
2021 SCSG
GI SYMPOSIUM

Esophageal Disorders

Edy Soffer MD

Keck School of Medicine,

University of Southern California

I have no disclosures

Dietary Therapy for EoE

Efficacy of One-food versus Six-Food Elimination Diet for Treatment of Eosinophilic Esophagitis in Adults: Results from the Multicenter Randomized Controlled "SOFEED" Trial

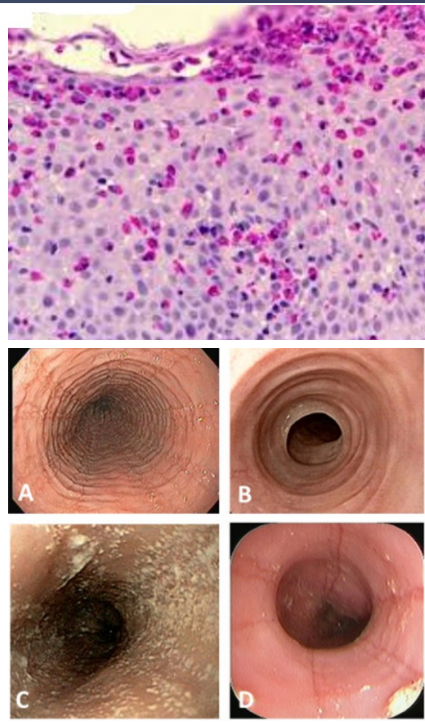
Kara Kliewer[1], **Nirmala Gonsalves**[2], **Evan Dellon**[3], **David Katzka**[4], Seema Aceves[5], Nicoleta Arva[6], Kelly Capocelli, Mirna Chehade[7], Margaret Collins[1], Gary Falk[8], Sandeep Gupta[9], Ikuo Hirano[2], John Leung[10], Lisa Martin[1], Paul Menard-Katcher[11], Vincent Mukkada[1], Kathryn Peterson[12], Amanda Rudman Spergel[13], Jonathan M. Spergel[14], Guang-Yu Yang[2], Xue Zhang[1], Glenn Furuta[15], Marc E. Rothenberg[1]

Consortium of Eosinophilic Gastrointestinal Disease Researchers (**CEGIR**)

DDW 2021, May 22, 12:30

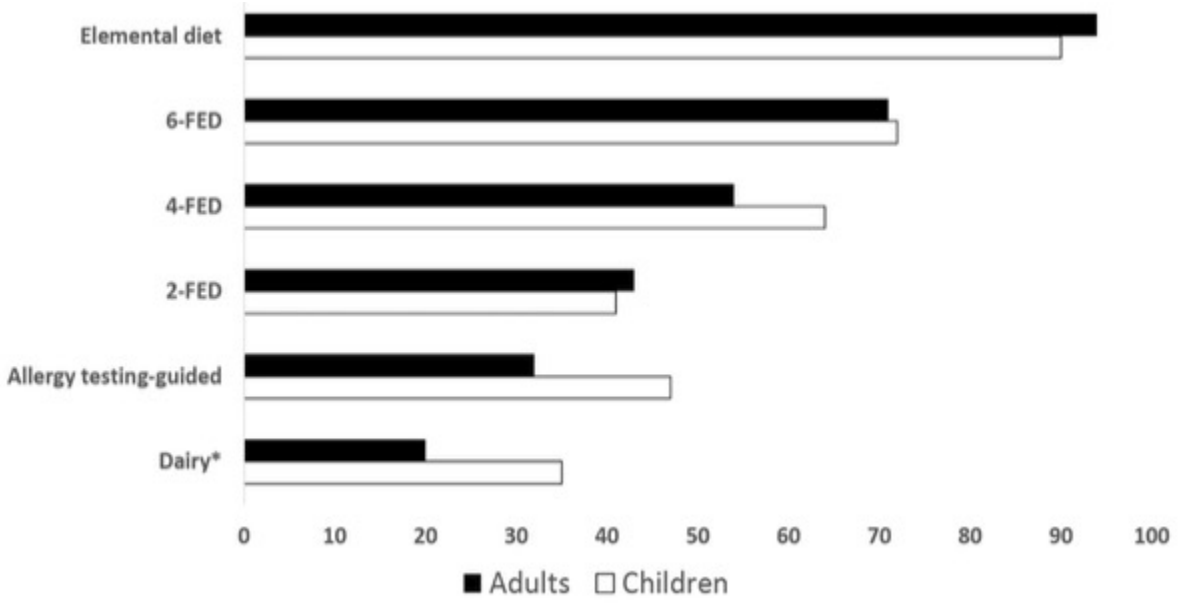
Background

- EoE: An antigen-mediated disease of the esophagus, mediated by offending foods.
- Presentation: Eosinophilic infiltration, endoscopic findings, symptoms (dysphagia)
- Therapy: PPI, swallowed steroids, diets
- Elimination diets: from **6** food (milk, wheat, egg, soy, nuts, sea food) to **1** (milk)



Diet Therapies for EoE

Review of published trials, efficacy assessed by histopathology



Molina-Infante, Lucendo JACI 2018

One-Food vs Six-Food Elimination Diet

Prospective, multi-site randomized trial in adults with active EoE

Aim

Determine and compare efficacy of 1FED (milk) vs 6FED (milk, wheat, egg, soy, nuts/peanuts, seafood) in improving histologic, endoscopic, and clinical outcomes in active EoE

Primary Outcome

- Percent achieving histologic remission (< 15 eos/hpf) in 1FED compared to 6FED

Secondary Outcomes

- Histologic response (≤ 1 eos/hpf) in 1FED vs 6FED
- Histology features score (EoE HSS)
- Endoscopic scoring system (EREFS)
- EoE activity index (EEsAI)
- EoE quality of life (EoE-QoL-A)
- EoE Diagnostic Panel (EDP)

