



14th ANNUAL
NCSCG
POST-DDW
SYMPOSIUM

Jointly provided by Rehoboth McKinley Christian Health Care Services (RMCHCS) and
the Northern California Society for Clinical Gastroenterology

Northern California Society
for Clinical Gastroenterology


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McKinley
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Yearly Updates in Motility Disorders

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Objectives & Disclosures

- Objectives
 - To review the most important motility updates over the past year:
 - Esophageal motility
 - Eosinophilic esophagitis
 - Gastroparesis
 - Irritable bowel syndrome
- Disclosures: none

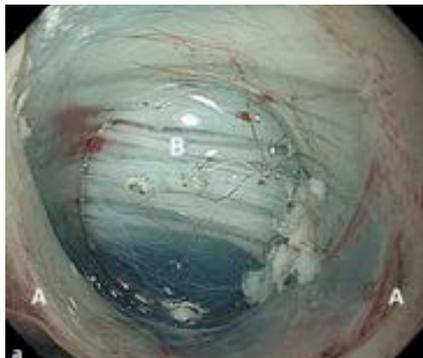
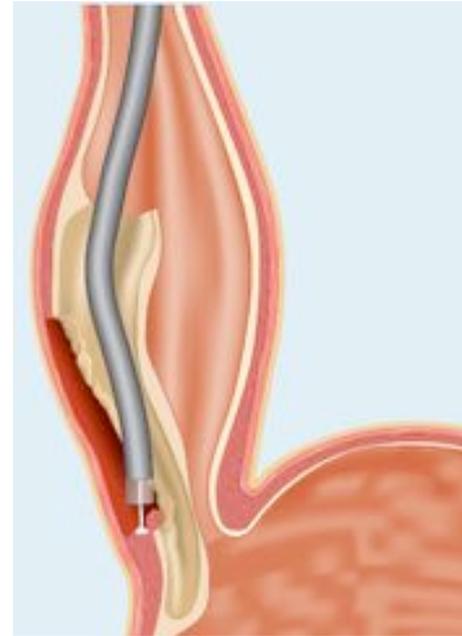
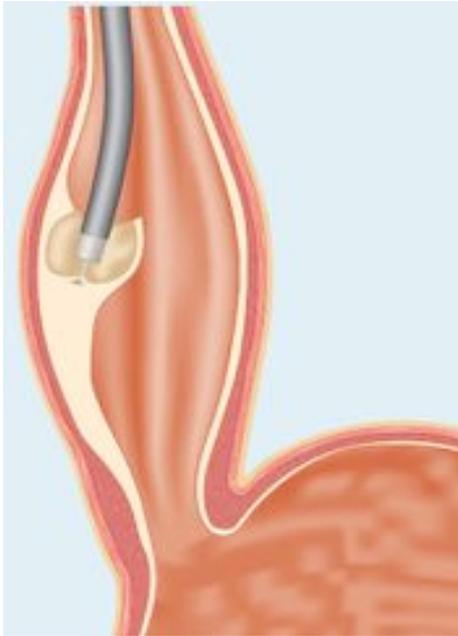
Esophageal Motility

- Key updates over the past year
 - Emerging literature on per-oral endoscopic myotomy (POEM)
 - Emergence of the Functional Lumen Imaging Probe (FLIP)
 - New Guidelines for reflux testing

Per-Oral Endoscopic Myotomy (POEM)

- Conceptualized by Jay Pasricha 2007
- First performed in a human subject by H. Inoue in 2008
- > 8000 procedures done worldwide (mostly China/Japan)
- Success rates > 90% reported in most series
- No randomized controlled trials at present

Per-Oral Endoscopic Myotomy (POEM)



Per-Oral Endoscopic Myotomy (POEM)

Peroral endoscopic myotomy (POEM) vs pneumatic dilatation (PD) in therapy-naive patients with achalasia: results of a randomized controlled trial

Fraukje Ponds, Paul Fockens, Horst Neuhaus, Torsten Beyna, Thomas Frieling, Philip Chiu, Justin Wu, Guido Costamagna, Pietro Familiari, Vivien Wong, Peter Kahrilas, John Pandolfino, André Smout
and Arjan Bredenoord

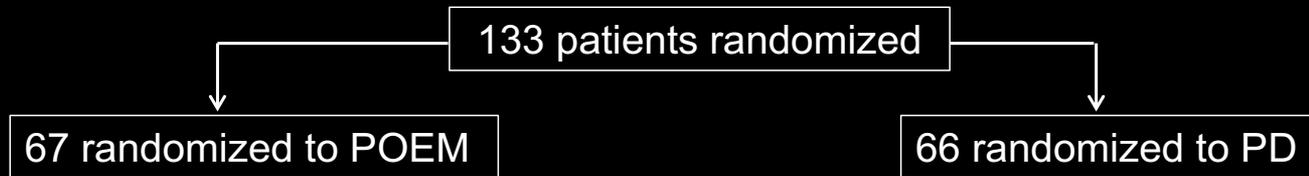
AMC, Amsterdam, the Netherlands
Evangelisches Krankenhaus, Düsseldorf, Germany
HELIOS Clinic, Krefeld, Germany
The Chinese University of Hong Kong, Hong Kong
Università Cattolica del Sacro Cuore, Rome, Italy
Northwestern University, Chicago, USA

Department of Gastroenterology and Hepatology — 

- Slides Courtesy of Arjan Bredenoord

Per-Oral Endoscopic Myotomy (POEM)

