

Single Administration of EP-104GI in RESOLVE, a Phase 1b/2 Trial in Eosinophilic Esophagitis, Improves Endoscopic Features of Inflammation and Fibrosis Over 36 Weeks

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a chronic, immune-mediated disease where esophageal inflammation and fibrosis lead to dysphagia, pain, and food impaction¹
- Upper endoscopy (EGD) plays a key role in diagnosis and monitoring of EoE by assessing inflammatory and fibrotic features characteristics of EoE¹⁻³
- EP-104GI is a novel, long-acting submucosal formulation of fluticasone propionate particles designed for sustained, localized drug, investigated for the treatment of EoE⁴

METHODS

- RESOLVE (NCT05608681) is a Phase 1b/2, multicenter, open-label, trial to evaluate 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 and dose per site) (Fig 1 & 2)
- Participants (n=3/cohort) were followed for up to 24 or 52 weeks

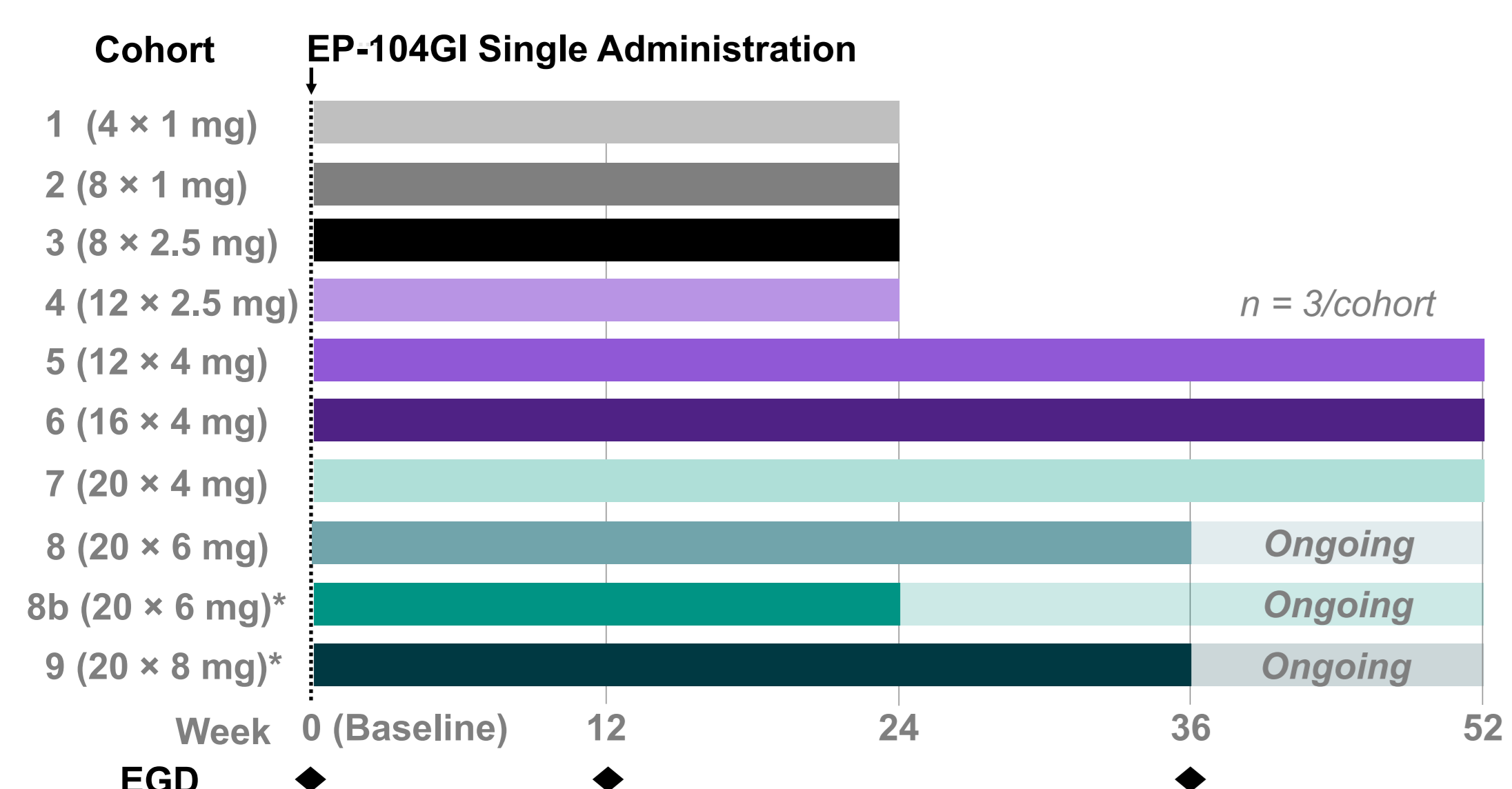


Figure 1. RESOLVE Part 1 Dose Escalation Design

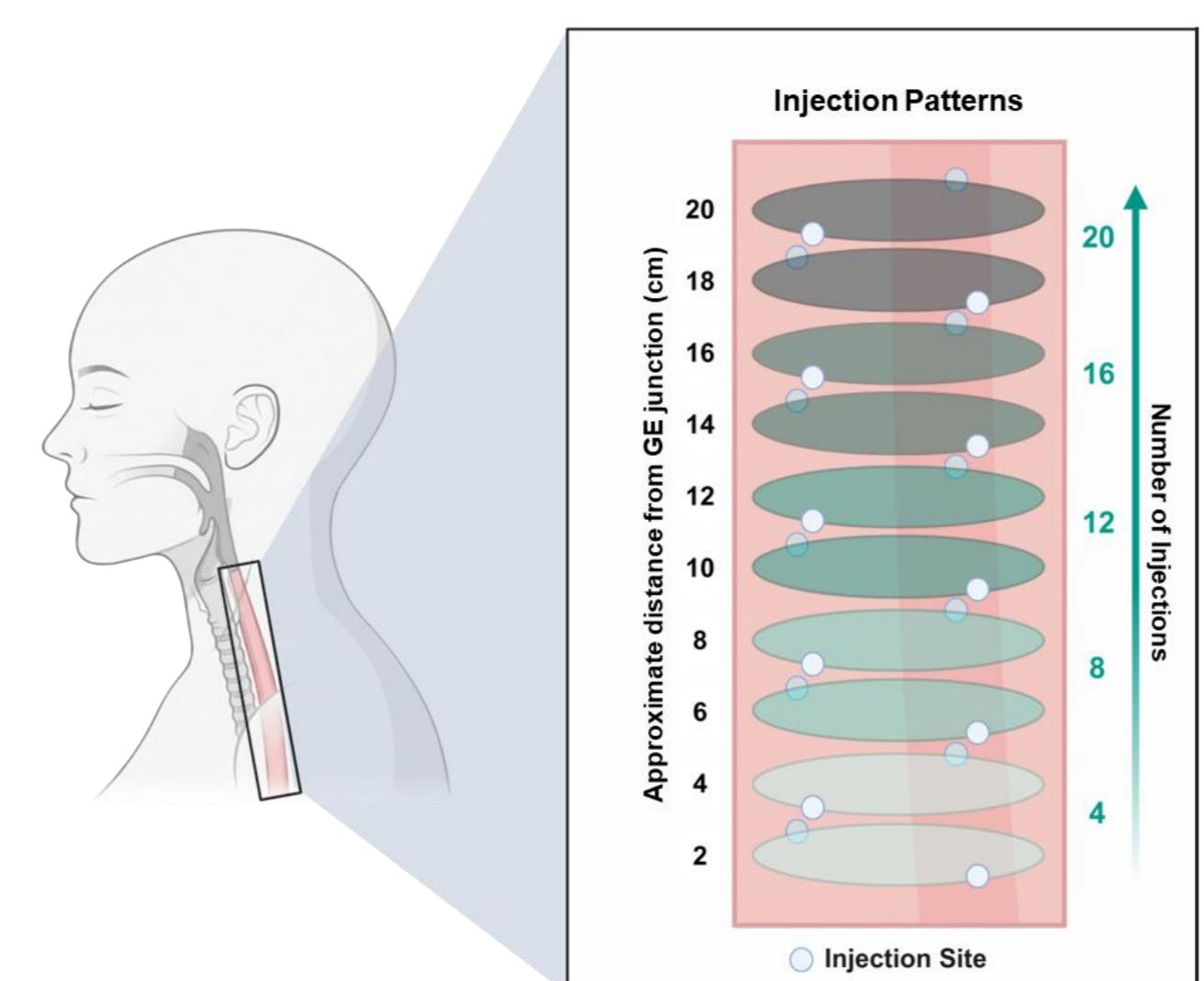


Figure 2. Injection pattern in RESOLVE Part 1

Endoscopic Assessment

- The Hirano EoE Endoscopic Reference Score (EREFS) assesses the severity of five endoscopic features (domains) of EoE: **edema, rings, exudates, furrows, and strictures** at their most severe location^{2,3}
- A score of 2 points has been validated as a response threshold for the EREFS score⁵
- EREFS assessments from EGD examinations were conducted on all cohorts at baseline, week 12, and week 36

REFERENCES

1. Dellon et al. (2025) AJG 120(1):31-59 2. Hirano et al. (2013) Gut. 62(4):489-95. 3. Ma et al. (2022) Gastrointest Endosc. 95(6):1126-1137.e2.4. Reed et al. (2025) Am J Gastroenterol 10.14309/ajg.0000000000003876. 4. Malone et al. (2025) Gastroenterology, 169:1 S-402. 5. Cotton et al. (2022) Endoscopy. 54(7):635-643.

