Welcome to the Virtual Grand Rounds Waiting Room – The educational activity will begin promptly at 12 Noon Eastern.
Welcome to the Virtual Grand Rounds Waiting Room – The educational activity will begin promptly at 12 Noon Eastern.

ACG VIRTUAL NAVIGATING, NETWORKING AND NEGOTIATING YOUR FIRST JOB WORKSHOP

MODERATORS

- Dr. Kara De Felice
- Dr. Shivangi Kothari
- Dr. Judy Trieu

PANELISTS

- Dr. Daniel Raines
- Dr. David Greenwald
- Dr. Harish Gagneja
- Dr. Margaret Schwiesow
- Dr. Amy Oksentenko
- Dr. Mark Pochapin
- Dr. Ripple Sharma
- Dr. Samir Sheh
- Dr. Vivek Kaul

Saturday, January 16, 2021 at 10 am to 1 pm EST

Fellows interested in gaining valuable insight on what he or she faces at the start of their career will find this workshop a must-attend event.

This event is hosted by the ACG Women In GI Committee and supported by Medtronic.
Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.

How to Receive CME and MOC Points

LIVE VIRTUAL GRAND ROUNDS WEBINAR
ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.
MOC QUESTION

If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.

ACG Virtual Grand Rounds

Join us for upcoming Virtual Grand Rounds!

Week 37: Choledochal Cysts: Recognition and Management
Laith H. Jamil, MD, FACG
December 17, 2020 at Noon EDT

PLEASE NOTE: There will be no ACG Virtual Grand Rounds on December 24 or 31 due to the holidays. We will begin again on Thursday, January 7, 2021.

Week 1, 2021: Management of Acute Kidney Injury in Patients with Cirrhosis
Paul Y. Kwo, MD, FACG
January 7, 2021 at Noon EDT

Visit gi.org/ACGVGR to Register
Disclosures:

Speaker:
Ikuo Hirano, MD, FACG
Clinical Trials Support: Celgene/Receptos, Regeneron, Shire/Takeda, Adare, Allakos
Consultant: Adare, Allakos, Arena, AstraZeneca, Celgene/Receptos, Eli Lilly, Esocap, Gossamer Bio, Parexel, Regeneron, Shire/Takeda

Moderator:
Christine Y. Hachem, MD, FACG
Dr. Hachem has no conflicts of interest related to this talk.

Off Label Discussion: Use of topical steroids and PPI

New Therapeutic Options for EoE and EGIDs on the Horizon

Ikuo Hirano, MD, FACG
Gastroenterology Division
Northwestern University Medical School
New Therapeutic Options for Eosinophilic Gastrointestinal Disease

- What’s wrong with symptom-based management in EoE?
- What’s new with the “old” therapeutic options for EoE?
- How do we manage refractory EoE?
- How do we treat EGIDs outside of the esophagus?

Case: 28 yo man with progressive dysphagia. Admission for esophageal tear post endoscopic food disimpaction

EGD on PPI with severe rings. Unable to pass standard endoscope. Biopsies: 94 eos/hpf
Case: 28 yo man with progressive dysphagia. Admission for esophageal tear post endoscopic food disimpaction

EGD on PPI with severe rings. Unable to pass standard endoscope. Biopsies: 94 eos/hpf

Post Fluticasone 880 mcg BID
Continued dysphagia.

Biopsies: 0 eos/hpf
Case: 28 yo man with progressive dysphagia. Admission for esophageal tear post endoscopic food disimpaction

EGD on PPI with severe rings. Unable to pass standard endoscope. Biopsies: 94 eos/hpf

Post Fluticasone 880 mcg BID
Continued dysphagia. Biopsies: 0 eos/hpf
EGD scope not traverse.

EoE Disease Activity: More than Just Counting Eosinophils!