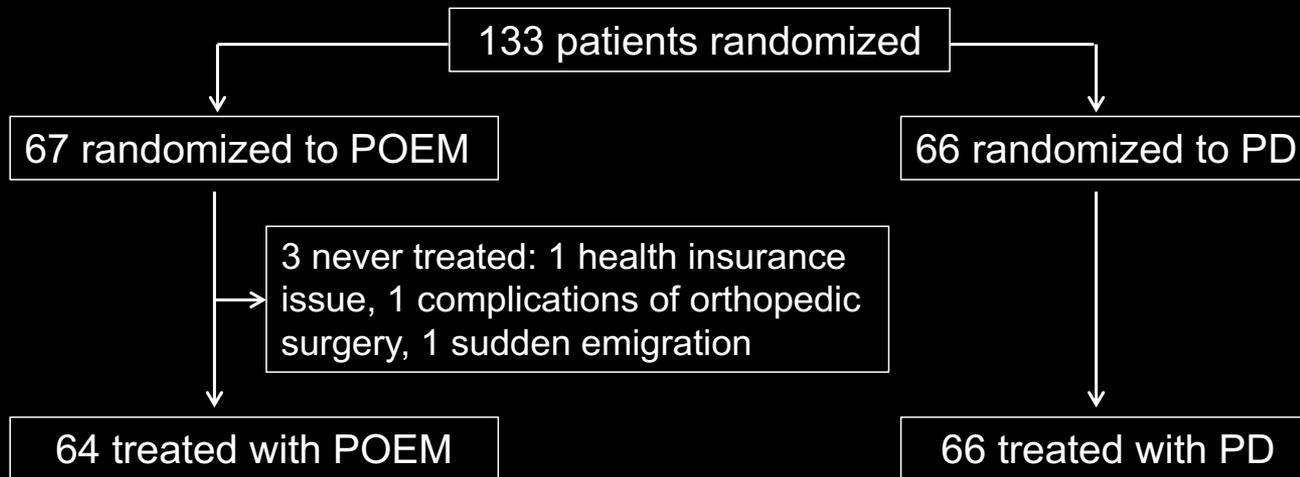
Results: Successful treatment



- Slides Courtesy of Arjan Bredenoord

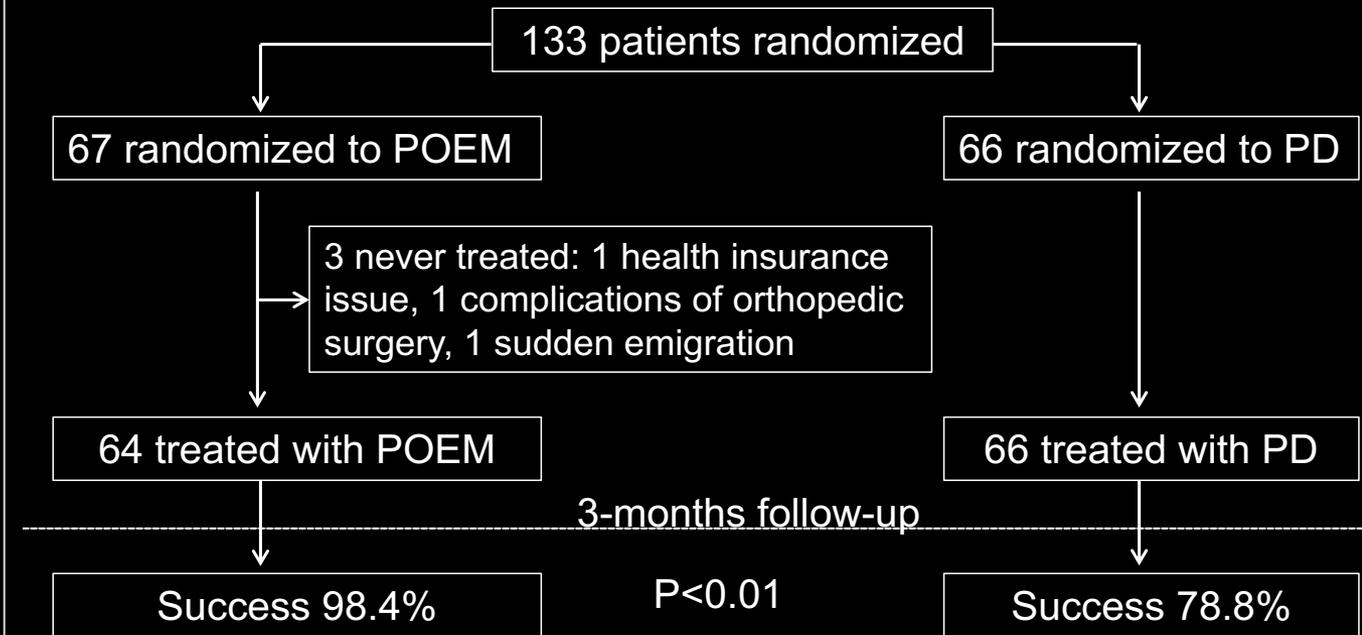
Per-Oral Endoscopic Myotomy (POEM)

Results: Successful treatment



Per-Oral Endoscopic Myotomy (POEM)

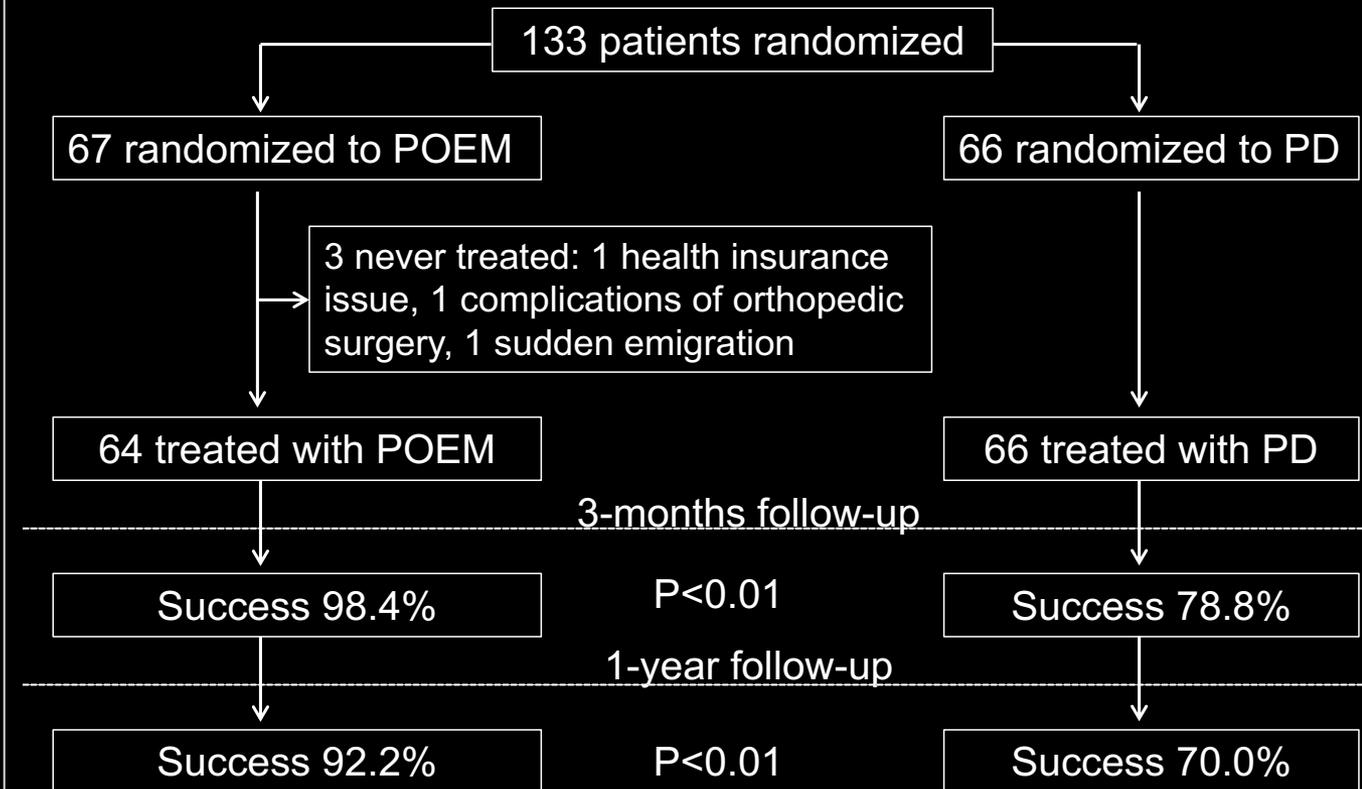
Results: Successful treatment



- Slides Courtesy of Arjan Bredenoord

Per-Oral Endoscopic Myotomy (POEM)

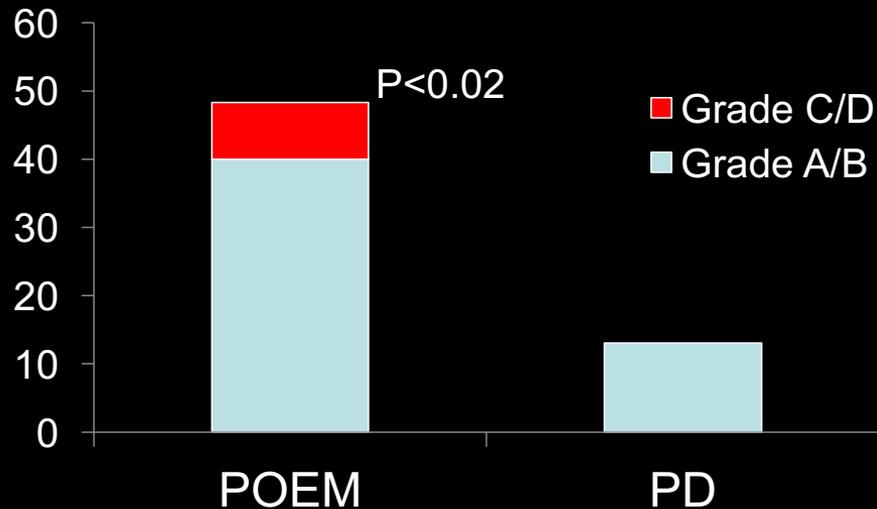
Results: Successful treatment



- Slides Courtesy of Arjan Bredenoord

Per-Oral Endoscopic Myotomy (POEM)