Hypothesis

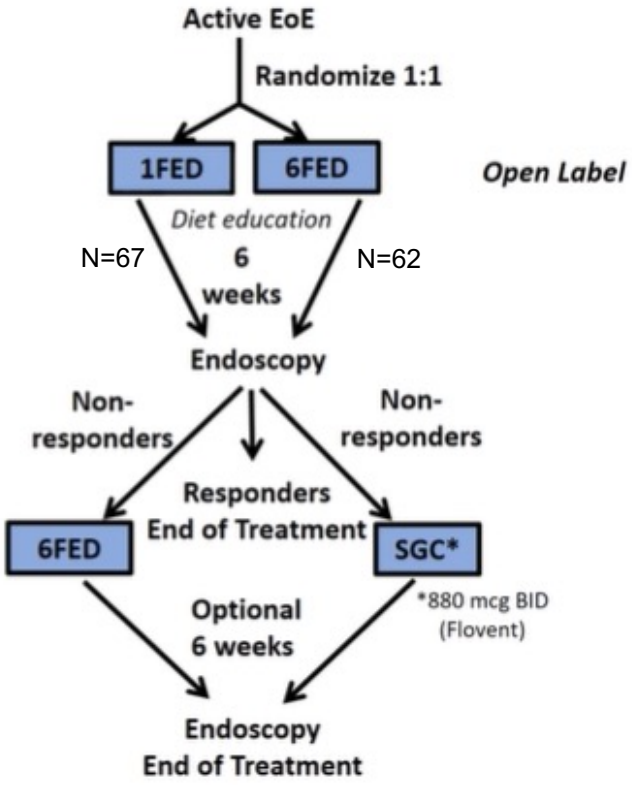
- 6FED will be superior to 1FED in achieving remission (< 15 eos/hpf)

Method

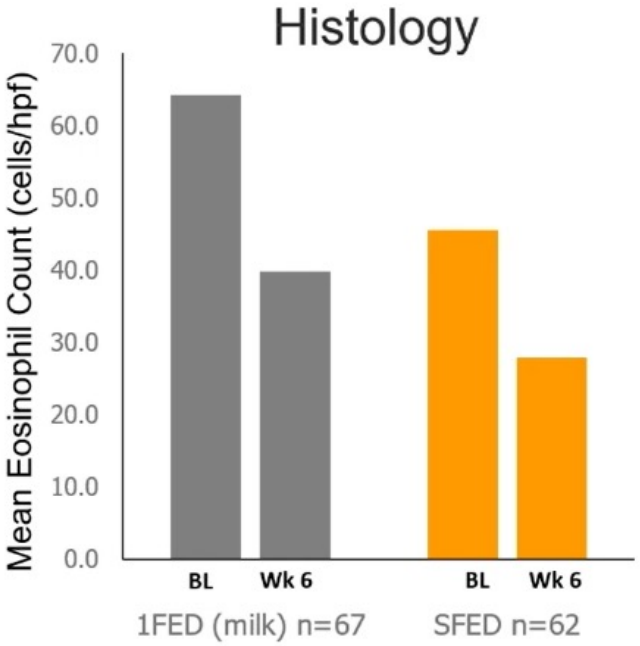
Key Entry Criteria

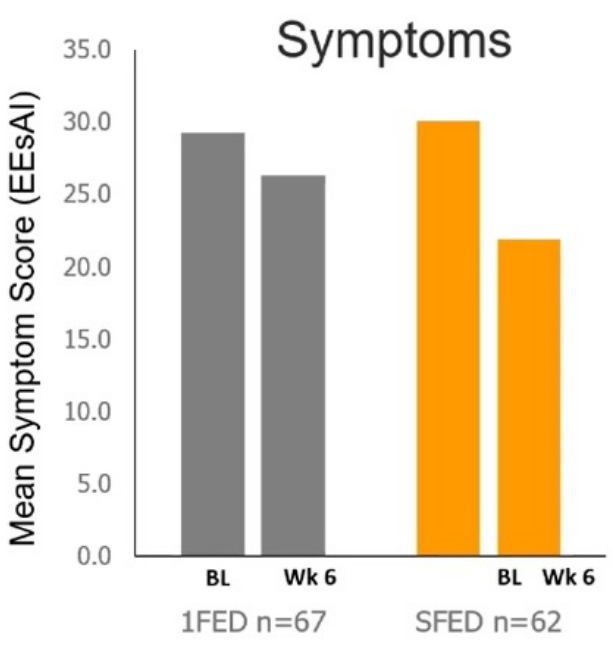
- 18 - 60 years
- Active EoE (≥15 eos/hpf)
- Failed high dose PPI after ≥ 8 weeks (either historically or at screening endoscopy)
- Symptomatic

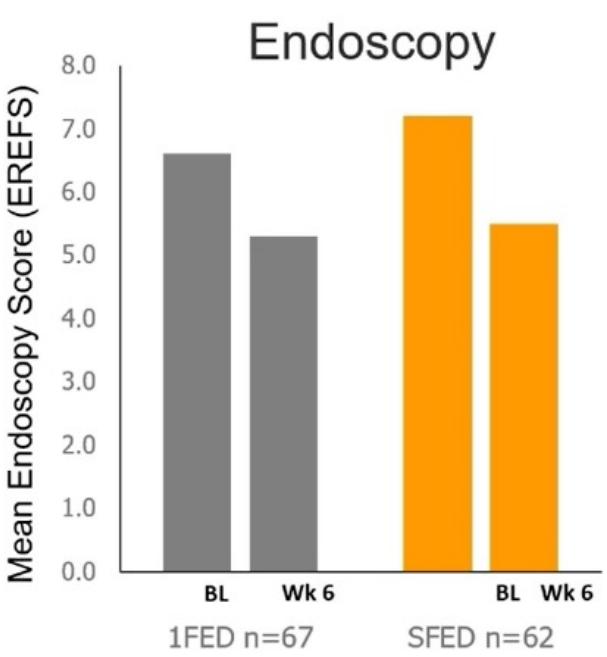
Design



Results







For those who failed first phase: 6 food effective in about ½ of failed 1 food. Swallowed steroids effective in most 6 food failures

