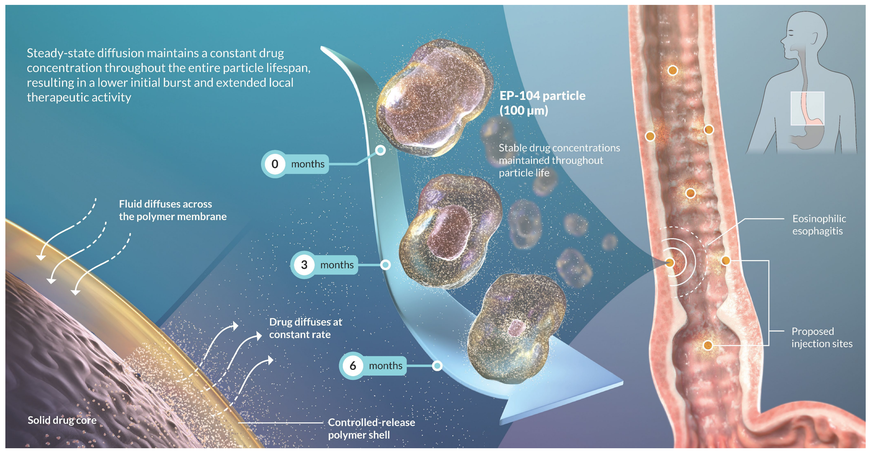
INTRODUCTION

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, proton pump inhibitors, and dietary elimination; but these are not always effective.

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 polymer-coated crystals of FP that release at a pre-defined rate via diffusion at the injection site, reducing peak concentrations while prolonging the therapeutic window (Fig 1).

Figure 1: Mechanism of action of EP-104GI



AIM & METHODS

RESOLVE (NCT05608681) is a Phase 1b/2a, multicenter, open-label, dose-escalation study to evaluate the safety, tolerability, feasibility, pharmacokinetics, and efficacy of EP-104GI in adults with histologically confirmed active EoE.

EP-104GI is administered as a single dose via 4-20 injections into the esophageal wall (Fig 2). Dose escalations increase the dose per site and/or number of sites. Participants in cohorts 1 and 2 were assessed for up to 24 weeks. Additional cohorts are planned to evaluate greater dose per injection site and/or increased number of injections with a longer duration of follow-up of 52 weeks.

Efficacy assessments include esophageal biopsies with histological endpoints including Peak Eosinophil Count (PEC) and Eosinophilic Esophagitis Histology Scoring System (EoEHSS), and patient-reported symptom outcomes.

Figure 2: EP-104GI injection and esophageal biopsy schematic

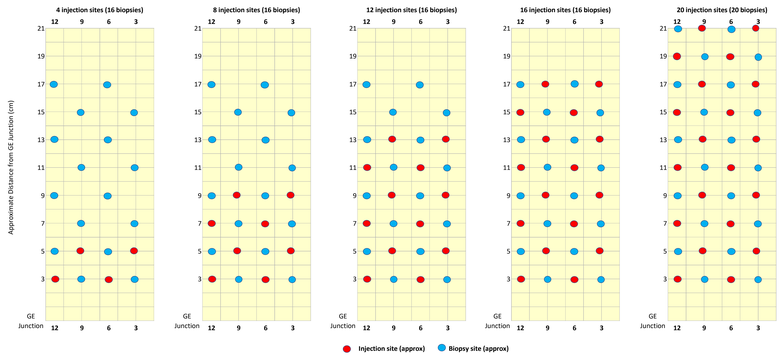
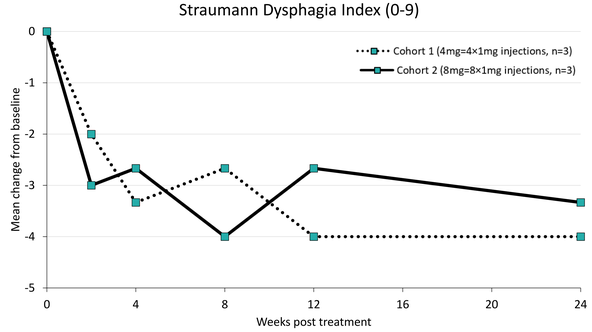
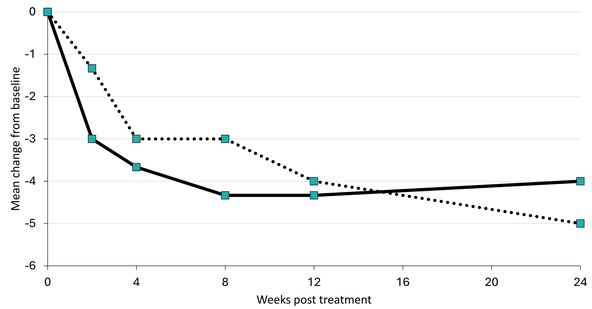