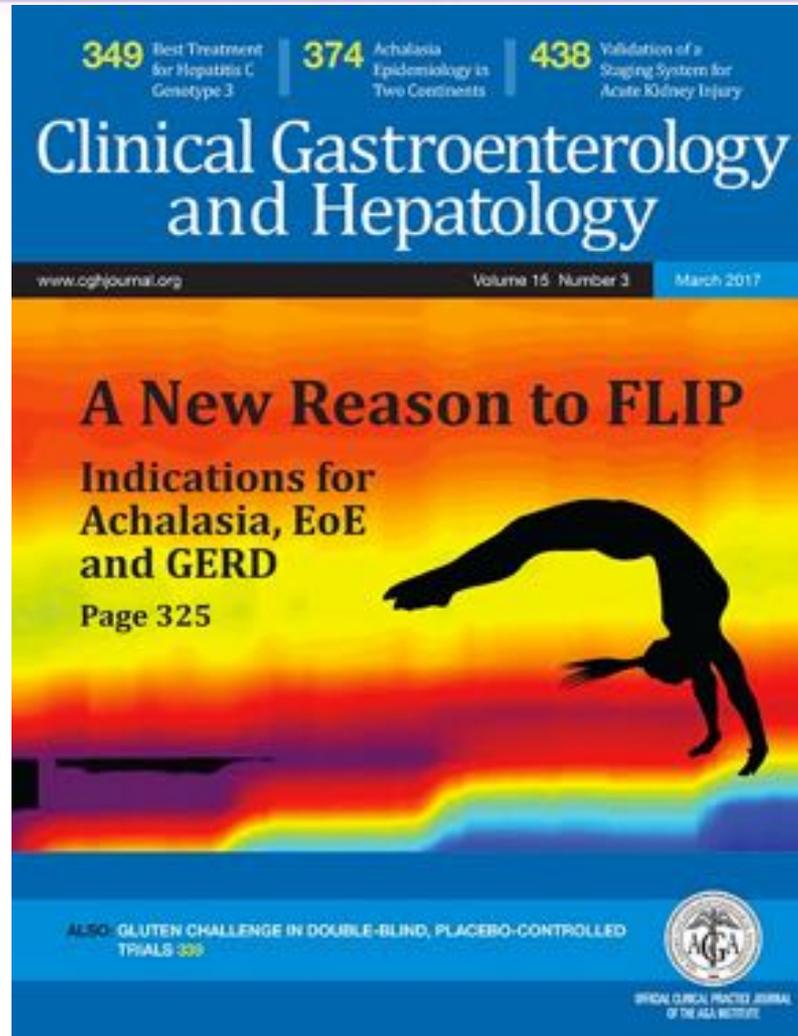
Reflux esophagitis after 1 year



Patients with pathological acid exposure (EAT>6%) on 24hr pH-metry

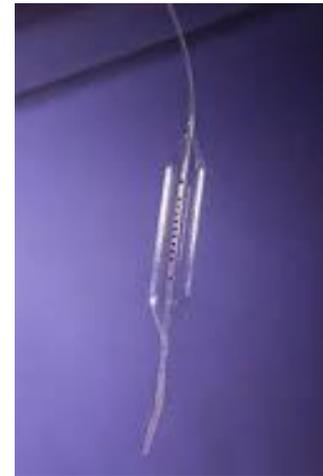
after POEM	49.1%
after PD	38.6%

Functional Lumen Imaging Probe (FLIP)



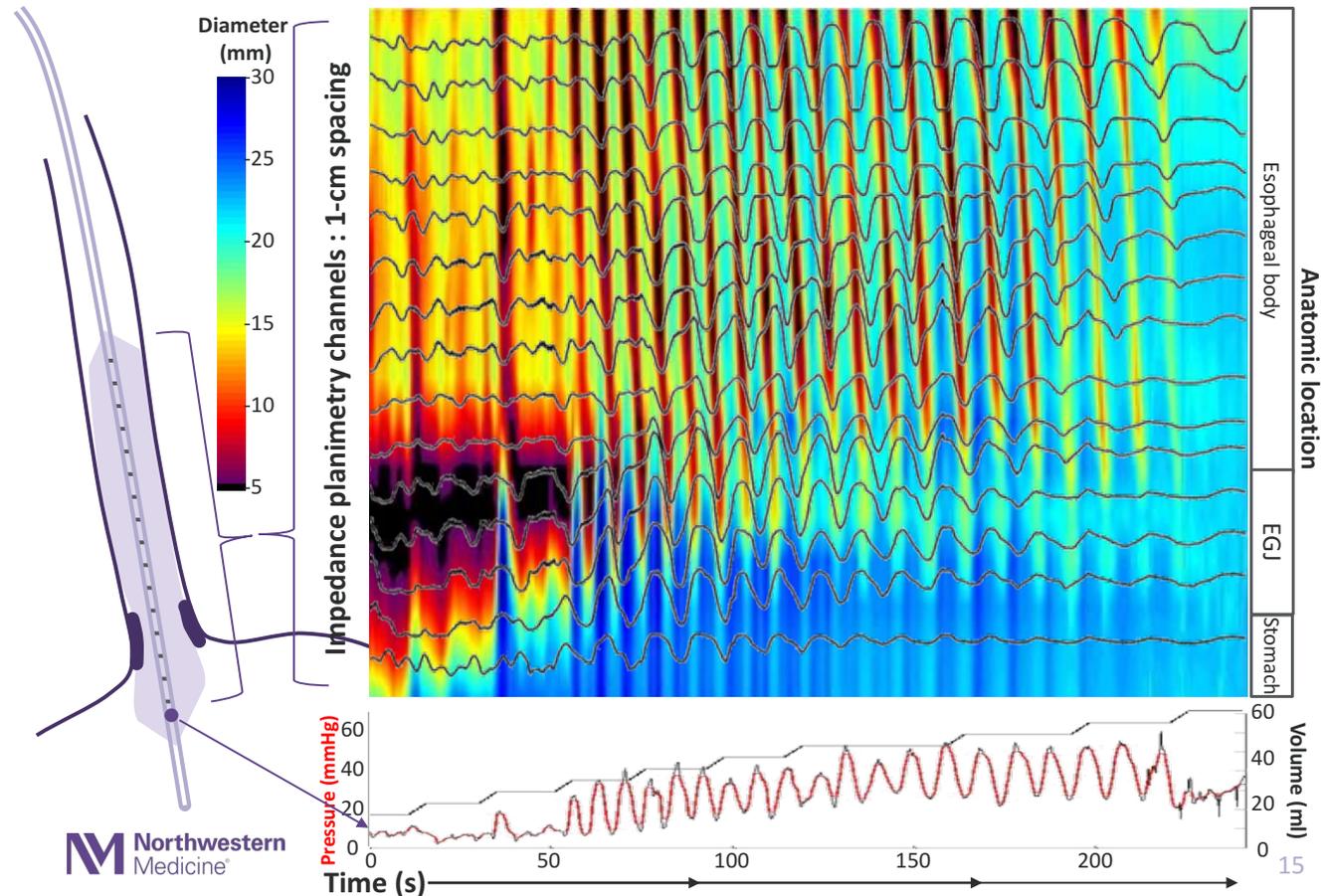
Functional Lumen Imaging Probe (FLIP)