Activity = Inflammation + Tissue Remodeling

Esophageal Eosinophilia

Mucosa/submucosa/muscularis expansion, Subepithelial fibrosis, Increased vascularity, Dysmotility

Treat to Target

**Symptoms**
Resolution of dysphagia without the need to avoid food based on texture

**Histopathology**
Resolution of esophageal eosinophilic inflammation (< 5-15 eos/hpf)

**Endoscopy**
Improvement in inflammatory features and strictures (Diameter > 15 mm)

Hirano, Furuta. Gastroenterology 2020;158:840-851

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**Treat to Target**

<table>
<thead>
<tr>
<th></th>
<th>Complete Response</th>
<th>Complete Non-Response</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom Activity</strong></td>
<td>😊 😖</td>
<td>Minimum</td>
</tr>
<tr>
<td><strong>Histologic Activity</strong></td>
<td>🍔</td>
<td>Minimum</td>
</tr>
<tr>
<td><strong>Endoscopic Activity</strong></td>
<td>😚</td>
<td>Minimum</td>
</tr>
</tbody>
</table>

Hirano, Furuta. Gastroenterology 2020;158:840-851
**EoE Treatment Failure: Medical Therapy**

*Persistent symptoms and EGD signs with normal histology*

- EGD on PPI with severe rings. Unable to pass standard endoscope. Biopsies: 94 eos/hpf

- Post Fluticasone 880 mcg BID x 6 mos. Continued dysphagia. Biopsies: 0 eos/hpf

EGD scope not traverse.

---

**Treat to Target: Symptoms, EGD, Pathology**

- EGD on pantoprazole 40 mg BID; weekly dysphagia. Path 100 eos/hpf

- EGD on fluticasone powder 1 mg BID; No dysphagia; Path 3 eos/hpf
New Therapeutic Options for Eosinophilic Gastrointestinal Disease

- What’s wrong with symptom-based management in EoE?
- What’s new with the “old” therapeutic options for EoE?
- How do we manage refractory EoE?
- How do we treat EGIDs outside of the esophagus?
Initial Therapeutic Choices for EoE

Medications
• Proton pump inhibition
• Swallowed topical corticosteroids
• Clinical trials

Diet therapy
• Elemental diet
• Empiric elimination diet
• Allergy-testing directed diet

Esophageal dilation
• For patients with symptomatic esophageal stricture
• Does not address underlying inflammatory process

2020 ACG Virtual Grand Rounds on Eosinophilic Gastrointestinal Disease

• 6/25/20 – Kathy Peterson - EOE and EGID: Pearls and Pitfalls
• 9/10/20 – Gary Falk has been invited - Management of EoE With Topical steroids: The When and How of Long-Term Management
• 10/22/20 – Nirmala Gonsalves - Special Considerations When Discussing Diet Elimination for EoE
Case Presentation: Patient JS

A 33-year-old man with history of allergic rhinitis and childhood asthma presents with an 8-year history of progressive dysphagia to meats and bread with recent ER food impaction.

The mucosa demonstrated edema, furrows, rings and exudates. Biopsies from the distal esophagus demonstrated 90 eos/HPF.

Case presentation

Which of the following statements regarding choice of initial therapy for EoE is most accurate?

a. Targeted elimination diets based on IgE based allergy testing are more effective than empiric six food elimination diets
b. To be effective in EoE, proton pump inhibitor therapy should be prescribed at double dose administered BID
c. Systemic corticosteroids are more effective at improving eosinophilic inflammation than swallowed topical corticosteroids
d. Systemic adverse effects are common with swallowed topical corticosteroids
e. In clinical guidelines, swallowed topical corticosteroids are the only initial therapeutic option for EoE recommended based on randomized, placebo-controlled clinical trials
Case presentation

Which of the following statements regarding choice of initial therapy for EoE is most accurate?

a. Targeted elimination diets based on IgE based allergy testing are more effective than empiric six food elimination diets
b. To be effective in EoE, proton pump inhibitor therapy should be prescribed at double dose administered BID
c. Systemic corticosteroids are more effective at improving eosinophilic inflammation than swallowed topical corticosteroids
d. Systemic adverse effects are common with swallowed topical corticosteroids
e. In clinical guidelines, swallowed topical corticosteroids are the only initial therapeutic option for EoE recommended based on randomized, placebo-controlled clinical trials

AGA-JTF Guidelines: Management of Eosinophilic Esophagitis

Proton pump inhibition in EoE

Recommendation: In patients with symptomatic esophageal eosinophilia, the AGA/JTF suggests using PPI over no treatment (conditional recommendation, very low quality evidence).