RESULTS

Table 1. EREFS Response And Improvements In Participants With Score >2 At Baseline

| No. Injections | 4X | | 8X | | 12X | | 16X | | 20X | |
|---|-------------|-------------|--------------|--------|--------------|-------------|-------------|-------------|--------------|--------------|
| | 1mg | 2.5mg | 1mg | 2.5mg | 4mg | 4mg | 6mg | 6mg* | 8mg* | |
| Dose/Injection | 4 mg | 20 mg | 8 mg | 30 mg | 48 mg | 64 mg | 80 mg | 120 mg | 120mg | 160 mg |
| Total Dose | 4 mg | 20 mg | 8 mg | 30 mg | 48 mg | 64 mg | 80 mg | 120 mg | 120mg | 160 mg |
| Cohort No. | 1 | 3 | 2 | 4 | 5 | 6 | 7 | 8 | 8b | 9 |
| Participants at Baseline >2, n | 3 | 3 | 3 | 3 | 2 | 3 | 3 | 1 | 3 | 1 |
| Responders (Participant with EREFS Score ≤2, With A Score At Baseline >2) | | | | | | | | | | |
| Week 12 | 0/3 | 0/3 | 0/3 | 1/3 | 0/2 | 1/2 | 0/2 | 0/1 | 3/3 | 1/1 |
| Week 36 | - | - | - | - | 1/2 | 1/3 | 1/3 | 0/1 | ongoing | 1/1 |
| Mean Change From Baseline / Mean Percentage Change From Baseline | | | | | | | | | | |
| Baseline Score, mean | 4.3 | 4.0 | 3.7 | 4.0 | 3.0 | 4.7 | 5.7 | 5.0 | 5.3 | 4.0 |
| Week 12 | +0.5 / +12% | -0.3 / -8% | +0.7 / +18% | 0 / 0% | +0.5 / +17% | -1.5 / -32% | -2.0 / -35% | 0 / 0% | -5.0 / -94% | -4.0 / -100% |
| Week 36 | - | - | - | - | -1.0 / -33% | -0.7 / -14% | -3.3 / -59% | 0 / 0% | ongoing | -3.0 / -75% |
| EREFS - Inflammatory (EREFS-i): Mean Change From Baseline / Mean Percentage Change From Baseline | | | | | | | | | | |
| Week 12 | +1.0 / +38% | -0.7 / -20% | 0 / 0% | 0 / 0% | +1.5 / +100% | 0 / 0% | 0 / 0% | -1.0 / -25% | -4.0 / -92% | -3.0 / -100% |
| Week 36 | - | - | - | - | -0.5 / -33% | 0 / 0% | -1.3 / -40% | 0 / 0% | ongoing | -3.0 / -100% |
| EREFS - Fibrosis (EREFS-f): Mean Change From Baseline / Mean Percentage Change From Baseline | | | | | | | | | | |
| Week 12 | -0.5 / -30% | +0.3 / +50% | +0.7 / +100% | 0 / 0% | -1.0 / -67% | -1.5 / -75% | -2.0 / -86% | 1.0 / +100% | -1.0 / -100% | -1.0 / -100% |
| Week 36 | - | - | - | - | -0.5 / -33% | -1 / -50% | -2.0 / -86% | 0 / 0% | ongoing | 0 / 0% |