- History
 - Developed by Barry McMahon & Hans Gregersen
 - First publication in 2005
 - Crospon established for commercialization in 2006
 - CE certification 2009
 - FDA approval 2010
- Measures:
 - Diameter
 - Compliance



Functional Lumen Imaging Probe (FLIP)

FLIP: Topography: Esophageal diameter topography



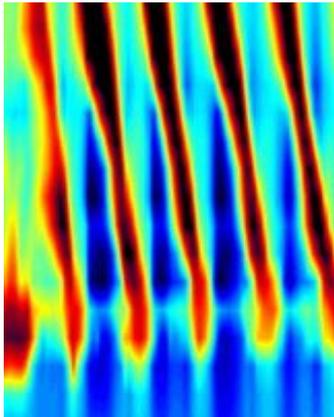
- Slides Courtesy of John Pandolfino
- Presented at Rome Foundation Lecture. DDW

Functional Lumen Imaging Probe (FLIP)

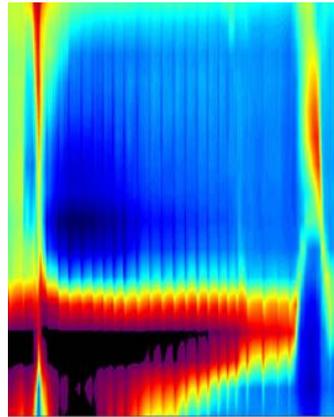
Contractility patterns

Methods: FLIP Analysis

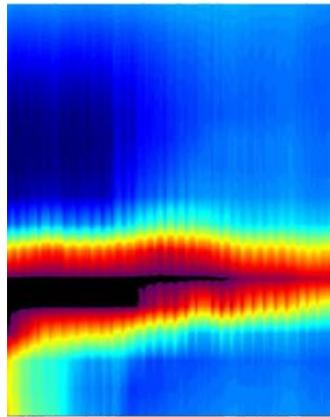
Repetitive,
ANTEGRADE
contractions
(RACs)



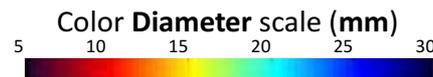
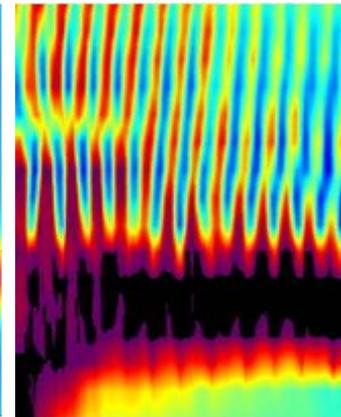
Contractility,
No RACs or RRCs



Absent
contractility



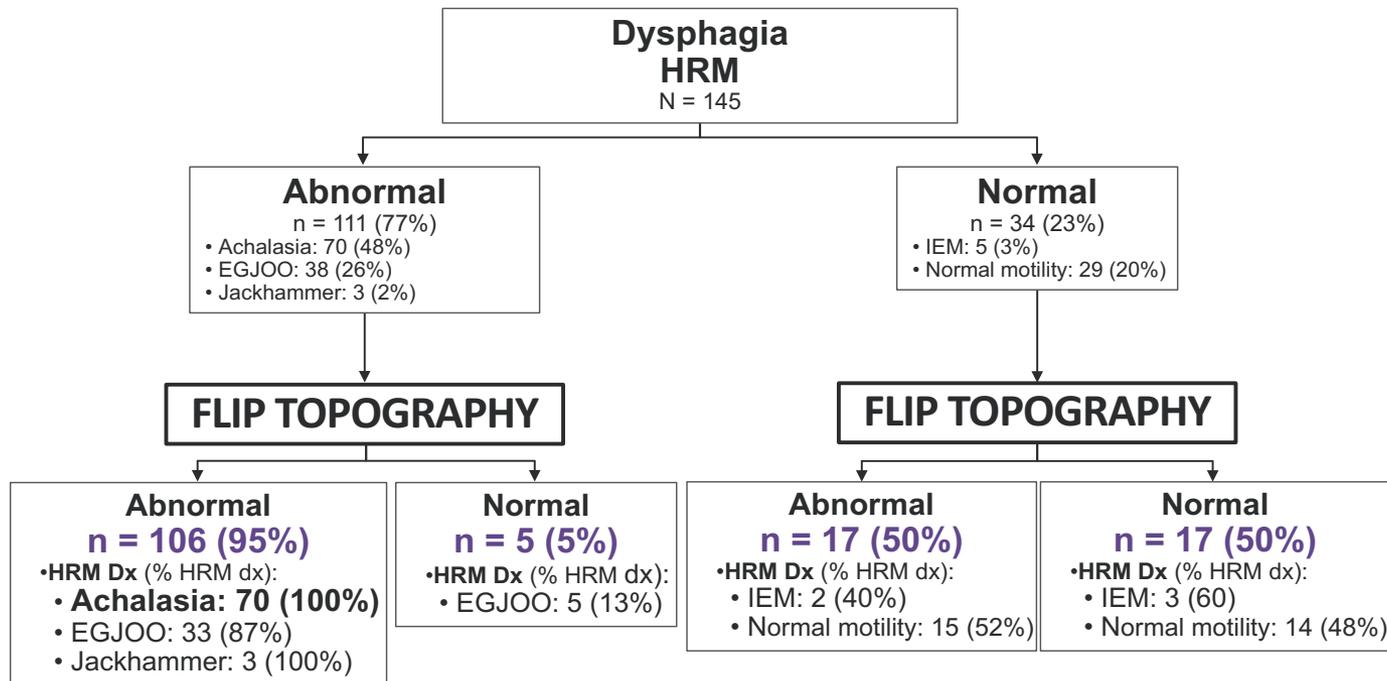
Repetitive,
RETROGRADE
contractions
(RRCs)



- Slides Courtesy of John Pandolfino
- Presented at Rome Foundation Lecture. DDW

Functional Lumen Imaging Probe (FLIP)

Relationship of HRM and FLIP topography Results: FLIP topography



- Slides Courtesy of John Pandolfino
- Presented at Rome Foundation Lecture, DDW

Functional Lumen Imaging Probe (FLIP)

Discrepant diagnoses: HRM and FLIP topography Results: FLIP topography

HRM diagnosis	n	FLIP topography motility classification (n, %)						
		Achalasia without contractility	Spastic Achalasia	EGJOO (achalasia or subtle mechanical obstruction)	Absent contractility	Spastic motor disorder	Diminished contractility	Normal motility
Type I Achalasia	19	13 (68)	2 (11)	3 (16)	1 (5)	0	0	
Type II Achalasia	3	1 (33)	0	0	0	0	0	
Type III achalasia	2	0	0	0	0	0	0	
EGJ outflow obstruction	3	0	0	0	0	0	5 (13)	
Jackhammer	0	0	0	0	0	0	0	
IEM	5	0	0	1 (20)	0	1 (20)	1 (20)	2 (40)
Normal	29	0	4 (14)	8 (28)	0	3 (10)	0	14 (48)
Controls ^{1,2}	10	0	0	0	0	0	2 (20)	8 (80)

50% (17/34) patients with normal/borderline HRM had an abnormal response to distension on FLIP topography

- Slides Courtesy of John Pandolfino
- Presented at Rome Foundation Lecture. DDW

New Guidelines for Reflux Testing

- Group of 50 international experts met over past 2 years
- Formulated more simple guidelines for reflux testing
- Key updates:
 - Abnormal:
 - Acid > 6%
 - Impedance > 80 events/day
 - Creation of a borderline group
 - Acid 4-6%
 - Impedance 40-80 events/day
 - Normal:
 - Acid < 4%
 - Impedance < 40 events/day
 - Less importance of other metrics
 - DeMeester Score
 - Supine/erect reflux

