Best of “GERD and Barrett’s Esophagus”

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Outline

• Best of GERD
  – PPI risks
  – Diagnostics
  – Pharmacology

• Best of Barrett’s esophagus
PPI Controversy

• Several abstract and clinical sessions dedicated to PPI controversy
  – J Kurlander et al found majority of internists are concerned about PPI and only half feel they are effective at preventing GI bleed
  – Dr. Colin Howell reviewed level of evidence behind claims of adverse risk
PPI Controversy

- *D Kruchko et al, Advocate Lutheran General Hospital, Chicago, IL*

- Searched FDA Adverse Event Reporting System (FAERS)
  - Years 2013-2018
  - 3,989,619 PPI-related
  - Examined proportions of physician and lawyer reports
PPI Controversy

Lawyer reported 9 in 2016 → 974 in 2018
10722% increase!
Novel GERD Diagnostic

- Workup of refractory GERD symptoms can be complicated
  - several options
  - pros/cons to each modality
  - Limitations- variable disease, difficult symptom correlation

- Mucosal Impedance may be surrogate for long-term mucosal changes 2/2 GERD
  - Dilated intracellular spaces decrease impedance

- Through the scope probe re-designed mounted on balloon
Novel GERD Diagnostic

- Balloon provides dynamic measurement along the esophagus, placed during EGD

RESULTS

MI pattern along the esophagus was significantly different ($p<0.01$) between GERD, EoE and normal subjects.
Novel GERD Diagnostic

- Program can provide “probability” of diagnoses like GERD, non-GERD, and EoE
- Will also have function of inputting clinical features (age, sex, symptom) to tailor this probability
Novel GERD Diagnostic

• Ultimate goal = simplify our complicated algorithms in defining cause of persistent symptoms + optimize patient comfort
Novel GERD Medication

- Phase 2b study IW-3718
- Mechanism: Extended release tablet that releases bile acid sequestrant in stomach, rendering bile acids inert
- RCT of pts on once daily PPI with ongoing symptoms >4x a week
Novel GERD Medication

• Inclusion: Pts with esophagitis or (+)wireless pH test with ongoing symptoms
• Intervention: PPI + placebo or PPI + various doses of IW-3718
• Outcomes: symptoms expressed as severity and frequency (modified reflux symptom questionnaire)
Novel GERD Medication

Symptoms Assessed for Severity

Heartburn

Burning Feeling Behind Breastbone / Center of Upper Stomach

Pain Behind Breastbone / Center of Upper Stomach

Least Squares Mean (SE) Change From Baseline

$\Delta = -0.4 \ (P = 0.03)$

$\Delta = -0.5 \ (P = 0.01)$

$\Delta = -0.4 \ (P = 0.03)$

Severity assessed on a 6-point scale: 0 = did not have, 5 = severe. No adjustment for multiplicity.

DDW 2019
Novel GERD Medication

• Adverse events:
  – 42% IW-3718 group, 41% placebo
  – Most common constipation, nausea

• Conclusion: Novel gastric-retentive bile acid sequestrant IW-3718 was efficacious to reduce severity and frequency of GERD symptoms
  – Best dose 1500mg BID
Barrett’s Esophagus

Esomeprazole and aspirin in Barrett’s oesophagus (AspECT): a randomised factorial trial

Janusz A Z Jankowski, John de Caestecker, Sharon B Love, Gavin Reilly, Peter Watson, Scott Sanders, Yeng Ang, Danielle Morris, Pradeep Bhandari, Claire Brooks, Stephen Attwood, Rebecca Harrison, Hugh Barr, Paul Moayyedi, the AspECT Trial Team

Lancet 2018;392: 400-408
Background

• Despite advancing technology for the treatment of Barrett’s, incidence of esophageal cancer continues to rise
• Is there a role for chemoprevention?
### Study Design

- **Inclusion:** 1cm or more of Barrett’s
- **2x2 factorial design**
  - High dose PPI (40mg BID) or Low dose PPI (20mg QD)
  - Aspirin 300mg or no aspirin

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Participants

- 2557 randomized → 20,095 person yrs of f/u
  - Length Barrett’s mostly 2-8cm (80%) - no diff between arms
  - Male 80%, Female 20%

| High dose PPI  | n=577 | Low dose PPI  | n=571 |
| High dose PPI | n=704 | Low dose PPI | n=705 |
| Aspirin       |       | Aspirin       |       |
| No aspirin    |       | No aspirin    |       |

- Outcome: Time to all-cause mortality, esophageal cancer, or HGD
Results

- High dose PPI > Low dose Aspirin = no aspirin
- High dose PPI+Aspirin has the best effect

- NNT 34 ppi, 43 Aspirin
What now?

• Should we add an Aspirin to those already on high dose PPI therapy for symptoms?
• Does this effect get even better? (First 5 years of f/u were non-significant)
Thank you