Results from Dose Escalation Cohorts 1-6 of RESOLVE, an Ongoing Phase 1b/2a Study of EP-104GI (Long-acting Fluticasone Propionate Injectable Suspension) For Eosinophilic Esophagitis

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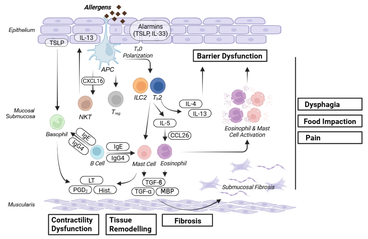
BACKGROUND

- Complex local inflammation in eosinophilic esophagitis (EoE) leads to burdensome symptoms such as dysphagia, but treatment options remain limited[1]
- The broad anti-inflammatory action of topical corticosteroids enables them to address EoE's complex pathogenesis[2]
  - Transient and indirect contact of swallowed topical corticosteroids with the mucosa may limit efficacy



Adapted and modified from: Choi et al. (2025) Korean J Helicobacter Up Gastrointest Res., O'Shea et al. (2018) Gastroenterology, Racca et al. (2022) Front. Physiol., Underwood et al. (2023) Ann Allergy Asthma Immunol., Young et al. (2022) Dig. Dis Sci. Created using BioRender

Fig 1. Eosinophilic Esophagitis Pathogenesis

- EP-104GI is as a submucosal, long-acting formulation of fluticasone propionate microparticles, engineered to provide controlled, localized drug release at a consistent rate.
  - It presents the potential to locally address esophageal inflammation[3]

METHODS

- RESOLVE part 1 (NCT05608681) is a Phase 1b, multicenter, open-label, dose-escalation trial to evaluate the safety, tolerability and feasibility of EP-104GI injection in adults with EoE (Fig 1)

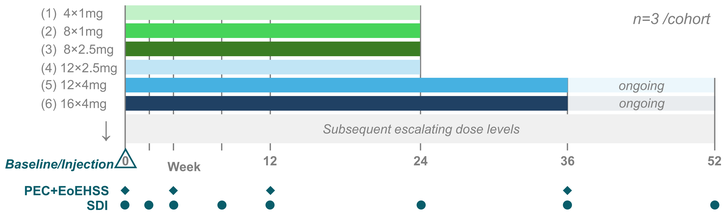


Figure 1. RESOLVE-I Dose Escalation Study Design

- EP-104GI was injected into the esophageal wall in alternating quadrants during endoscopy in escalating dose levels (number of sites x dose per site)
- Participants are followed for up to 24 (4×1mg to 12×2.5mg) or 52 weeks (12×4mg, 16×4mg and subsequent dose levels)

REFERENCES

1. Dellon et al. (2025) AJG 120(1):31-59. 2. Schoepfer et al. (2024) Inflamm Intest Dis. 9(1):199–209 3. Hasnoot et al. (2022) Am J Gastroenterol 117(9):1412-1418. 4. Malone et al. (2025) Gastroenterology, 169:1 S-402

RESULTS

Pharmacokinetics & Safety

- No dose limiting toxicity reported to date: no serious treatment-emergent adverse events, events of GI or oral candidiasis, or cases of adrenal suppression were reported
- TEAEs related to EP-104GI administration for doses reported included esophageal sensitivity, pressure sensation, chest pain, nausea, throat tightness
- Serum concentrations of cortisol and glucose were stable following EP-104GI administration (Fig. 3a/b)
- Plasma levels of fluticasone remained constant (<20 pg/ml) shortly following an initial peak (Fig. 3c)

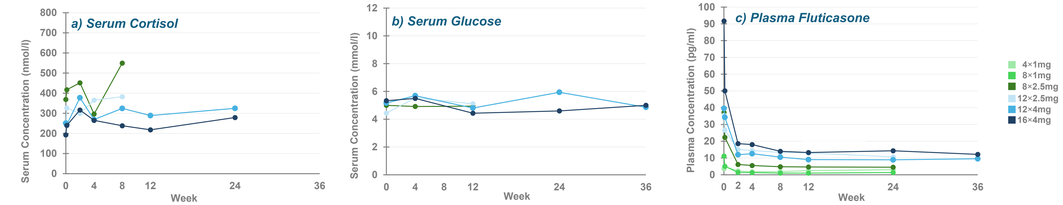


Figure 3. Mean Cortisol, Glucose and Fluticasone Concentrations Following Administration of EP-104GI