Received 22 December 2016 | Accepted 20 February 2017
DOI: 10.1111/nmi.12067

REVIEW ARTICLE

WILEY 

Ambulatory reflux monitoring for diagnosis of gastro-esophageal reflux disease: Update of the Porto consensus and recommendations from an international consensus group

S. Roman¹ | C. P. Gyawali² | E. Savarino³ | R. Yadlapati⁴ | F. Zerbib⁵ |
J. Wu⁶ | M. Vela⁷ | R. Tutuian⁸ | R. Tatum⁹ | D. Sifrim¹⁰ | J. Keller¹¹ |
M. Fox¹² | J. E. Pandolfino⁴ | A. J. Bredeoord¹³ | the GERD consensus group^a

Eosinophilic Esophagitis

- More papers published on EoE in the past 5 years than in the entirety prior
- Several big developments but two that peaked my interest:
 - Oral topical steroid tablet formulations
 - Esophageal pin-prick allergy testing

Eosinophilic Esophagitis

- The mainstay of medical therapy for EoE is topical steroid
- Most commonly used is swallowed fluticasone
- Other option is oral viscous budesonide
- Neither is FDA-approved for EoE

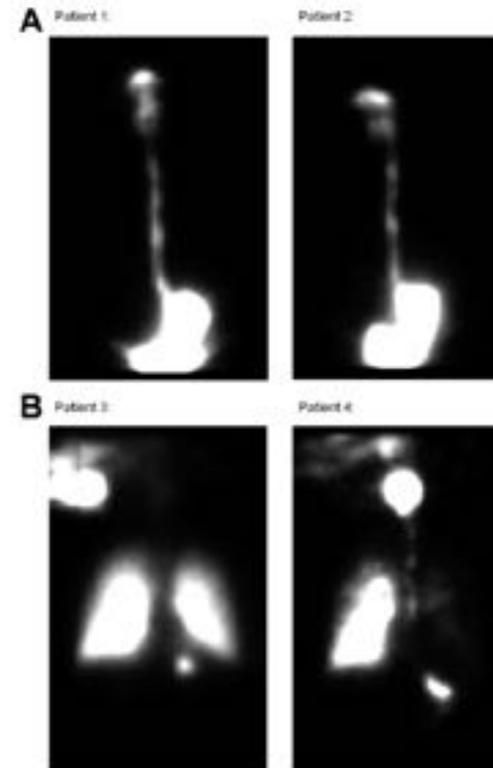


Figure 1. Illustrative examples of nuclear scintigraphy esophageal emptying scans for the (A) OEB and (B) NEB groups. These images represent the total distribution of ^{99m}Tc-DTPA tracer throughout the imaging period. Note that for OEB, the medication deposits only in the oropharynx, esophagus, and stomach, whereas for NEB there is also medication deposition in the lungs. In addition, there is qualitatively more deposition in the esophagus and stomach of OEB compared with NEB.

- Slide Courtesy of David Katzka
- Presented at DDW EoE Session Saturday afternoon

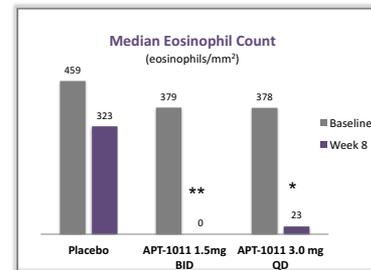
Eosinophilic Esophagitis

Orodispersible budesonide tablets in EoE

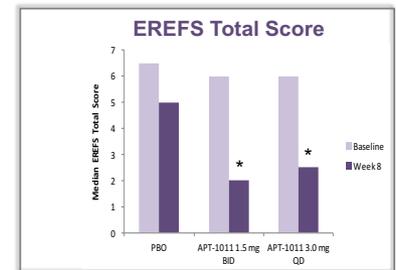
- Multicenter, randomized, double blind, placebo controlled trial
- 88 adults
- Budesonide tablets 1 mg BID vs placebo for 6 weeks
- Histologic remission 93% budesonide; 0% placebo ($p < 0.0001$)
- Symptom resolution: 59% budesonide; 14% placebo ($p < 0.0001$)
- Esophageal Candidiasis: 5%

Randomized, double-blind, placebo controlled trial of fluticasone orally disintegrating tablet in adolescents and adults with EoE

Median Eosinophil Count (eos/mm²)



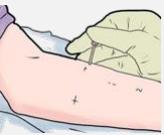
Endoscopic Score (EREFS)



- Slide Courtesy of Ikuo Hirano
- Presented at EoE Sessions. DDW

Eosinophilic Esophagitis

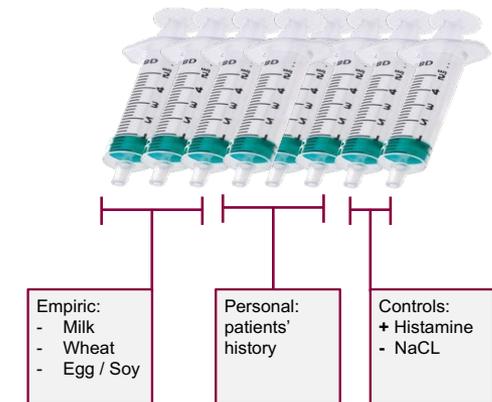
Background: Dietary treatment of EoE

Elimination		Elemental
Empiric (4FED/SFED)	Allergy Test-Directed	
		
72.1 %	45.5 %	90.8 %

Arias et al. Am. J. Gastroenterol. 2014.



Esophageal Prick Test



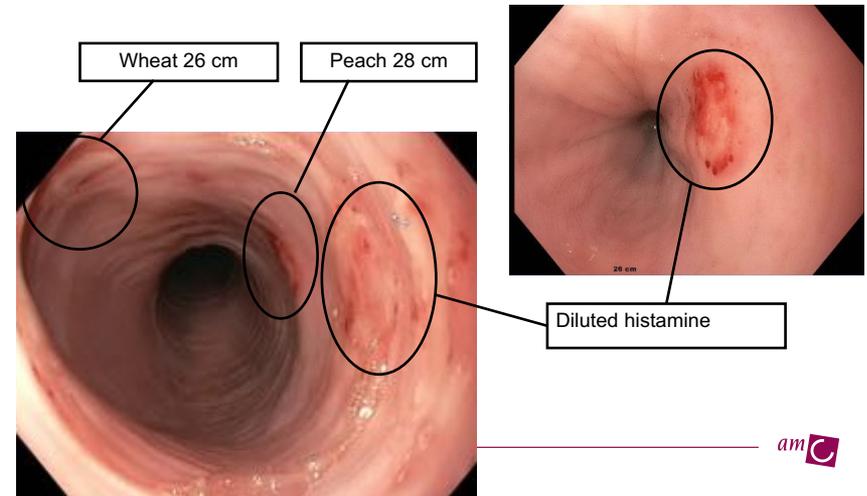
- Slides Courtesy of Arjun Bredenoord
- Presented at EoE Session Tuesday 4pm. DDW

Eosinophilic Esophagitis

Acute EPT response



Delayed response EPT



- Slides Courtesy of Arjun Bredenoord
- Presented at EoE Session Tuesday 4pm. DDW

Gastroparesis

Relamorelin in Patients with Diabetic Gastroparesis: Efficacy and Safety Results from a Phase 2B Randomized, Double-blind, Placebo-controlled, 12-Week Study (RM-131-009)