Conclusions

- A one-food elimination diet: An option for initial therapy
- Why are the results so much better than previous reports?
- An attractive adjunct to other therapies achieving suboptimal results

PPI Therapy for EoE

- ~ 42% efficacy in achieving histological response
- Certainty of evidence (GRADE) : Very low
  -- Uncontrolled , no placebo
  -- marked heterogeneity in published data

I. Hirano et al. Technical Review on the Management of Eosinophilic Esophagitis: A Report From the AGA Institute and the Joint Task Force on Allergy-Immunology Practice Parameters. Gastroenterology 2020;158:1789–1810

PPI Therapy for EoE

OP077 Efficacy of proton pump inhibitor therapy for eosinophilic oesophagitis in real-world practice: Results from the EoE connect registry

Laserna-Mendieta et al

Aims

- ✓ To provide data on the efficacy of PPI treatment for EoE in actual clinical practice
- ✓ To clarify some of the questions that remain regarding this anti-inflammatory treatment approach

- EoE Connect database

(European Registry of Clinical, Environmental and Genetic Determinants in Eosinophilic esophagitis)

842 patients with demographical data completed

630 had PPI as an induction treatment

172 patients on PPI to maintain remission

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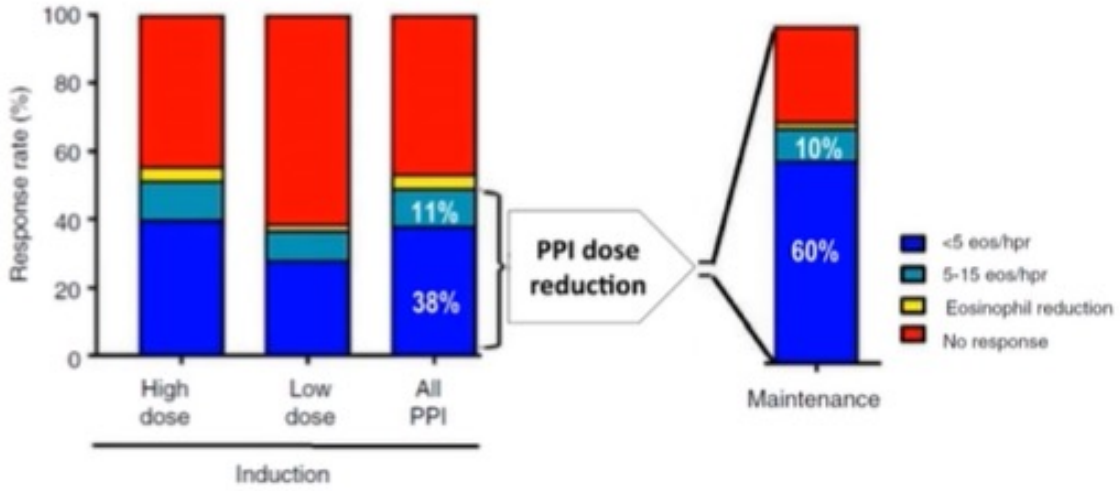
PPI Therapy for EoE

OP077 Efficacy of proton pump inhibitor therapy for eosinophilic oesophagitis in real-world practice: Results from the EoE connect registry

Laserna-Mendieta et al



Predictive factor of response (multivariate analysis)

- ✓Inflammatory phenotype
- ✓Prolonged treatment (71-90 days)

Therapy for EoE

Choosing an Initial EoE Therapy

	PPI	Steroids	Diet
Effectiveness	30-50%	50-90%	50-70% *(SFED)*
Administration	Easy	Cumbersome *(with current use of asthma products)*	Very difficult *(impact on social QoL)*
Safety	Very high	High *(long-term under evaluation)*	Very high
Cost	Low	Variable *(insurance coverage)*	High up-front (Multiple EGDs
Availability	Widespread	Not FDA approved	Widespread
Additional PRO	Addresses concomitant GERD	Strongest evidence-base *(Histo/symptoms/endoscopy)*	Conceptual appeal; Non-pharmacologic
Additional CON	Loss efficacy with prolonged use (?)	Loss efficacy in subset with prolonged use	Repeated endoscopies; long-term adherence

I. Hirano, DDW 2021

Eosinophilic Gastrointestinal Diseases

Endoscopy and Systematic Biopsy of Patients with Chronic Gastrointestinal Symptoms Leads to High Discovery Rate of Patients Who Meet Histologic Criteria for Eosinophilic Gastritis and/or Eosinophilic Duodenitis

Nicholas J. Talley MD PhD[*1], Amol P. Kamboj MD[2], William D. Chey MD[3], Henrik S. Rasmussen MD PhD[2], Brian E. Lacy MD PhD[4], Ikuo Hirano MD[5], Mirna Chehade MD MPH[6], Nirmala Gonsalves MD[5], Kathryn A. Peterson MD[7]; Anthony Lembo MD[8]; Colleen M. Schmitt MD MHS[9]; Marc E. Rothenberg MD PhD[10], Robert M. Genta MD[11]; Maria A. Pletneva MD PhD[7]; Kevin O. Turner DO[12]; Malika Pasha MBA[2], Evan S. Dellon MD MPH[*13], William J. Sandborn MD[*14]

