Novel Therapy in Gastroesophageal Reflux Disease (GERD)

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Goals of Treatment

• Primary endpoint for treatment GERD is
  – To eliminate symptoms
  – Normalization of quality of life
• To heal esophageal injury
• To manage and prevent complications e.g. strictures
• To prevent recurrence
GERD: Management

- Lifestyle modifications
- Prokinetic drugs and mucosal protective agents
- Acid-suppressive medications
- Drug manipulates TLESRs
- Endoscopic treatment
- Surgical treatment
Possible etiologic factors involved in GERD

- Decreased Salivation
- Impaired Esophageal Acid Clearance
- Impaired Tissue Resistance
- Transient LES Relaxation
- Decreased Resting Tone of LES
- Delayed Gastric Emptying

Acid pocket

Lower Esophageal Sphincter (LES)

Duodenum
The “acid pocket”

an area of unbuffered gastric acid that accumulates in the proximal stomach after meals and serves as the reservoir for acid reflux in healthy individuals and GERD patients*

In the fasting state, average intragastric pH was 1.4. After a meal, intragastric pH increased to 4.4, but was still pH 1.6 in the region adjacent to the GE pH step-up point.

# Acid reflux during TLESRs: HV vs GERD patients

<table>
<thead>
<tr>
<th></th>
<th>HVs (n=12)</th>
<th>s-HH (n=12)</th>
<th>I-HH (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLOSRs (median (IQR))</td>
<td>12.5 (7.8–16.8)</td>
<td>11.0 (9.0–12.0)</td>
<td>11.0 (8.0–13.0)</td>
</tr>
<tr>
<td>TLOSRs with reflux (%)</td>
<td>88.0±4.7</td>
<td>89.8±3.1</td>
<td>92.1±3.2</td>
</tr>
<tr>
<td>▶ liquid (%)</td>
<td>36.9±10.0</td>
<td>13.5±2.5</td>
<td>21.9±7.7</td>
</tr>
<tr>
<td>▶ mixed (%)</td>
<td>39.8±8.0</td>
<td>69.3±6.4*</td>
<td>63.5±10.1</td>
</tr>
<tr>
<td>▶ gas (%)</td>
<td>23.3±8.1</td>
<td>17.2±6.0</td>
<td>14.6±4.9</td>
</tr>
</tbody>
</table>

![Graph 1](image1.png)

![Graph 2](image2.png)

Mechanisms underlying increased acid exposure in hiatal hernia patients

Increased risk (x2) to have acid reflux during a TLESR in GERD

• Increased compliance – more liquid reflux
• Changes in size or position in acid pocket?

Fletcher J, et al. Gastroenterology 2001;121:775-783
Scintigraphy: **Position of the acid pocket and hiatal hernia**

- HV and small HH GERD patients: acid pocket distal to the SCJ and diaphragm
- Large HH GERD:
  - in 40% extending above the diaphragm during entire study
  - In rest of large HH patients: intermittent migration of pocket into HH sac above diaphragm

• The position of the acid pocket is largely determined by the presence of a HH.

• Entrapment of the pocket above the diaphragm, especially in patients with I-HH, is a major risk factor underlying the increased occurrence of acidic reflux during a TLESR in patients with GERD.

3D reconstruction of MRI images of the stomach postprandially showing the disposition of an administered alginate / antacid combination

Effect of PPI on the acid pocket

Acid pocket size

\[ p < 0.01 \]

Acid pocket position

Rohof et al., submitted
Effect of Baclofen on Gastric Acid Pocket in GERD Patients
Emidio Scarpellini, Rita Vos, Veerle Boecxstaens, Ans Pauwels, Jan F. Tack

• To study the effect of baclofen on the location and the extent of the postprandial AP in GERD.