Esophageal Inflammation

- Eosinophil counts and histologic severity show an escalating response for increasing doses (Tab 1)
- Week 36: Improvements **>25%** in Biopsies With Peak Eosinophil Count (PEC) ≤6/hpf (Fig. 4)
- Week 36: Improvements **>45%** in EoE Histology Scoring System (EoEHSS) grade and stage (Fig. 5)

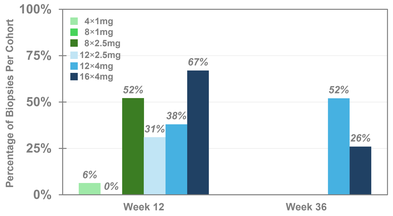


Figure 4. Mean Percentage of Esophageal Biopsies With Peak Eosinophil Count ≤6/hpf Following EP-104GI Administration

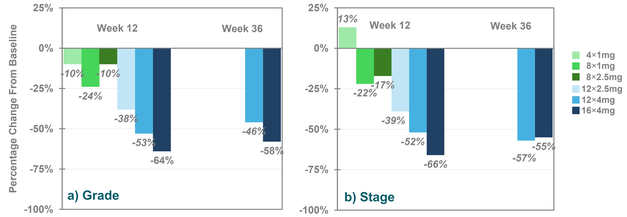


Figure 5. Mean Percentage Change In EoEHSS Total Score†

Dysphagia

- Persistent, long-term improvements in patient-reported dysphagia following single administration of EP-104GI
- Week 24: Most cohorts demonstrate a response in Straumann Dysphagia Index (SDI) ≥3[4] (Fig. 6)
- Week 36: Doses of 12×4mg and 16×4mg maintained mean improvements >2.5 (Fig. 6)

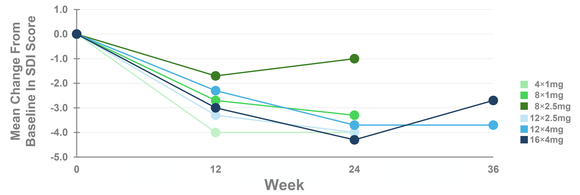


Figure 6. Straumann Dysphagia Index (SDI) Following EP-104GI Administration

***Table 1**: Histological and Symptom Responses to EP-104GI*

Cohort No.	(1)	(2)	(3)	(4)	(5)	(6)
Sites X Dose	4×1 mg	8×1 mg	8×2.5 mg	12×2.5 mg	12×4 mg	16×4 mg
Total Dose	4 mg	8 mg	20 mg	30 mg	48 mg	64 mg
Percentage Change From Baseline In Composite‡ EoE Histology Scoring System (grade/stage)						
Week 12	-10% / 13%	-24% / -22%	-7% / -15%	-37% / -39%	-54% / -54%	-65% / -66%
Week 36	-	-	-	-	-45% / -56%	-58% / -55%
Percentage of biopsy sites with Peak Eosinophil Count ≤6 eosinophil/hpf						
Week 12	6%	0%	52%	31%	38%	67%
Week 36	-	-	-	-	52%	26%
Percentage of biopsy sites with Peak Eosinophil Count <15 eosinophil/hpf						
Week 12	9%	8%	38%	38%	48%	81%
Week 36	-	-	-	-	60%	34%
Percentage Change From Baseline In Straumann Dysphagia Index						
Week 12	-75%	-40%	-28%	-45%	-41%	-47%
Week 24	-75%	-50%	-17%	-55%	-65%	-68%
Week 36	-	-	-	-	-65%	-42%

† calculated by summing all individual items and dividing by the maximum score for evaluated items (range, 0-3)

‡ calculated by summing the individual available items and dividing by the maximum score for evaluated items (range, 0-1)

CONCLUSIONS

- EP-104GI administration has been feasible, safe and well tolerated to date, with no gastrointestinal candidiasis, signs of adrenal suppression, or other dose-limiting toxicity reported
- Escalating improvements in inflammation and long-term improvements in dysphagia support the investigation of escalating dose levels over a 52-week post-dose period