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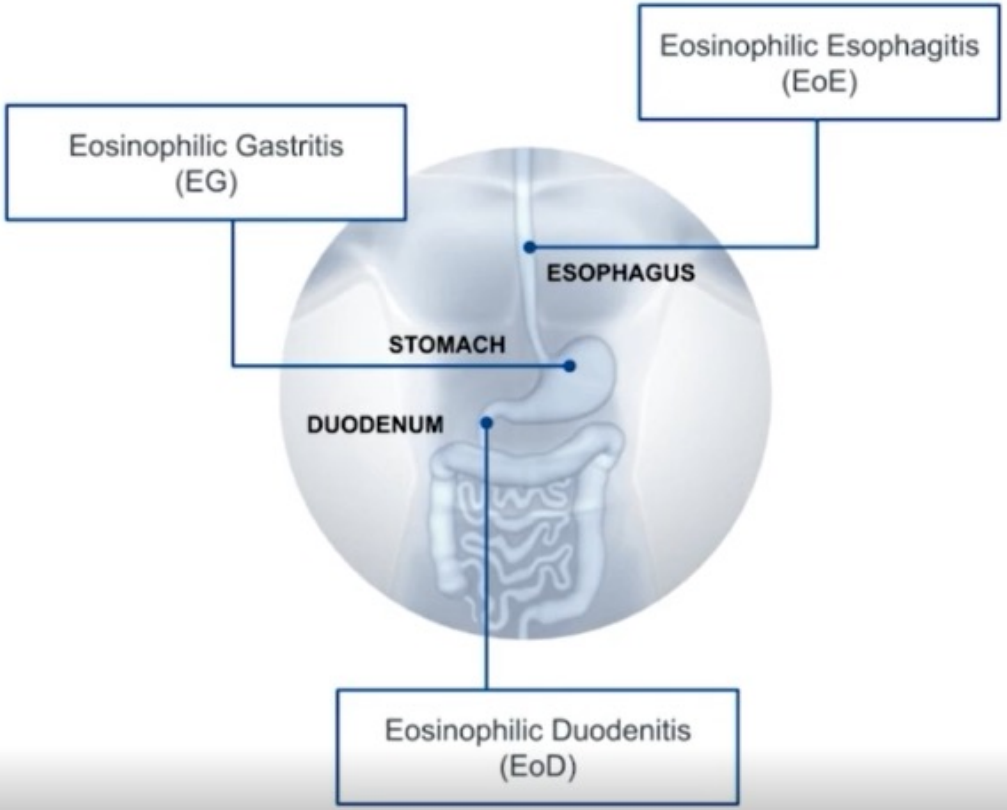
Eosinophilic Gastrointestinal Diseases (EGIDs)



EG, EoD, EoE

Chronic Eosinophilic Inflammation of the Stomach, Duodenum, or Esophagus

- Eosinophils and mast cells are important drivers of disease
- Symptoms: abdominal pain, nausea, early satiety, loss of appetite, bloating, abdominal cramping, vomiting, diarrhea, and dysphagia
- No FDA approved treatment for EG, EoD, or EoE
- Current standard of care: diet and/or steroids

Egan M et al. Ann Allergy Asthma Immunol 2018;121:162-167. Gonsalves N. Clin Rev Allergy Immunol 2019

Eosinophilic Gastrointestinal Diseases (EGIDs)

- A previous study involving a new agent for treatment of EGID, reported a high rate of gastroduodenal eosinophilia
- ~ 30% were patient with chronic nonspecific functional GI symptoms or diagnoses with, who received a de novo diagnosis of EGID