Methods:
• 13 treatment-naive GERD patients
• PH electrode stepwise pull-through (1 cm/min, LES -10 to +5 cm) was performed at 30 min intervals for 150 minutes, with administration of placebo or baclofen 40 mg after the first and ingestion of a meal (200 ml Nutridrink®, 300 Kcal) after the second pull-through.
• Upper GI symptoms were recorded as VAS

Results:
• The proximal extent of the AP above the LES was not significantly altered by baclofen compare to placebo
• Heartburn severity ratings tended to be lower after baclofen both pre- and postprandially
• Preprandially, symptoms of epigastric burning, retrosternal cramps and abdominal pain were significantly lower after baclofen compared to placebo
• Postprandially, belching and epigastric burning were significantly lowered by baclofen in comparison with placebo
Effect of Baclofen on Gastric Acid Pocket in GERD Patients
Emidio Scarpellini, Rita Vos, Veerle Boecxstaens, Ans Pauwels, Jan F. Tack

<table>
<thead>
<tr>
<th>*P&lt;0.05</th>
<th>pH drop at the LES</th>
<th>30 min after the meal</th>
<th>60 min after the meal</th>
<th>90 min after the meal</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH drop at the LES</td>
<td>Placebo</td>
<td>2.9±0.6</td>
<td>4.8±0.4</td>
<td>4.4±0.2 units</td>
</tr>
<tr>
<td>Baclofen</td>
<td>2.5±0.4</td>
<td>3.6±0.4</td>
<td>2.8±0.4 units</td>
<td></td>
</tr>
<tr>
<td>Nadir pH</td>
<td>Placebo</td>
<td>3.9±0.6</td>
<td>2.3±0.6</td>
<td>2.1±0.4 units</td>
</tr>
<tr>
<td>Baclofen</td>
<td>2.5±0.4</td>
<td>2.8±0.4</td>
<td>2.5±0.3 units</td>
<td></td>
</tr>
</tbody>
</table>

Gastric pH drops in the postprandial period. Baclofen did not affect pH drops nor the nadir pH at all the time points after the meal (p=NS).

Conclusion:
• Baclofen does not alter the AP
• The effects of baclofen on the LES are associated with a significant reduction of upper GI symptoms both pre- and postprandially
TRPV1 and GERD

Increased TRPV1 gene expression in esophageal mucosa of patients with NERD and EE

TRPV1 = Transient receptor potential channel vanilloid subfamily member-1 (TRPV1)

Transient lower esophageal sphincter relaxation (TLESR) reducers

- \( \text{GABA}_B \) receptor agonists and metabotrophic glutamate receptor 5 (mGluR5) antagonists

- \( \text{GABA}_B \) agonist (Baclofen)
  - ↓ TLESR rate by 40–60%
  - ↓ reflux episodes by 43%
  - ↑ LES basal pressure
  - ↑ gastric emptying
  - significantly ↓ DGER and weakly acidic reflux as well as DGER-related symptoms
  - 10 mg QID up to 20 mg TID

Van Hewaarden et al. Aliment Pharmacol Ther 2002
# Effect of Baclofen on Reflux Symptoms

43 GERD pts randomized to baclofen 10-20 mg vs. placebo tid x 2 wks

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Placebo</th>
<th>Baclofen</th>
<th>Pre</th>
<th>Post</th>
<th>$P$-value</th>
<th>Pre</th>
<th>Post</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heartburn</td>
<td>5 (1.8-6)</td>
<td>1.5 (0-4)</td>
<td>0.001*</td>
<td></td>
<td></td>
<td>6 (2.5-6)</td>
<td>3 (1-6)</td>
<td>0.186</td>
</tr>
<tr>
<td>Belching</td>
<td>4.5 (2-6)</td>
<td>3 (1-4.5)</td>
<td>0.481</td>
<td></td>
<td></td>
<td>4 (1.3-8.3)</td>
<td>1 (1-6)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>2.5 (0.8-6)</td>
<td>0 (0-3)</td>
<td>0.017*</td>
<td></td>
<td></td>
<td>3.5 (1-4)</td>
<td>1 (0-3.5)</td>
<td>0.036*</td>
</tr>
<tr>
<td>Symptom Score</td>
<td>14 (11-18)</td>
<td>6.5 (4.5-11)</td>
<td>0.000*</td>
<td></td>
<td></td>
<td>14 (7.3-20)</td>
<td>6 (2.3-17)</td>
<td>0.004*</td>
</tr>
</tbody>
</table>