Michael Camilleri *Mayo Clinic, Rochester, MN*

Richard W. McCallum *Texas Tech University Health Sciences Center, El Paso, TX,*

Jan Tack *University Hospital, Leuven, Belgium*

Sharon Spence, Keith Gottesdiener, Fred T. Fiedorek
Motus, Boston, MA,

for the RM-131-009 Study Group



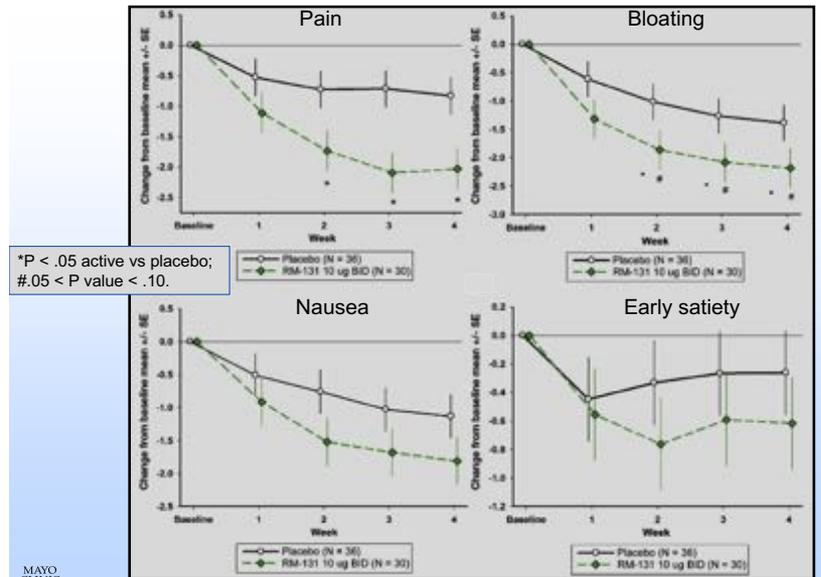
- Slides Courtesy of Michael Camilleri
- Presented at AGA Presidential Plenary Session. DDW

Gastroparesis

Background

- Relamorelin (RM-131) is a selective pentapeptide ghrelin receptor agonist:
 - ~15-130 fold more potent prokinetic than ghrelin in animal models
 - Large margins of safety (>750-fold) in toxicology studies
 - SC injection with small insulin needle
 - Potent effects on gastric emptying in Phase 1 studies
 - 10 µg BID for 4 weeks: prokinetic and relief of symptoms of diabetic gastroparesis in Phase 2A study especially in patients with vomiting at baseline

Lembo et al Gastroenterology 151:87-96, 2016

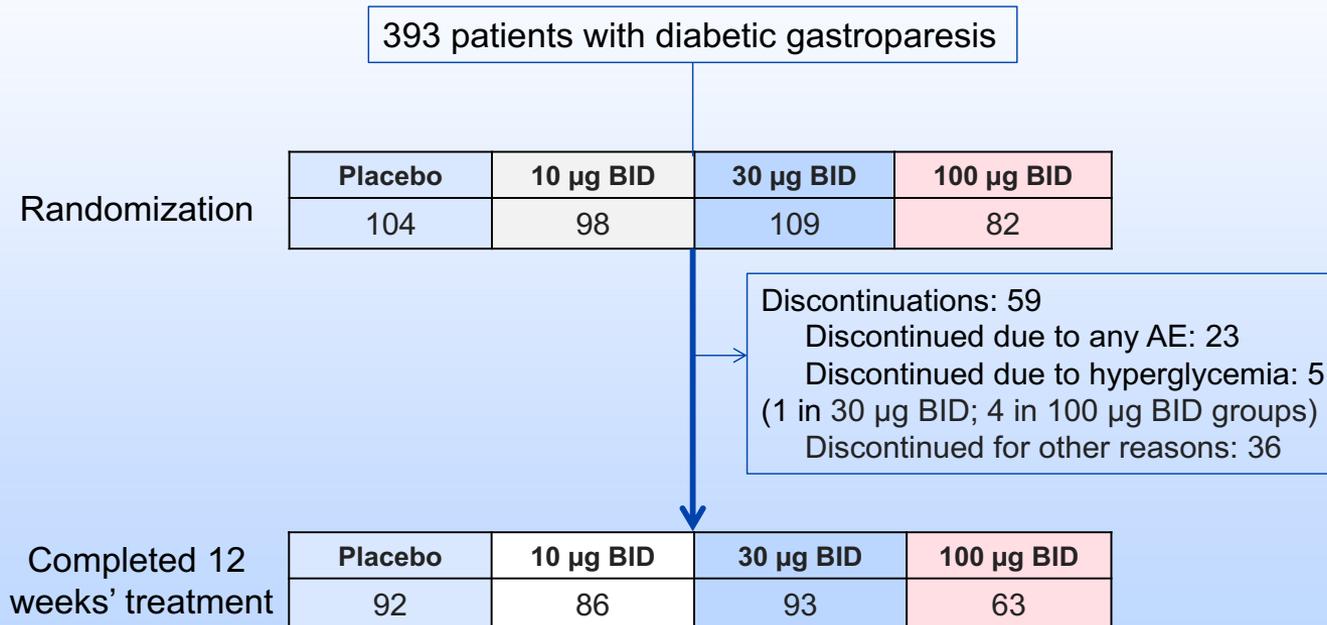


Lembo et al Gastroenterology 151:87-96, 2016

- Slides Courtesy of Michael Camilleri
- Presented at AGA Presidential Plenary Session, DDW

Gastroparesis

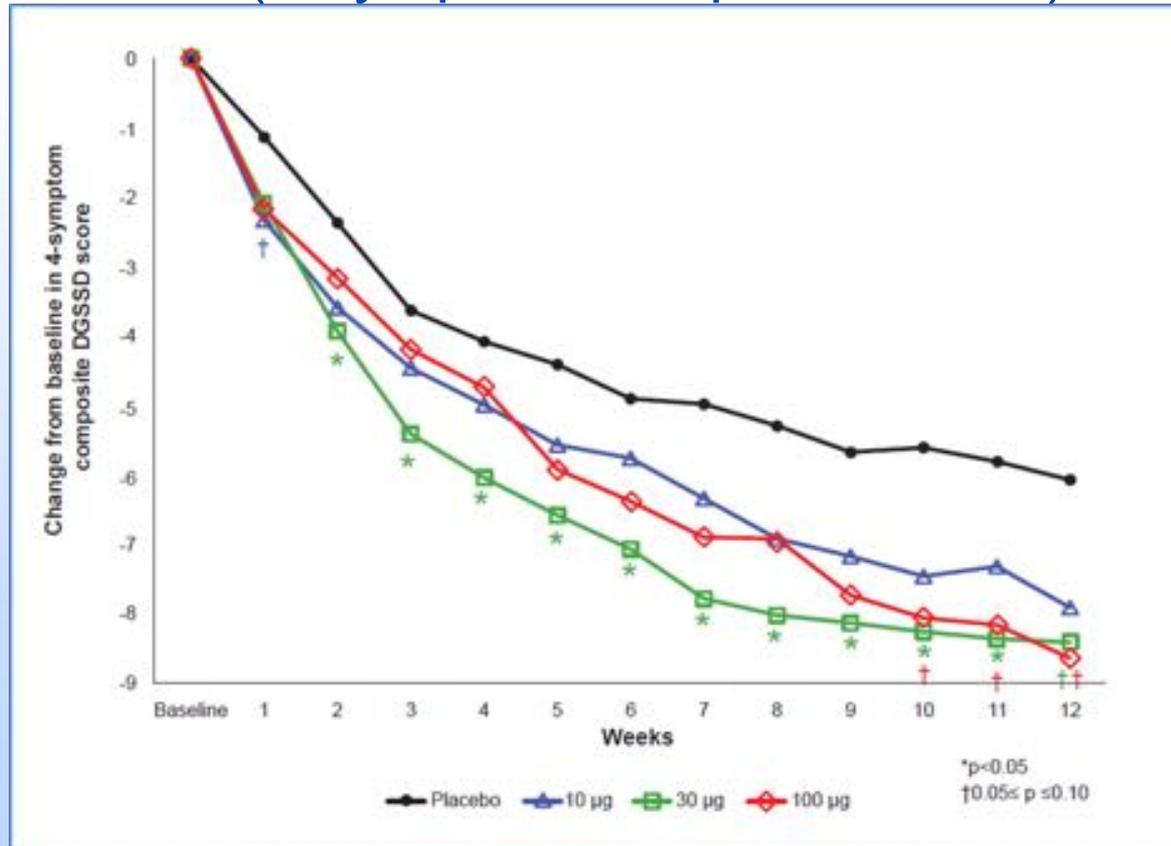
CONSORT FLOW CHART Discontinuations and Completers