Dellon ES et al. NEJM 2020;383:1624

Design / Aim

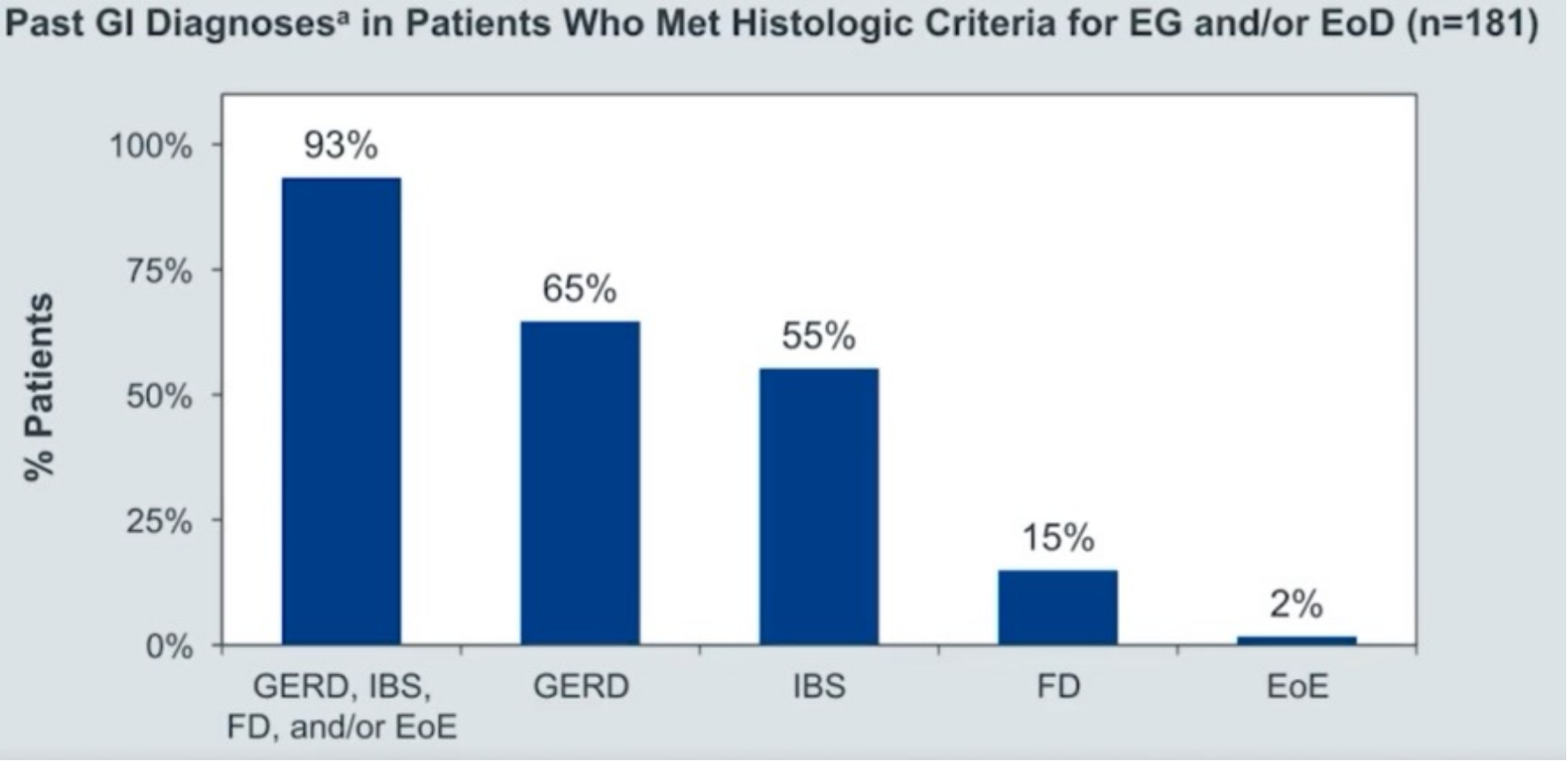
- **Study Design**
  - Prospective, multi-center study to assess the prevalence of EG and/or EoD in symptomatic patients with chronic functional GI symptoms
    - At least a 6-month history of abdominal pain, abdominal cramping, nausea, vomiting, diarrhea, bloating or early satiety without identifiable cause and unresponsive to pharmacologic or dietary intervention

    and/or

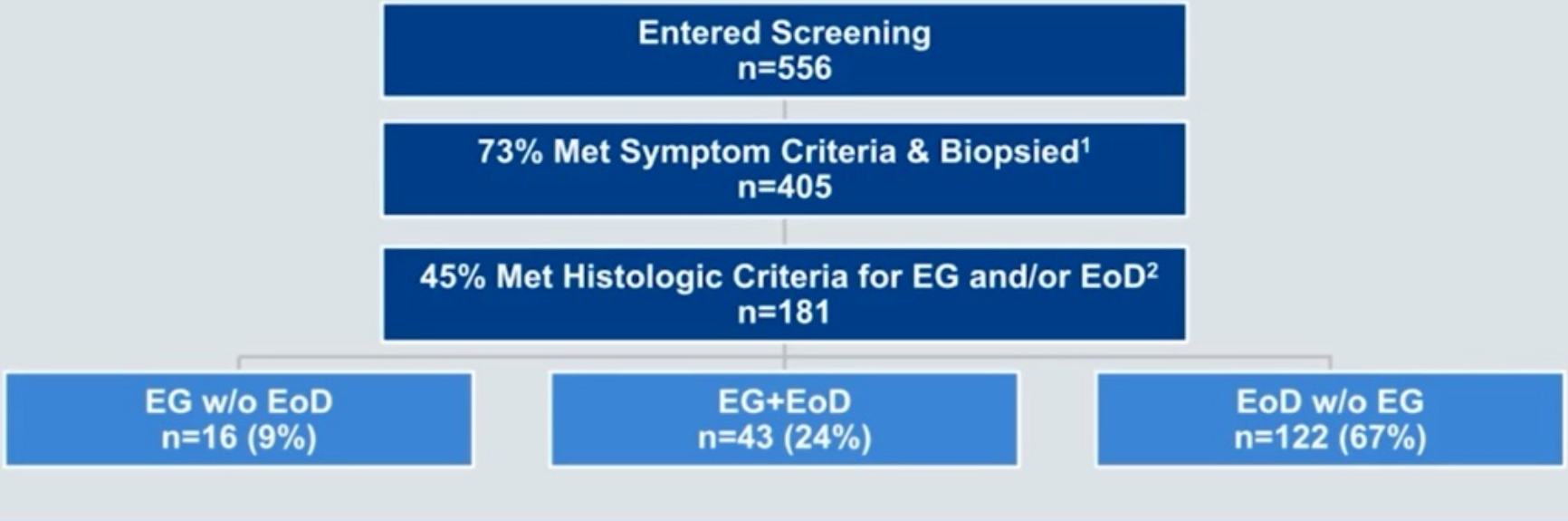
    - a diagnosis of IBS or functional dyspepsia (FD), indicating a chronicity of symptoms
  - **An asymptomatic healthy volunteer study was conducted for comparison**

- **Co-Primary Endpoints**
  - Proportion of symptomatic patients that underwent biopsy and met the histologic criteria for EG and/or EoD (≥30 eos/hpf in 5 gastric or 3 duodenal hpf)
  - Proportion of symptomatic patients that underwent biopsy with ≥30 mast cells/hpf in 5 gastric hpfs and/or ≥30 mast cells/hpf in 3 duodenal hpfs and < 30 eos/hpf

Characteristics of Patients



Results



33% (181/556) of patients with chronic functional GI symptoms and 45% (181/405) of patients with moderate-severe symptoms undergoing biopsy met histologic criteria for EG and/or EoD