Data are expressed as median (interquartile range). $P$-values shown are results of Friedman test. *$P<0.05$.

metabotropic glutamate receptor 5 (mGluR5) antagonists

Table 2: Effects of repeated ADX10059 and placebo on the main reflux parameters in the total 5 h and Postprandial 4 h pH impedance monitoring periods. Data are shown as median (range) change at day 6 from predose day 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Placebo</th>
<th>50 mg b.i.d.</th>
<th>125 mg b.i.d.</th>
<th>250 mg b.i.d.</th>
<th>Overall treatment effect (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total reflux episodes (n)</td>
<td>6.5 [1, 21]</td>
<td>4.0 [-2, 7]</td>
<td>-0.5 (-18, 8)</td>
<td>1.5 (-7, 9)</td>
<td>0.115</td>
</tr>
<tr>
<td>Postprandial reflux episodes (n)</td>
<td>7.0 [1, 18]</td>
<td>3.5 [-2, 8]</td>
<td>1.0 (-18, 8)</td>
<td>2.0 (-4, 7)</td>
<td>0.131</td>
</tr>
<tr>
<td>Total acid reflux episodes (n)</td>
<td>3.0 [1, 21]</td>
<td>2.0 [-1, 8]</td>
<td>1.0 (-16, 11)</td>
<td>3.5 (-2, 7)</td>
<td>0.523</td>
</tr>
<tr>
<td>Postprandial acid reflux episodes (n)</td>
<td>4.0 [1, 18]</td>
<td>2.0 [-1, 9]</td>
<td>1.0 (-16, 11)</td>
<td>3.5 (-1, 5)</td>
<td>0.448</td>
</tr>
<tr>
<td>Total weakly acidic reflux episodes (n)</td>
<td>0.5 [0, 4]</td>
<td>0.0 [-3, 3]</td>
<td>-2.5 (-5, 2)</td>
<td>-2.0 (-6, 2)</td>
<td>0.071</td>
</tr>
<tr>
<td>Postprandial weakly acidic reflux episodes (n)</td>
<td>1.0 [0, 4]</td>
<td>0.0 [-1, 3]</td>
<td>-2.0 [-3, 2]</td>
<td>-1.0 [-4, 2]</td>
<td>0.041</td>
</tr>
<tr>
<td>Total reflux with proximal extent &gt;15 cm (n)</td>
<td>5.0 [0, 16]</td>
<td>1.0 [-1, 2]</td>
<td>-0.5 (-12, 12)</td>
<td>1.5 [-2, 5]</td>
<td>0.164</td>
</tr>
<tr>
<td>Total acid exposure (%)</td>
<td>2.6 [0.7, 4.9]</td>
<td>2.0 [0.2, 2.9]</td>
<td>-0.1 [-6.6, 0.2]</td>
<td>1.0 [-2.6, 5.0]</td>
<td>0.048</td>
</tr>
<tr>
<td>Postprandial acid exposure (%)</td>
<td>2.3 [0.9, 6.3]</td>
<td>2.6 [0.3, 3.7]</td>
<td>0.1 [-8.1, 0.3]</td>
<td>1.4 [-4.2, 6.7]</td>
<td>0.078</td>
</tr>
<tr>
<td>Total bolus exposure (%)</td>
<td>1.05 [0.2, 2.9]</td>
<td>0.70 [-0.4, 2.6]</td>
<td>-0.05 [-2.6, 1.8]</td>
<td>0.05 [-1.0, 3.4]</td>
<td>0.118</td>
</tr>
<tr>
<td>Postprandial bolus exposure (%)</td>
<td>1.3 [0.2, 3.1]</td>
<td>0.9 [-0.6, 3.5]</td>
<td>-0.05 [-3.3, 2.4]</td>
<td>0.2 [-0.9, 4.5]</td>
<td>0.198</td>
</tr>
</tbody>
</table>

*P = 0.028, **P = 0.008.
The bold values are statistically significant.

