Durability of Dysphagia Improvements Following Single Administration of EP-104GI in Participants With Eosinophilic Esophagitis During Dose Escalation in the RESOLVE Trial

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease where local inflammation and fibrosis negatively impact quality of life by leading to dysphagia (difficulty swallowing), pain, and food impaction [1]
- EP-104GI is a novel, long-acting submucosal formulation of fluticasone propionate particles designed for sustained, localized drug release within esophageal tissue, currently investigated for the treatment of EoE [2]
- We report here the durability of improvements for dose cohorts reporting over 36 and 52 weeks in the RESOLVE trial

METHODS

- RESOLVE (NCT05608681) is a Phase 1b/2, multicenter, open-label trial, evaluating the safety, tolerability and feasibility of EP-104GI injection in adults with EoE
- In part 1, EP-104GI was injected at baseline in the esophageal wall during endoscopy in escalating dose cohorts (number of sites or dose per site) (Fig 1)
- Participants (n = 3/cohort) were followed for up to 24 or 52 weeks

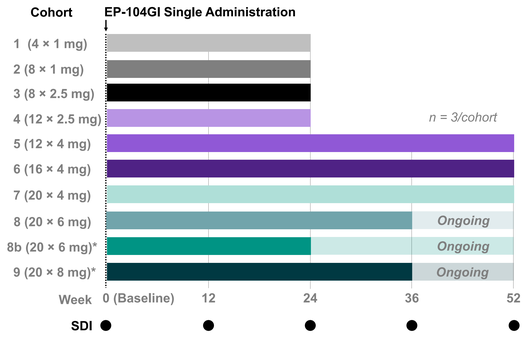

Figure 1. RESOLVE-I Dose Escalation Study Design

Straumann Dysphagia Index

- The **Straumann Dysphagia Index (SDI)** quantifies the **severity** and **frequency** of dysphagia over a 7-day recall period [3,4]
- In RESOLVE part 1, SDI assessments were conducted on all cohorts at baseline, week 12, 24, 36, and 52

RESULTS

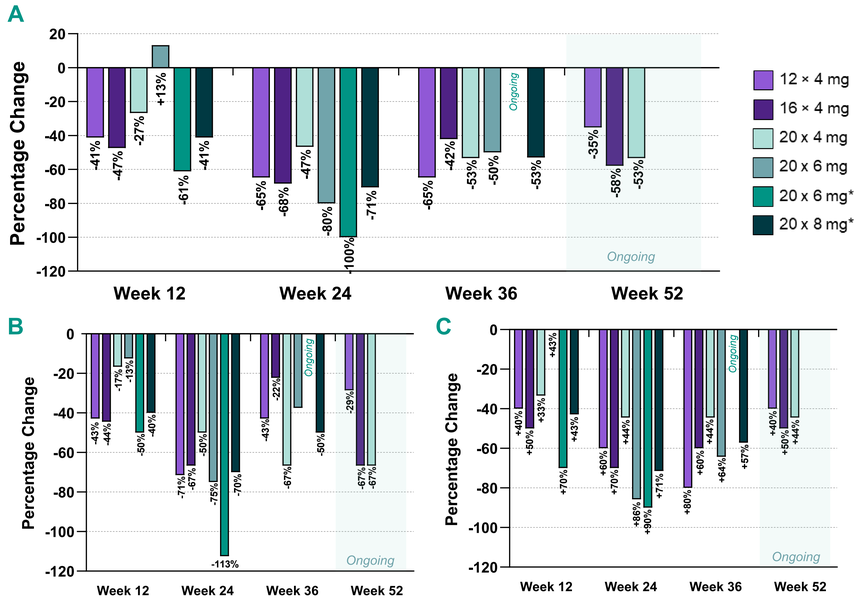

Figure 2. Mean Percentage Change From Baseline in SDI Score (A), Frequency (B) and Intensity (C) Sub Scores

Table 1. SDI Scores Across Cohorts

Cohort No. Sites x Dose Total Dose	1 4 x 1 mg 4 mg	2 8 x 1 mg 8 mg	3 8 x 2.5 mg 20 mg	4 12 x 2.5 mg 30 mg	5 12 x 4 mg 48 mg	6 16 x 4 mg 64 mg	7 20 x 4 mg 80 mg	8 20 x 6 mg 120 mg	8b* 20 x 6 mg 120 mg	9* 20 x 8 mg 160 mg
Mean SDI Score at Baseline										
Baseline	5.33	6.67	6.00	7.33	5.67	6.33	5.00	5.00	6.00	5.67
Mean Change From Baseline SDI Score										
Week 12	-4.00	-2.67	-1.67	-3.33	-2.33	-3.00	-1.33	+0.66	-3.67	-2.33
Week 24	-4.00	-3.33	-1.00	-4.00	-3.67	-4.33	-2.33	-4.00†	-6.00†	-4.00
Week 36	-	-	-	-	-3.67	-2.67	-2.67	-2.50†	*ongoing*	-3.00
Week 52	-	-	-	-	-2.00	-3.67	-2.67	*ongoing*	*ongoing*	*ongoing*
Number of Participants with Reduction of ≥3 Points From Baseline										
Week 12	1/2	1/3	2/3	2/3	2/3	2/3	1/3	0/3	2/3	2/3
Week 24	1/1	2/3	1/2	2/3	2/3	3/3	2/3	2/2†	2/2†	2/3
Week 36	-	-	-	-	3/3	1/3	2/3	1/2†	*ongoing*	2/3
Week 52	-	-	-	-	2/3	2/3	2/3	*ongoing*	*ongoing*	*ongoing*

† : n=2

- All dose cohorts available to date showed substantial reductions in SDI total scores at week 24, 36 and 52, indicating consistent improvement from baseline (Fig 2)
- At week 36, all dose cohorts reported to date showed mean improvements of 2.5 points or more (Tab 1)
- A reduction of 3 points or more in SDI has been proposed as a clinical response threshold [3]
  - At week 36, 3/3, 1/3, 2/3, 1/2 and 2/3 participants in dose cohorts 5, 6, 7, 8 and 9, respectively, reported SDI improvements of ≥3 points (9/14 in total) (Tab 1)
- Patients reported generally consistent improvements in both frequency and intensity of dysphagia with EP-104GI treatment (Fig 2b-c)
  - *Cohort 8 (20x6mg) reported a transient increase in intensity concomitant with a decrease in frequency of dysphagia at week 12*

CONCLUSIONS

- Administration of EP-104GI has been feasible, generally safe and well tolerated to date, with no clinically significant signs of adrenal suppression, glucose derangement, or other dose-limiting toxicity reported
- The study found persistent improvement in dysphagia over 24, 36, and 52 weeks following a single administration of EP-104GI in participants with EoE
- Overall, our results support the continued development of EP-104GI for the treatment of EoE

REFERENCES

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Abbreviations: EoE, Eosinophilic esophagitis; SDI, Straumann Dysphagia Index

** Administration for 2 dose cohorts (8b & 9) was performed using updated needle/catheter combinations*