Conclusions

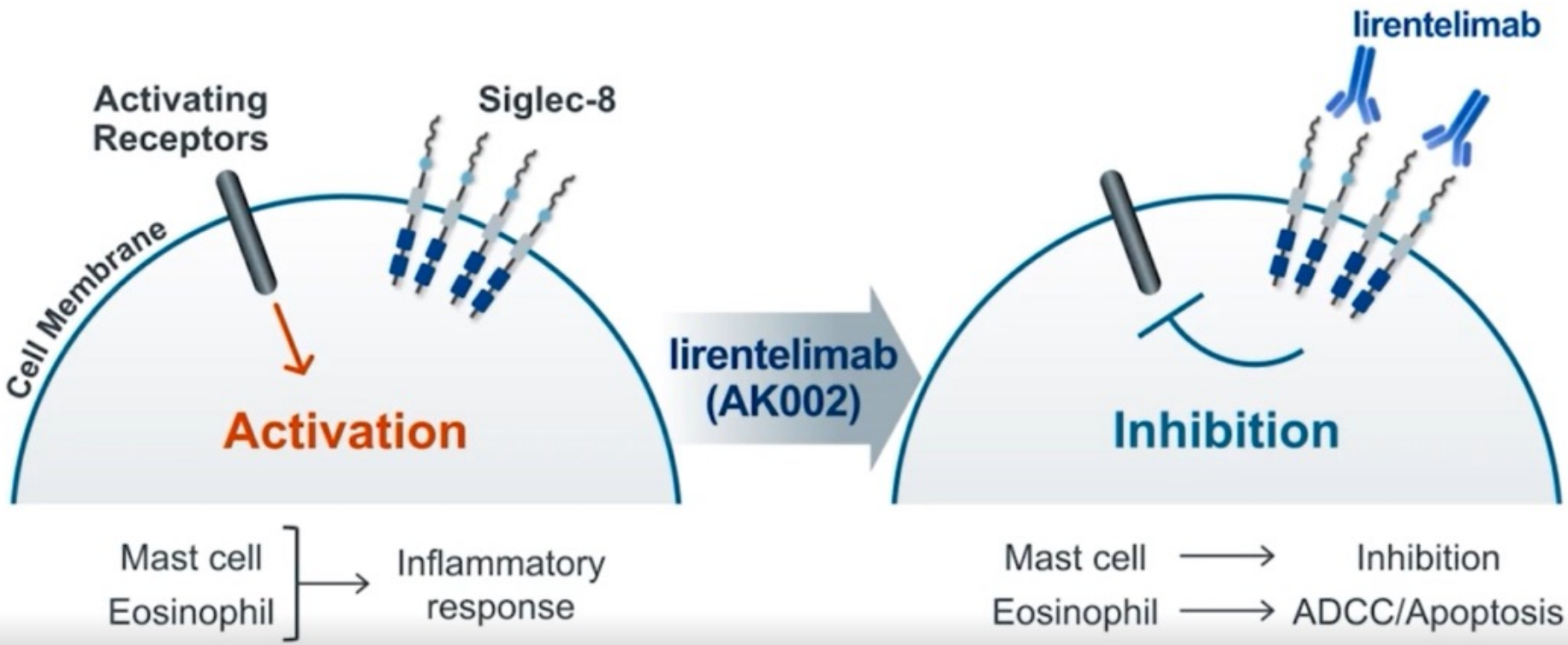
- 45% of patients with moderate-severe unexplained GI symptoms met strict histologic criteria for gastric or duodenal eosinophilia
- Eosinophilic gastrointestinal diseases should be considered in patient moderate-severe unexplained GI symptoms

Lirentelimab trial

Long-term Treatment of Patients with Eosinophilic Gastritis and/or Eosinophilic Duodenitis with Lirentelimab, a Monoclonal Antibody Against Siglec-8

Kathryn A. Peterson MD[1], Mirna Chehade MD MPH[2], Joseph A. Murray MD[3], Gary W. Falk MD[4], Nirmala Gonsalves MD[5], Robert M. Genta MD[6], Marc E. Rothenberg MD PhD[7], Adam C. Bledsoe MD[3], Sandy R. Durrani MD[7], Michael Vaezi MD[8], Camilla Shaw BSN RN[9], Henrik S. Rasmussen MD PhD[9], Bhupinder Singh MD[9], Alan T. Chang[9], Amol P. Kamboj MD[9], Ikuo Hirano MD[5], Evan S. Dellon MD MPH[10]

Lirentelimab



Enigma Phase 2 Study

- 59 patients with moderate/ severe UGI symptoms
- Histology: ≥ 30 Eos/hpf stomach or duodenum or both
- 4 months therapy with lirentelimab (eosinophilic depletion, mast cell stabilizer)

RANDOMIZED STUDY RESULTS			
Prespecified Endpoints		**lirentelimab (n=39)**	**Placebo (n=20)**
1° - Tissue Eosinophils	% Δ	-95%	+10%
	p-value	**<0.0001**	-
2° - Treatment Responders	%	69%	5%
	p-value	**0.0008**	-
2° - TSS	% Δ	-53%	-24%
	p-value	**0.0012**	-