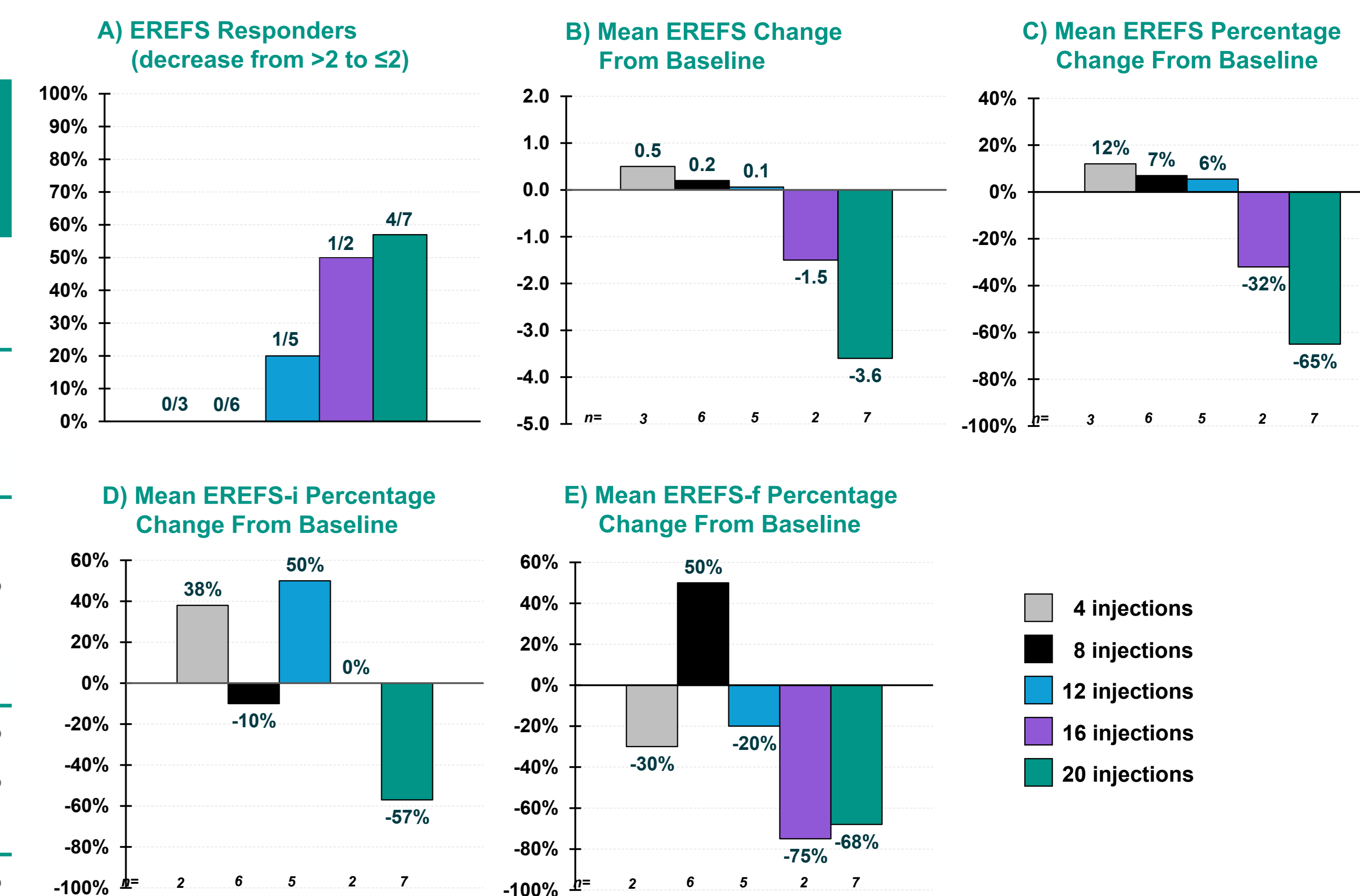


Figure 2 A-E. Pooled Analyses For Week 12 Per Number of Injection Sites For Participants With EREFS Scores >2 At Baseline

- In total, 25/30 (83%) of participants enrolled presented with an EREFS score >2 at baseline (Tab 1)
- Participants with a score ≤2 at baseline were distributed disproportionately in higher dose cohorts (8; 20x6mg and 9; 20x8mg) (Tab 1)
- Participants with baseline scores >2 tended to demonstrate a greater proportion of responders (achieving EREFS ≤2), greater mean absolute improvement and greater relative percentage improvements at higher dose cohorts (Tab 1)
 - Highest improvements were overall observed in participants included in dose cohorts 8b and 9 (20x6mg and 20x8mg)
- As the EREFS score assesses the most severe location at any point of the esophagus, the relative surface coverage may impact the treatment effect on EREFS
 - An analysis of cohorts pooled according to number of sites injected for all completed cohorts (week 12) showed a clear injection sites – dependent response (Fig 2 A-C)
- Review of EoEHSS inflammatory and fibrosis sub scores also indicate that higher dose cohorts overall tend to demonstrate greater improvements in either inflammatory or fibrotic features (Tab 1)
 - Consistent improvements in both sub scores were observed only for participants dosed using 20 injection sites (Fig 2 D-E)

CONCLUSIONS

- A relationship between the number of injection sites and overall improvements in endoscopic findings during dose escalation in RESOLVE supports the selection of dose levels using 20 injections for dose optimization
- Injections at 20 sites resulted in consistent improvements in both inflammatory and fibrotic findings, suggesting an appropriate coverage of the esophageal surface

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

EGD, esophagogastroduodenoscopy; EoE, eosinophilic esophagitis; EREFS, EoE Endoscopic Reference Score; EREFS-f, EREFS-Fibrotic; EREFS-i, EREFS-Inflammatory.