ADX10059 decreased reflux episodes in healthy subjects

Transient lower esophageal sphincter relaxation (TLESR) reducers

- **GABA$_B$ receptor agonist:**
  - **Arbaclofen placarbil** (XP19986)
    - an active R-isomer of baclofen
    - well absorbed from the colon, allowing the drug to be delivered in a **sustained release** formulation that may allow **less frequent dosing** (QD)

Transient lower esophageal sphincter relaxation (TLESR) reducers

- **GABA\(_B\) receptor agonist:**
  - Lesogaberan (AZD3355)
    - 244 refractory GERD patients
    - DBCT, received either lesogaberan (65 mg BID) or placebo

**RESULTS:**
- Lesogaberan, compared with placebo, resulted in a significantly larger proportion of responders to treatment (16% vs 8% of patients; \(p=0.026\))

→ Lesogaberan add-on therapy to PPIs significantly improved heartburn and regurgitation symptoms

How Is Dexlansoprazole Different?

Dexlansoprazole is the first and only PPI with a Dual Delayed Release (DDR) formulation, which provides a second release of drug.

Dexlansoprazole capsules contain 2 types of enteric-coated granules:

- **Granule 1** begins releasing drug within an hour of dosing.
- **Granule 2** provides a second release of drug several hours later.

**Release 1** (25% at pH 5.5)

**Release 2** (75% at pH 6.75)
Pharmacokinetics of Dexlansoprazole and Lansoprazole

Randomized, open-label, multiple-dose, crossover study evaluating dexlansoprazole 60 mg and lansoprazole 30 mg once daily for 5 days in healthy subjects (n=40). Dexlansoprazole 60 mg was also compared to lansoprazole 30 mg for the healing of EE. Additional information is available in the presentation.

Eight-Week Healing Rates in Erosive Esophagitis

P < 0.05 after adjusting for the number of doses compared. Pairwise treatment comparisons performed with Cochran-Mantel-Haenszel test for crude rate analysis and with log-rank tests for life table analysis.

Non-Erosive GERD
Nighttime Heartburn Relief Results

Percentage of Nights Without Heartburn

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Median Percent Nights</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>52</td>
<td>317</td>
</tr>
<tr>
<td>DEXILANT 30 mg</td>
<td>81*</td>
<td>315</td>
</tr>
<tr>
<td>DEXILANT 60 mg</td>
<td>77*</td>
<td>315</td>
</tr>
</tbody>
</table>

ITT analysis
*P<.00001, pairwise comparison using Wilcoxon rank-sum test. Hochberg’s method of multiple comparisons used to maintain overall significance of .0025.

The LINX Reflux Management System
One Hundred Consecutive Patients Treated with Magnetic Sphincter Augmentation for Gastroesophageal Reflux Disease: 6 Years of Clinical Experience from a Single Center

Luigi Bonavina, MD, FACS, Greta Saino, MD, Davide Bona, MD, Andrea Sironi, MD, Veronica Lazzari, MD

Table 4. Esophageal pH Measurements

<table>
<thead>
<tr>
<th>Measure</th>
<th>Baseline</th>
<th>Last follow-up*</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total time pH &lt; 4, %</td>
<td>8.0</td>
<td>3.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total upright time, %</td>
<td>9.2</td>
<td>3.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total supine time, %</td>
<td>3.5</td>
<td>0.4</td>
<td>0.002</td>
</tr>
<tr>
<td>Total reflux episodes, n</td>
<td>51.7</td>
<td>31.5</td>
<td>0.002</td>
</tr>
<tr>
<td>Reflux episodes &gt; 5 min, n</td>
<td>4.0</td>
<td>1.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Longest reflux episode, min</td>
<td>35.3</td>
<td>9.5</td>
<td>0.024</td>
</tr>
<tr>
<td>DeMeester score</td>
<td>30.1</td>
<td>11.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Last follow-up pH measurements for patients 1 through 30 per protocol.
†p Values are from Wilcoxon signed rank test for continuous outcomes and McNemar’s test for categorical normalization outcomes.
‡Percent reported as median.
Prucalopride Decreases Esophageal Acid Exposure and Accelerates Gastric Emptying in Healthy Subjects

Boudewijn F. Kessing, Andreas J. Smout, Roelof J. Bennink, Noémie Kraaijpoel, Jac. Oors, Albert J. Bredenoord