- Slides Courtesy of Michael Camilleri
- Presented at AGA Presidential Plenary Session, DDW

Gastroparesis

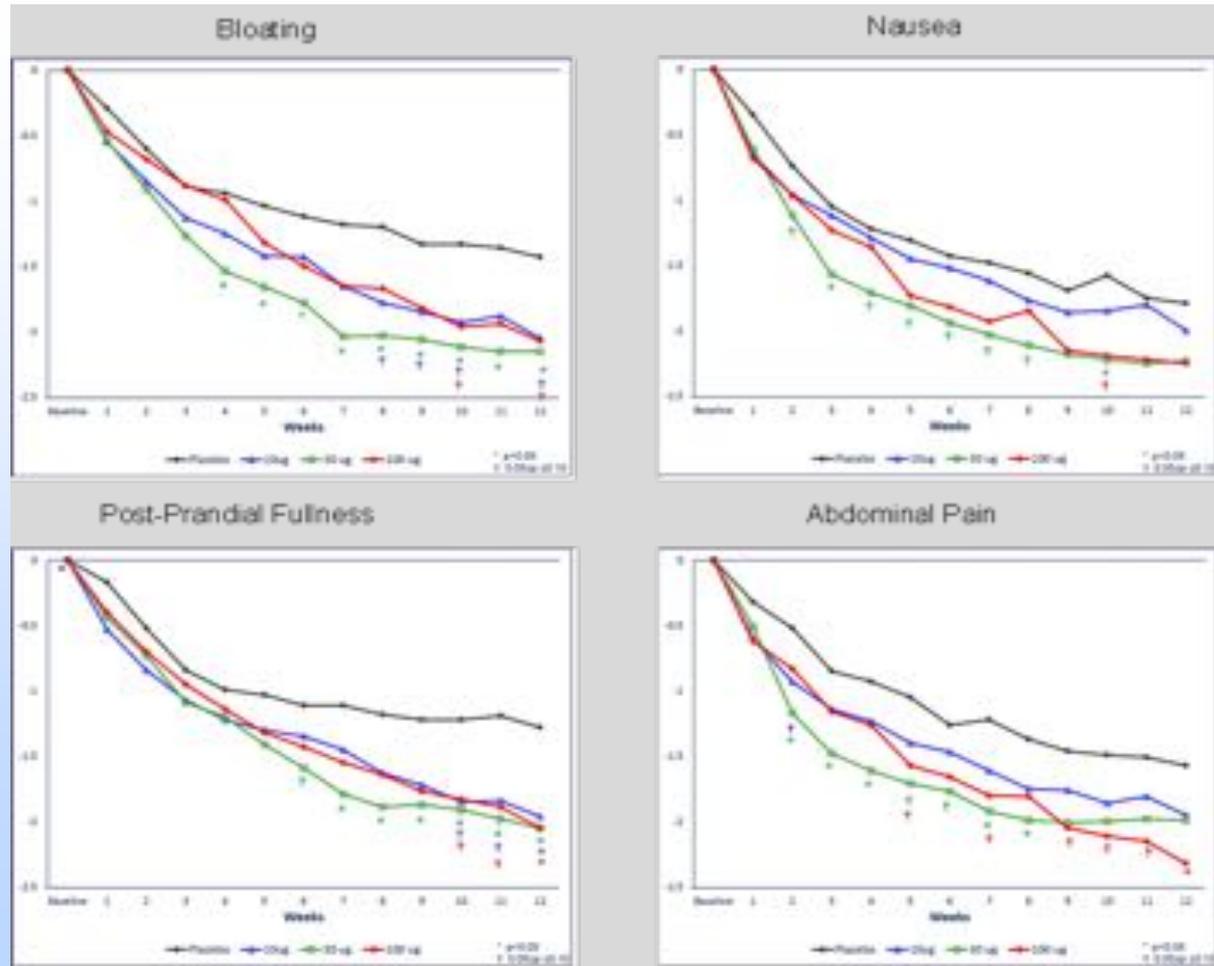
Change from Baseline through Week 12 in DGSSD (4-symptom composite score)



- Slides Courtesy of Michael Camilleri
- Presented at AGA Presidential Plenary Session, DDW

Gastroparesis

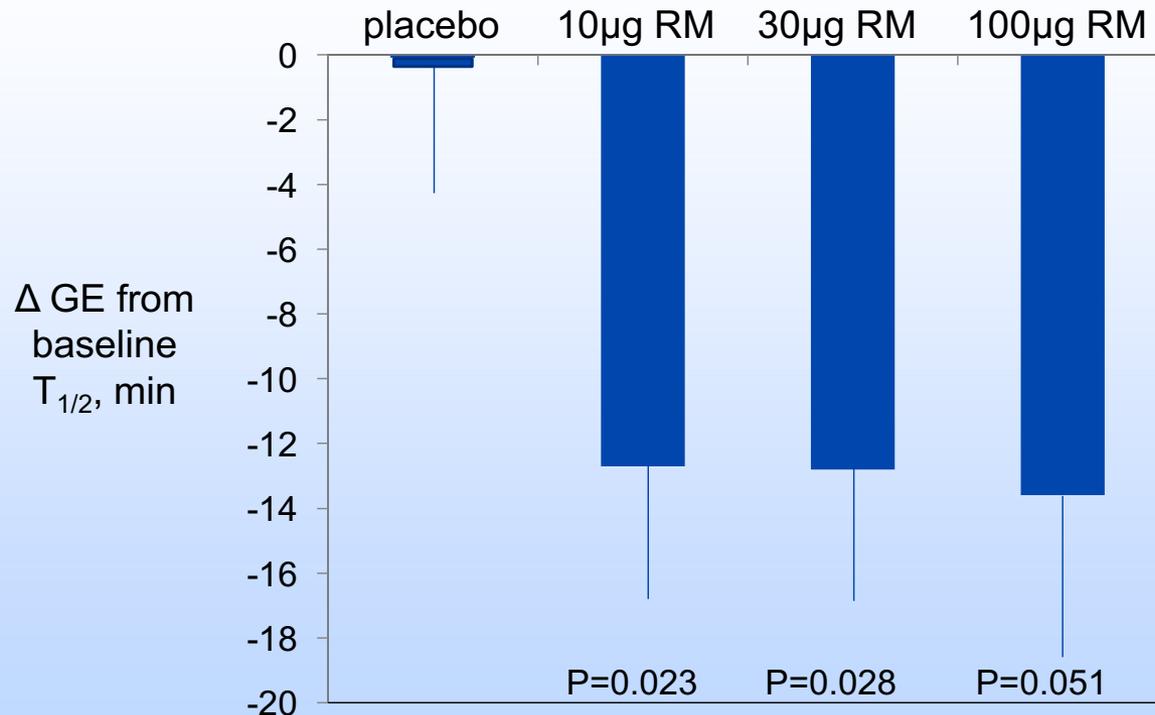
Change from Baseline through Week 12 in each symptom score



