Enteryx®: Worldwide Pivotal Studies in 237 Patients

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I. Introduction

- Enteryx is a biocompatible copolymer designed for endoscopic injection into the lower esophageal sphincter (LES) to relieve the symptoms of gastroesophageal reflux disease (GERD).
- Enteryx has been shown to decrease proton pump inhibitor (PPI) use and to enhance quality of life in PPI-dependent GERD patients.

II. Aim

- Report on the safety and effectiveness of Enteryx in two prospective, open-label, international, multicenter clinical trials that followed similar study protocols.

III. Methods & Materials

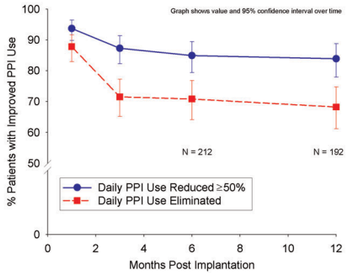
- PPI-dependent patients with GERD (N = 237) underwent endoscopic Enteryx implantation under fluoroscopic guidance using moderate sedation. Patients participated in one of two single-arm, multicenter studies:
  - a US expanded IDE study (N = 144) conducted at 6 sites in the United States, 1 site in Canada, and 1 site in Europe, or
  - a European prospective study (N = 93) conducted at 17 sites in 6 European countries (Germany, France, the United Kingdom, Belgium, the Netherlands, and Spain).
- PPI usage, GERD health-related quality of life (GERD-HRQL) score, retreatment rate, adverse events, and esophageal pH were recorded during the 12 mo follow-up.
- Major inclusion criteria:
  - Daily PPI-dependency for ≥ 3 months (GERD-HRQL ≤ 11 on PPIs, increasing to ≥ 20 off PPIs).
  - Heartburn and/or regurgitation prior to PPI therapy; and esophageal pH < 4 for ≥ 5% of a > 12-hour monitoring period or for ≥ 3% of a supine period.
- Major exclusion criteria:
  - Savary-Miller grade III or IV esophagitis
  - Significant esophageal motility disorder
  - Esophageal/gastric cancer or varices
  - Prior gastric or esophageal surgery
  - Hiatus hernia ≥ 3 cm
  - Barrett's esophagus

IV. Results

Table 1. Patient Demographics

	N
Gender	
Male	151 (63.7%)
Age (yrs)	
Mean	48.3
SD	12.79
Range	22-85
BMI ($kg \cdot m^{-2}$)	
Mean	27.4
SD	3.94
Range	19-37

Figure 1.
PPI use following Enteryx implantation (N = 237)



- At 6 mo, PPI use was eliminated in 70.8% (CI, 64.1-76.8%) and was reduced by ≥ 50% in an additional 14.2% (CI, 9.8-19.6%) of 212 evaluable patients.
- At 12 mo, PPI use was eliminated in 68.2% (CI, 61.1-74.8%) and was reduced by ≥ 50% in an additional 15.6% (CI, 10.8-21.6%) of 192 evaluable patients.

Figure 2a.
GERD-HRQL heartburn following Enteryx implantation

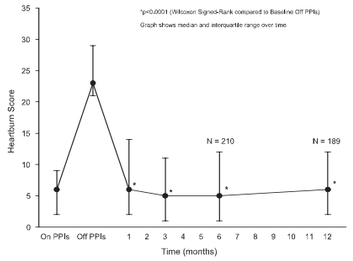
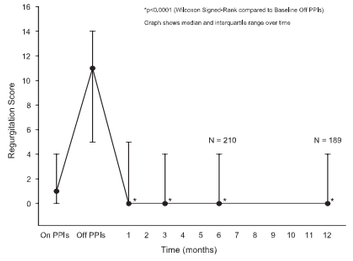


Figure 2b.
GERD-HRQL regurgitation following Enteryx implantation



- Both GERD-HRQL heartburn and regurgitation scores were significantly improved (p < 0.0001) at all timepoints relative to baseline (off PPIs).
- Median GERD-HRQL scores exhibited little fluctuation during all post-implantation timepoints.

Table 2. Re-treatment following Enteryx implantation

Site	N (%)
Berlin	1 (2.3)
Brussels	1(2.3)
Düsseldorf	1 (2.3)
Hamburg	1 (2.3)
Indianapolis	7 (16.3)
Lancaster	4 (9.3)
Marseille – Timone	2 (4.7)
Minneapolis	12 (27.9)
New York	7 (16.3)
Norfolk	6 (13.9)
Rotterdam	1 (2.3)
Total	43 (18.1)

- Higher re-treatment rates were observed in the United States compared with European sites

Table 3. Adverse events following Enteryx implantation

Adverse Event	Mild	Moderate	Severe	Total	Percent
Chest/Epigastric Pain	102	83	16	201	84.8%
Dysphagia/Odynophagia†	32	25	2	59	24.9%
Fever	23	14	1	38	16.0%
Belching	13	7	0	20	8.4%
Bloating/Flatulence	7	3	2	12	5.1%
Regurgitation	0	4	0	4	1.7%
Body Odor	1	2	0	3	1.3%
Flu	2	0	0	2	0.8%
Bradycardia	1	0	0	1	0.4%

†Three patients with dysphagia underwent dilatation (2 patients received a single dilatation, and 1 patient received 2 dilatations). In addition, 1 patient in the US IDE study experienced persistent dysphagia requiring hospitalization 6 wks after implantation. A paraesophageal collection was demonstrated on CT scan. The patient recovered completely with IV antibiotics.

- Retrosternal chest pain (85%) was the most frequent adverse event, with dysphagia/odynophagia occurring in one-quarter of patients.

Table 4. Esophageal acid exposure (total time pH < 4) at months 6 and 12 relative to baseline

Statistic	Baseline	Month 6	Baseline	Month 12
N	180	180	156	156
Mean	15.3	10.9	15.7	12.2
Median	10.8	8.3	10.3	7.2
SD	14.56	12.00	15.38	13.64
Q1	7	3	7	3
Q3	18	3	18	15
p-value*		<0.0001		.0002

*Wilcoxon rank test

- Esophageal acid exposure (total time pH < 4) was significantly improved at months 6 and 12 relative to baseline.

Table 5. Esophagitis grades at baseline and month 12

Baseline (N = 237)		Month 12 (N = 165)			
	N	NONE	GRADE I	GRADE II	GRADE III
NONE	153	71	15	23	1
GRADE I	51	11	10	11	2
GRADE II	29	5	5	10	1
GRADE III	4	0	0	0	0
TOTAL	**237**	**87**	**30**	**44**	**4**

- Esophagitis at month 12 was evaluable in 165 patients. Approximately two-thirds of these patients (68%) had either improvement or no change in their esophagitis scores (shaded cells in table).

V. Conclusions

- These data augment previous findings that Enteryx is safe and effective in the treatment of GERD symptoms.
- At 12 mo post-implantation, there were significant improvements in PPI use, GERD-HRQL score, and esophageal acid exposure.
- On the basis of the findings in this report, we believe that Enteryx is an appropriate therapy for patients with GERD who respond to PPIs and require long-term treatment.