- DBCT, crossover study in 21 healthy volunteers receiving 4 mg prucalopride or placebo x 6 days
- At day 5 subjects underwent HRM followed by 120 minutes combined HRM-pH-impedance monitoring after a standardized meal in order to study reflux mechanisms and the effect on TLESR
- The next day gastric emptying for solids was assessed scintigraphically

Results:

- Esophageal motility and basal pressure of the LES were not affected by prucalopride.
- Prucalopride significantly \(
\downarrow \text{total acid exposure time (AET)} \ (3.4 \ (2.5-5.6) \ \% \ vs \ 1.7 \ (0.8-3.5) \ %, \ p<0.05) \ \text{and upright AET} \ (4.8 \ (3.5-7.6) \ \% \ vs \ 2.6 \ (1.4-4.3) \ %, \ p<0.05).\)
Prucalopride Decreases Esophageal Acid Exposure and Accelerates Gastric Emptying in Healthy Subjects
Boudewijn F. Kessing, Andreas J. Smout, Roelof J. Bennink, Noémie Kraaijpoel, Jac. Oors, Albert J. Bredenoord

Results:
• The total number of reflux events was not affected by prucalopride,
• The number of reflux events extending to the proximal esophagus was significantly reduced as well as the proportion of reflux episodes reaching the proximal esophagus
• Prucalopride significantly improved acid clearance time (77.5 (47.8-108.8) vs 44.0 (30.0-67.8) s, p<0.05).
• Prucalopride did not affect the # of TLESRs or their association with reflux events.
• Prucalopride increased gastric emptying (T1/2 (49.8 (37.7-55.0) vs 32.7 (27.9-44.6) min, p<0.05)

Conclusion:
• Prucalopride accelerates gastric emptying and reduces esophageal acid exposure in healthy volunteers
227 patients with inadequate GERD symptom control despite BID PPI underwent Stretta.

All procedures were performed by a single endoscopist.

Baseline and follow-up GERD-HRQL scores (0-50), heartburn (0-5), satisfaction (0-5) and medication use

RESULTS:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before treatment, off meds</th>
<th>Before procedure, on meds</th>
<th>0.5 years</th>
<th>1 year</th>
<th>2 years</th>
<th>3 years</th>
<th>4 years</th>
<th>10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Med Scores</td>
<td>8.3±3.8</td>
<td>4.9±3.9</td>
<td>3.8±3.5</td>
<td>3.7±4.2</td>
<td>4.6±3.6</td>
<td>4.3±3.2</td>
<td>4.7±3.3</td>
<td></td>
</tr>
<tr>
<td>GERD Scores</td>
<td>27.8±10.7</td>
<td>21.4±11.5</td>
<td>11.1±10.0</td>
<td>6.9±7.5</td>
<td>5.0±6.9</td>
<td>6.9±8.2</td>
<td>7.3±8.5</td>
<td>8.1±9.9</td>
</tr>
<tr>
<td>Satisfaction</td>
<td>1.3±0.9</td>
<td>1.9±1.1</td>
<td>3.4±1.3</td>
<td>3.9±1.3</td>
<td>4.3±1.0</td>
<td>3.8±1.3</td>
<td>3.8±1.3</td>
<td>3.8±1.2</td>
</tr>
</tbody>
</table>

CONCLUSION:

Stretta for refractory GERD demonstrates a significant and sustained improvement of GERD-HQoL, patient satisfaction, and improved PPI use.
Methods:

• GERD with an abnormal pH study underwent targeted band ligation with/without mucosectomy. Band ligation was performed in all four quadrants < 5 mm distal to the Z-line and in 3 or 4 quadrants not more than 5 mm proximal to the Z-line.

• Six months after the procedure, all patients completed a medication history, GERD-HQRL questionnaire and underwent repeat pH testing.

Results:

• **10 patients** participated in the trial, half of whom underwent band ligation with mucosectomy.

• No procedural complications occurred.

• Three patients reported de novo dysphagia, one required dilation.