Figure 3: Patient reported outcomes following a single dose of EP-104GI

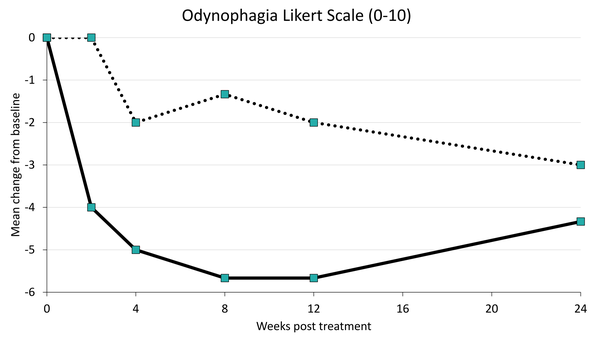
Straumann Dysphagia Index (0-9)



Dysphagia Likert Scale (0-10)



Odynophagia Likert Scale (0-10)



RESULTS

Safety observations from the ongoing dose escalation are mild-moderate treatment-emergent AEs, not related to EP-104GI (Table 1). Glucose levels post-dose have remained stable. Transient decreases in serum cortisol of up to 88 nmol/L were observed in one participant in each cohort on Day 2 post-dose, however, levels remained within normal range. There have been no symptoms of adrenal insufficiency.

Efficacy assessments demonstrate decreased from baseline in symptom scores extending to Week 24 (Fig 3). Reductions in PEC and EoEHSS Grade and Stage representing severity and extent of disease have been observed in all participants in Cohort 2 (Table 2).

Plasma concentration of FP has increase with EP-104GI dose, demonstrating a similar profile to that observed in previous clinical trials of the EP-104 injectable suspension in osteoarthritis (Fig 4).

Table 1: Treatment emergent adverse events occurring after a single dose of EP-104GI

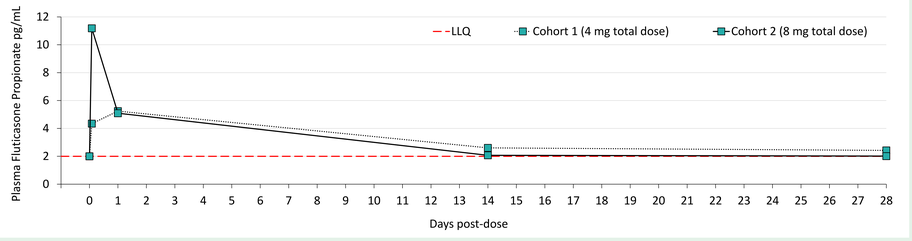
Cohort 1 (4 mg = 4×1 mg injections, n=3)			Cohort 2 (8 mg = 8×1 mg injections, n=3)		
Event	Severity	Relationship to EP-104GI	Event	Severity	Relationship to EP-104GI
Procedural pain	Mild	Unrelated[a]	Throat tightness	Mild	Unlikely[a]
Left occipital lymphadenopathy	Mild	Unrelated			
Back pain	Moderate	Unrelated			
Non-cardiac chest pain	Moderate	Unrelated[a]			
Nausea	Mild	Unlikely[a]			
Viral gastroenteritis	Mild	Unrelated			

[a] At least possibly related to injection procedure

Table 2: Mean reduction from baseline in mean PEC and EoEHSS Grade and Stage

	Week 4			Week 12		
	PEC (cells/hpf)	EoEHSS Grade (0-1 scale)	EoEHSS Stage (0-1 scale)	PEC (cells/hpf)	EoEHSS Grade (0-1 scale)	EoEHSS Stage (0-1 scale)
Cohort 1 (4 mg = 4×1 mg injections, n=3)	No reduction No reduction -3 (-10%)	-0.10 (-22%) -0.07 (-10%) -0.09 (-21%)	-0.08 (-19%) -0.02 (-4%) +0.01 (+2%)	No reduction		
Cohort 2 (8 mg = 8×1 mg injections, n=3)	-51 (-41%) -73 (-70%) +16 (+9%)	-0.29 (-49%) -0.26 (-47%) -0.11 (-18%)	-0.19 (-30%) -0.17 (-33%) -0.01 (-2%)	-50 (-41%) -54 (-51%) -78 (-43%)	-0.14 (-23%) -0.13 (-23%) -0.12 (-19%)	-0.15 (-23%) -0.11 (-21%) -0.11 (-17%)

Figure 4: Plasma concentration of fluticasone propionate following a single dose of EP-104GI



CONCLUSIONS

The initial results indicate that the novel diffusion-based localized delivery of FP via EP-104GI injection is feasible and safe in patients with EoE.

Efficacy data, although limited at this point, show improvement in symptom outcomes and histological findings which may increase with dose.

These findings support the potential for extended intervals between inter-esophageal injections, which may be further extended at the higher doses to be investigated in this study. Recruitment is ongoing.

DISCLOSURE AND CONTACT INFORMATION

JH, AM, MMK, CD and VP: employees of Eupraxia Pharmaceuticals. **ED:** Research funding: Adare/Ellodi, Allakos, Arena/Pfizer, AstraZeneca, Eupraxia, Ferring, GSK, Meritage, Miraca, Nutricia, Celgene/Receptos/BMS, Regeneron, Revolo, Shire/Takeda Consultant: Abbott, Abbvie, Adare/Ellodi, Aimmune, Akesobio, Alfasigma, ALK, Allakos, Amgen, 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, Upstream Bio Educational grant: Allakos, Aqilion, Holoclara, Invea. **HHK:** advisory board and speaker's bureau for Sanofi. **AJB:** received research funding from 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. **NG:** nothing to declare.

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Resolve