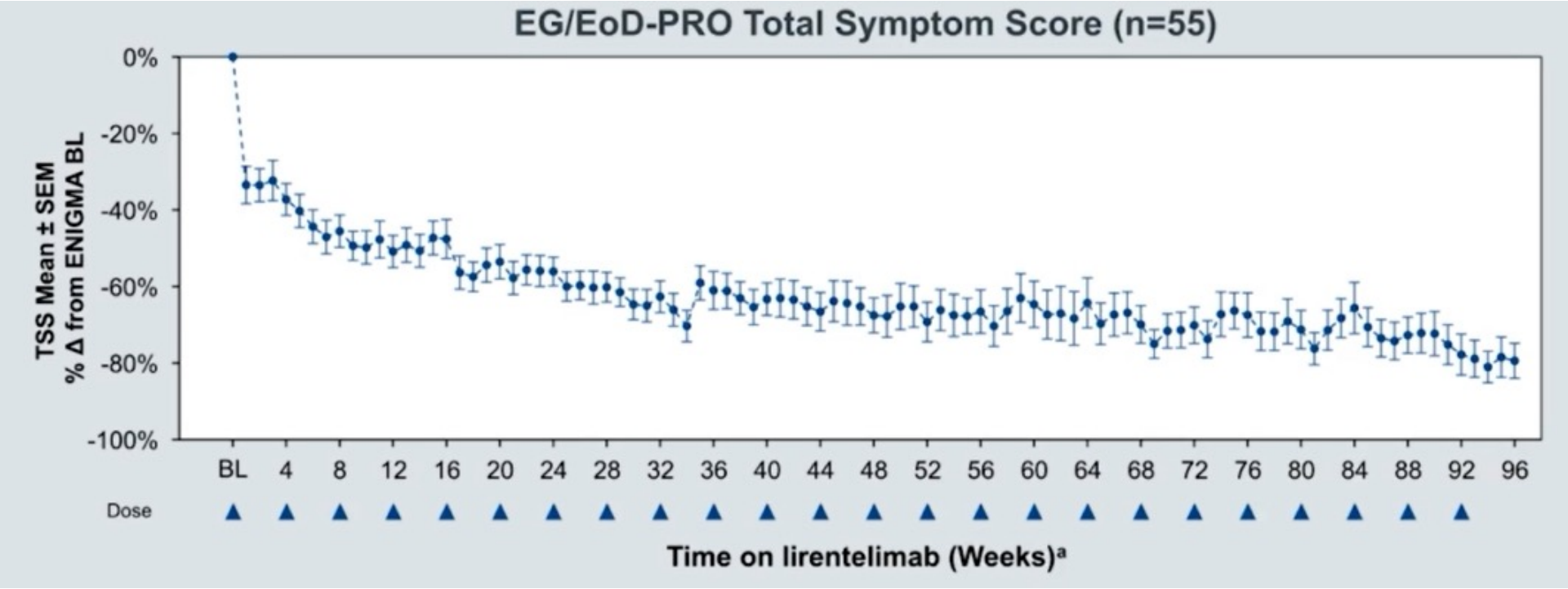
- All primary and secondary endpoints met in the first randomized trial in patients with EG and EoD
- Generally well tolerated

Dellon ES et al. NEJM 2020;383:1624

Open-label Extension Study: AIM / Design

- **Study Aim**
  - Determine safety and efficacy of long-term use of lirentelimab for treatment of EG and/or EoD
- **Study Design**
  - Patients who completed ENIGMA had the option to receive lirentelimab in an OLE study
  - Patients enrolled in the OLE received up to 26 monthly lirentelimab infusions, administered intravenously every 28 days, titrated up to 3.0 mg/kg
  - Patients underwent an upper endoscopy with biopsy on Days 323 (week 46) and 659 (week 94) from entering ENIGMA

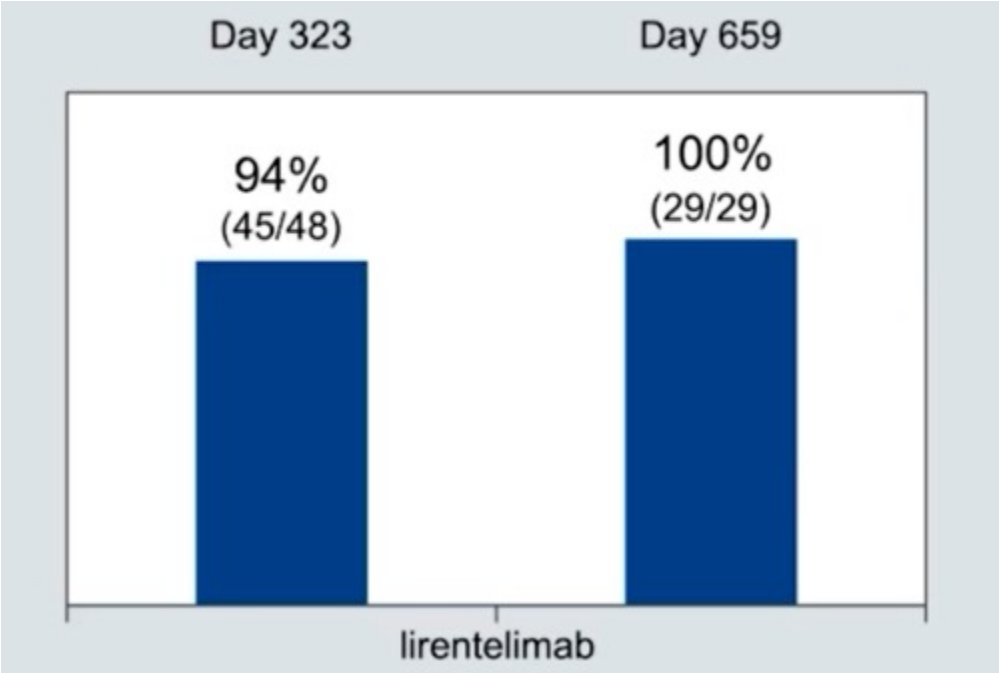
Results: Symptoms



Results: Histology

Proportion of Patients Meeting Histologic Remission Criteria

Eosinophils ≤4/hpf (Stomach) and/or ≤15/hpf (Duodenum)[a]