• Mean HQRL scores (off medications) improved from 26.6 to 9 at 6 months and 6.9 at 12 months, with 60% and 71% of scores normalizing at those respective time points.
A Prospective, Randomized Study on the Effect of Band Ligation With or Without Mucosectomy As a Treatment for GERD: Pilot Study, 12 Month Experience
William R. Kessler, Gail McNulty, Glen A. Lehman

Results:

• Improvement was noted in the band-ligation with mucosectomy group, with mean HQRL scores improving from 26.2 to 7.4 at 6 months and 7.5 at 12 months with bandligation alone, with mean HQRL scores improving from 27 to 10.6 at 6 months and 6 at 12 months

• The % total time pH < 4 improved from baseline 8.3% to 5.9% with more notable improvement in the band-ligation with mucosectomy group, 8.3% to 4.7% vs. band-ligation alone, 8.4% to 7.0%.

Discussion:

• Band ligation both with and without mucosectomy appears to be safe and effective in improving GERD symptom scores as well as reducing both acid exposure and PPI use in patients with PPI responsive GERD.
GERD symptom score in FH and Esophageal hypersensitivity

**Imipramine and Placebo**

<table>
<thead>
<tr>
<th>Time</th>
<th>Imipramine</th>
<th>Placebo</th>
<th>N=124</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 wk</td>
<td>0.42</td>
<td>30.2</td>
<td></td>
</tr>
<tr>
<td>8 wk</td>
<td>0.98</td>
<td>37.5</td>
<td></td>
</tr>
<tr>
<td>4 wk</td>
<td>0.25</td>
<td>36.4</td>
<td></td>
</tr>
<tr>
<td>8 wk</td>
<td>0.72</td>
<td>45.5</td>
<td></td>
</tr>
</tbody>
</table>

Limsrivilai J and Leelakusolvong S, Abstract Submission for DDW 2014
SF-36

Mean Total SF36

Baseline 1st Visit 2nd Visit

Error Bars: 95% CI

Case

Placebo

0.048 0.26

Limsrivilai J and Leelakusolavong S, Abstract Submission for DDW 2014
METHODS:

• PPI-refractory NERD patients with FSSG ≥ 8 despite therapy with a standard dose of rabeprazole (RPZ, 10 mg/day) for 4 weeks or more

• 242 patients with PPI-refractory NERD randomly assigned to 8 wks of either RPZ (10 mg/o.d.) plus rikkunshito (7.5 g/t.i.d.) (RKT group) or RPZ plus placebo (PL group).

• Assessed symptoms and quality of life (QOL) After the 4-wk and 8-wk treatments

• The primary endpoints were the degree of improvement of FSSG, GSRS and SF-8 score after treatment
Results:

• The FSSG in both the RKT and PL, groups significantly decreased after the treatments.
• The overall GSRS score also decreased significantly.
• There was no significant difference in the degree of improvement of FSSG and GSRS scores between the two groups after the 4-week and 8-week treatments.
• Improvement rates of SF-8 mental component summary (MCS) score were significantly (p<0.05) higher in the RKT group > the PL group after the 4-week treatment.
• Data showed the improvement of acid-related dysmotility (ARD) score (FSSG) in female patients or in geriatric patients (age>65 years) was significantly higher in the RKT group after the 8-week treatment.
• Improvement of SF-8 MCS score indicated that rikkunshito was more effective in patients with a low BMI (<22).

Conclusion:

• Rikkunshito may be useful for improving mental QOL in patients with PPI-refractory NERD.
• Additionally, rikkunshito improved ARD symptoms of GERD in female patients and in geriatric patients.
What is new for GERD?

• New medications:
  – New PPI: Dexlansoprazole, Tenatoprazole
  – P-CAB (Potassium-competitive acid blockers)
  – Drug acting on acid pocket
  – Prokinetic drugs: prucalopride
  – TLESR reducer: GABA_{B} receptor agonists and metabotropic glutamate receptor 5 (mGluR5) antagonists (ADX10059)
  – Esophageal perception: TRPV1
  – TCA and SSRI: TCA and SSRI
  – Herbal medicine: Rikkunshito
What is new for GERD?

• Endoscopic Rx:
  – Stretta
  – LINX system
  – Band ligation with or without mucosectomy
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