- Slides Courtesy of Michael Camilleri
- Presented at AGA Presidential Plenary Session, DDW

Gastroparesis

Decreased Gastric Emptying $T_{1/2}$ at Week 12



Data mean + SEM

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- Slides Courtesy of Michael Camilleri
- Presented at AGA Presidential Plenary Session, DDW

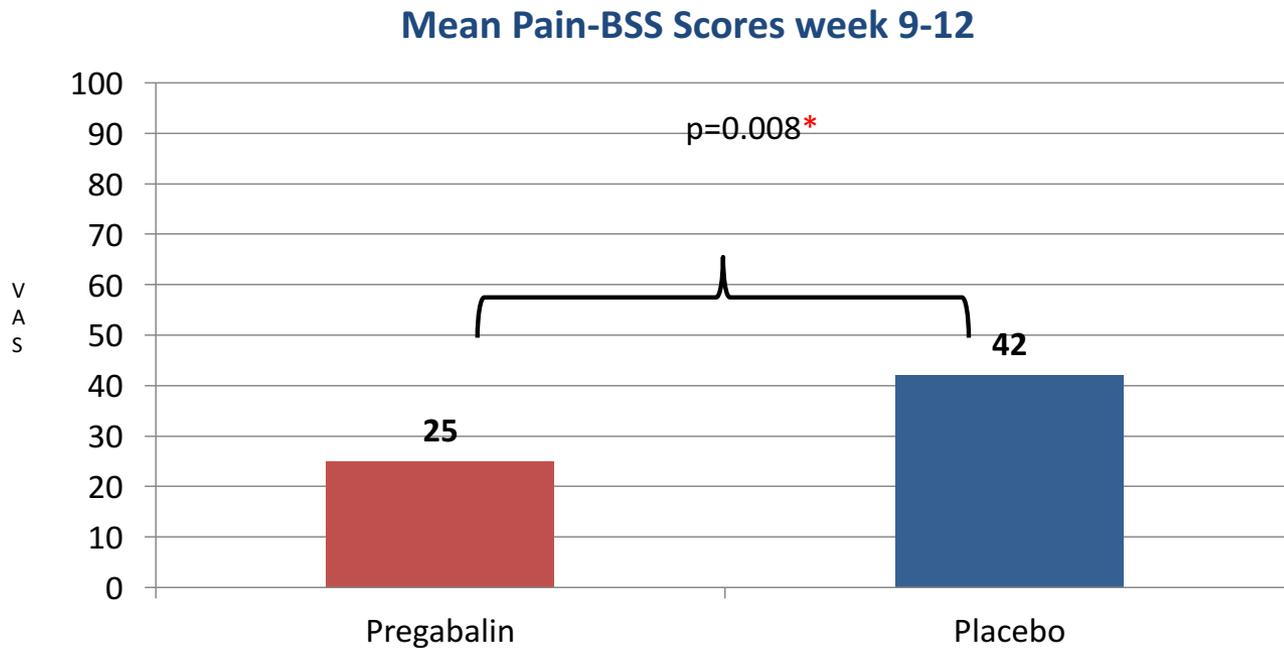
Irritable Bowel Syndrome

- A Placebo-Controlled Trial of Pregabalin for Irritable Bowel Syndrome
- 85 Subjects with IBS and abdominal pain were randomized to receive pregabalin twice daily versus placebo
- 12 week duration
- Primary endpoint: pain scores over the last 4 weeks of treatment

- Slides Courtesy of Yuri Saito
- Presented at ACG Presidential Plenary Session (October 2016)

Irritable Bowel Syndrome

Results: Primary Outcome



*Intention-to-treat analysis

- Slides Courtesy of Yuri Saito
- Presented at ACG Presidential Plenary Session (October 2016)

Irritable Bowel Syndrome

Mean BSS Scores (sd) weeks 9-12

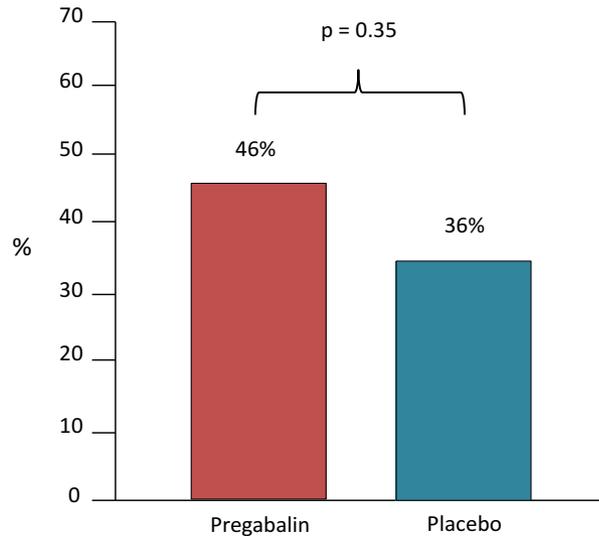
	Pregabalin N=32	Placebo N=35	ITT P-value
Pain-BSS	25 (16)	42 (27)	0.008*
Overall-BSS	26 (15)	42 (26)	0.009*
Diarrhea-BSS	17 (18)	32 (26)	0.049*
Constipation-BSS	26 (27)	22 (25)	N.S.
Bloating-BSS	29 (23)	44 (29)	0.016*

- Slides Courtesy of Yuri Saito
- Presented at ACG Presidential Plenary Session (October 2016)

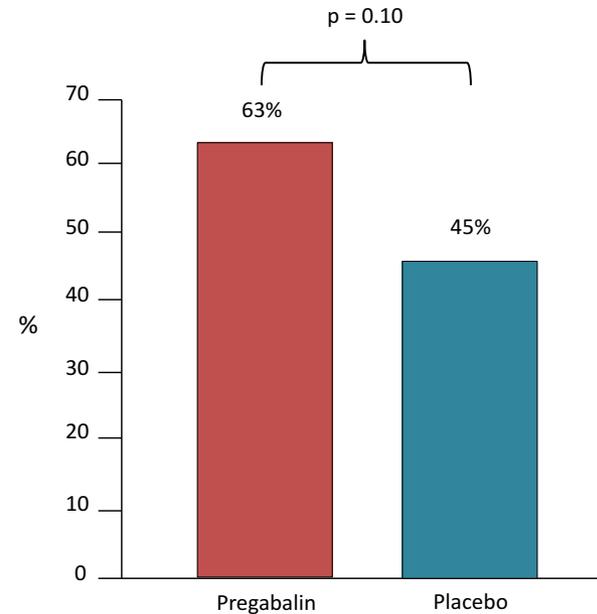
Irritable Bowel Syndrome

Other Secondary Endpoints

Adequate relief – weeks 9-12



Change in pain ≥ 30 – week 12



*Intention-to-treat
-Not adjusted for age and gender

- Slides Courtesy of Yuri Saito
- Presented at ACG Presidential Plenary Session (October 2016)

Irritable Bowel Syndrome

Adverse Events

	Pregabalin	Placebo	p-value
Total	28 (68%)	24 (55%)	N.S.
Diarrhea	6 (15%)	7 (16%)	N.S.
Abdominal pain	13 (32%)	13 (30%)	N.S.
Upset stomach	4 (10%)	1 (2%)	N.S.
Constipation	9 (22%)	4 (9%)	N.S.
Nausea	6 (15%)	2 (5%)	N.S.
Fullness	2 (5%)	0 (0%)	N.S.
Blurred vision	6 (15%)	1 (2%)	0.05*
Dizzy	13 (32%)	2 (5%)	0.01*
High or tipsy	4 (10%)	0 (0%)	0.05*

-One non-study related SAE: death

- Slides Courtesy of Yuri Saito
- Presented at ACG Presidential Plenary Session (October 2016)

Thank you



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