Conclusions

- Long-term treatment with lirentelimab results in sustained histologic & symptomatic improvements in patients with EG and/or EoD through week 94
  - Sustained response of blood and tissue eosinophil depletion
  - Symptomatic responses improved with increased duration of treatment
- Long-term treatment with lirentelimab was generally well-tolerated
- Additional lirentelimab studies:
  - Phase 3 randomized trial in EG and/or EoD (NCT04322604)
  - Phase 2/3 randomized trial in EoE (NCT04322708)

Laryngo-Pharyngeal Reflux

EFFICACY OF REFLUX BAND (UPPER ESOPHAGEAL SPHINCTER ASSIST DEVICE) FOR LARYNGOPHARYNGEAL REFLUX: A PROSPECTIVE TWO PHASE TRIAL

Rena Yadlapati[1], Samir Gupta[1], Madeline Greytak[1], John E. Pandolfino[2], Jonathon Cahoon[3], Paul Menard-Katcher[3], Daniel Fink[3], Matthew Clary[3], Andrew Vahabzadeh-Hagh[1], Mary Clarke[1], Philip Weissbrod[1], Alexander Kaizer[3], Sachin Wani[3]

DDW 2021, Sunday, May 23rd

Laryngo-Esophageal Reflux (LPR)

- Refers to various symptoms believed to be caused by acid reflux above the upper esophageal sphincter: cough, dysphonia, throat clearing, sore throat
- Relation to GERD? association vs causation

External UES Compression Device (Reflux Band)

- Device worn around the neck, typically at bedtime
- Individually adjusted to augment UES pressure by 20-30 mmHg

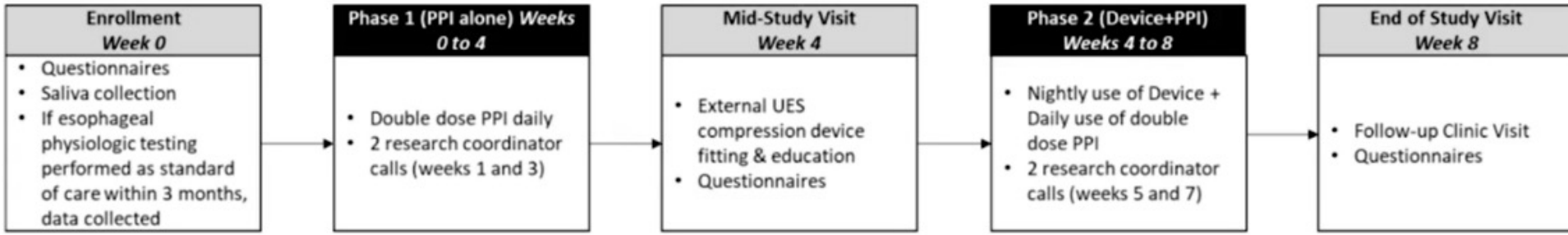
- It has been shown to induce a sustained increase in UES pressure, reduce esophago-pharyngeal reflux and improve symptoms

Shaker R et al. Laryngoscope. 2014 ;124 (10)

Methods

- Aim: Assess efficacy of the device as an adjunct to PPI therapy in patients with LPR
- Study Design: Two-phase prospective clinical trial over 26 months at two tertiary centers
- Subjects: Adults experiencing ≥ 8 weeks of laryngeal symptoms (throat clearing, sore throat, dysphonia, cough) not on PPI

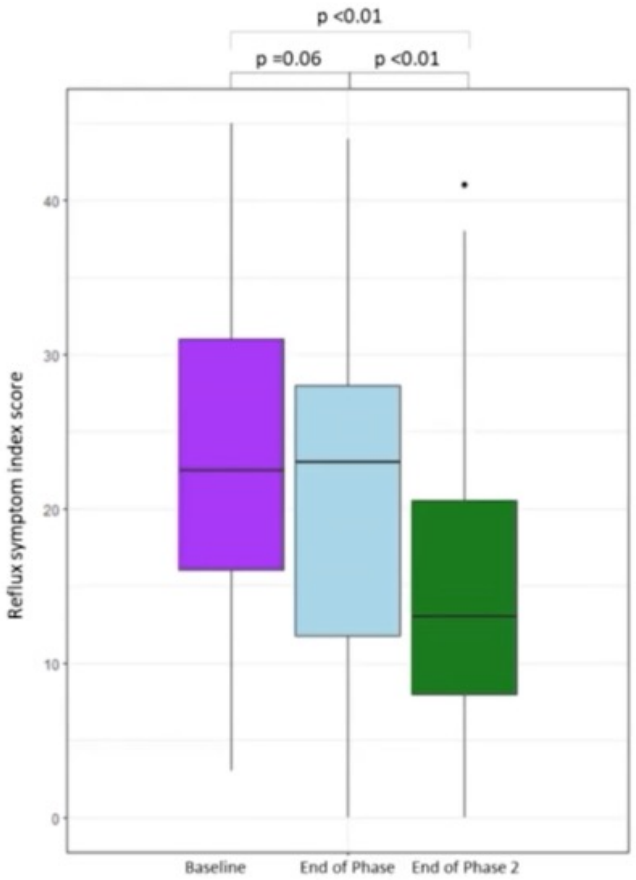
Study Design



- Primary end point: LPR symptom response , measured by the Reflux Symptom Index (RSI), categorized as response or non-response.
  Symptom response was defined as an RSI of ≤ 13 and /or 50% reduction from baseline RSI
- Of 154 eligible patients, 31 completed the second phase

Results

- No different in RSI in phase 1, PPI alone
- Significant decrease in RSI in phase 2, PPI+device
- Response at phase 1=11/31 (35%)
  Response at phase 2 = 17/31 (55%)
- Responders had lower BMI and smaller hernia



Conclusion

- The External UES Compression Device, is a potentially efficacious, non-invasive therapy to LPR
- Larger, randomized studies, can better clarify its role in LPR