Overall, unweighted histologic response rate (<15 eos/hpf) 42%
Swallowed Topical Corticosteroid Therapy

- 8 double-blind, placebo-controlled RCTs in 437 patients
- Overall, unweighted histologic response rate (<15 eos/hpf): 65%
- Strong recommendation based on moderate quality evidence

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Steroids Events Total</th>
<th>Placebo Events Total</th>
<th>Weight</th>
<th>Risk Ratio M−H, Random, 95% CI</th>
<th>Risk Ratio M−H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alexander 2012</td>
<td>4 21</td>
<td>14 21</td>
<td>9.4%</td>
<td>0.29 [0.11, 0.73]</td>
<td></td>
</tr>
<tr>
<td>Butz 2014</td>
<td>10 28</td>
<td>13 14</td>
<td>14.9%</td>
<td>0.38 [0.23, 0.65]</td>
<td></td>
</tr>
<tr>
<td>Dhillon 2017</td>
<td>32 51</td>
<td>41 42</td>
<td>19.0%</td>
<td>0.64 [0.52, 0.80]</td>
<td></td>
</tr>
<tr>
<td>Dohi 2010</td>
<td>2 15</td>
<td>16 16</td>
<td>7.5%</td>
<td>0.16 [0.06, 0.45]</td>
<td></td>
</tr>
<tr>
<td>Gupta 2015</td>
<td>30 60</td>
<td>19 21</td>
<td>18.2%</td>
<td>0.55 [0.41, 0.74]</td>
<td></td>
</tr>
<tr>
<td>Konikoff 2006</td>
<td>11 21</td>
<td>14 15</td>
<td>16.2%</td>
<td>0.56 [0.37, 0.86]</td>
<td></td>
</tr>
<tr>
<td>Mechle 2016</td>
<td>1 57</td>
<td>13 19</td>
<td>3.3%</td>
<td>0.03 [0.00, 0.18]</td>
<td></td>
</tr>
<tr>
<td>Straumann 2010</td>
<td>5 18</td>
<td>16 18</td>
<td>11.5%</td>
<td>0.31 [0.15, 0.67]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>271 166</td>
<td>100.0%</td>
<td>0.39 [0.26, 0.58]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 95\% 146

Heterogeneity: $I^2 = 0.20, \chi^2 = 31.85, df = 7$ ($p < 0.0001$); $I^2 = 78$

Test for overall effect: $Z = 4.68$ ($p < 0.00001$)

*1-sided.

Budesonide Orodispersable Tablet as Induction Therapy in EoE

- Randomized phase 3 trial in 88 adult patients with active EoE
- 1 mg BOT twice daily (n = 59) vs placebo (n = 29) for 6 weeks
- Primary endpoint: rate of combined clinical-histologic remission at week 6
- Secondary endpoint: rate of histologic remission (<16 eos/mm², <5 eos/hpf) at week 6

\[ P < .0001 \]

\[ P < .0001 \]

\[ P < .0001 \]

Budesonide Oral Suspension in EoE
Randomized Phase 3 Trial

- Randomized, double-blind, placebo-controlled trial of BOS in patients (11 to 55 years) with EoE and dysphagia
- 318 patients randomized 2:1 to 2 mg BOS or placebo twice daily for 12 weeks (BOS, n = 213; placebo, n = 105)
- Co-primary endpoints: histologic (peak eosinophil count ≤ 6 eos/hpf) and dysphagia symptom response after 12 weeks

Histologic Response

Symptom Response

Fluticasone Oral Disintegrating Tablet (APT-1011) Induces Histological Response at Week 12

All APT-1011 dosing regimens showed statistically significant responder rates compared to placebo at Week 12
Choosing an Initial EoE Therapy

<table>
<thead>
<tr>
<th></th>
<th>PPI</th>
<th>Steroids</th>
<th>Diet</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness</td>
<td>30-50%</td>
<td>50-90%</td>
<td>50-70% (SFED)</td>
</tr>
<tr>
<td>Administration</td>
<td>Easy</td>
<td>Cumbersome (with current use of asthma products)</td>
<td>Very difficult (impact on social QoL)</td>
</tr>
<tr>
<td>Safety</td>
<td>Very high</td>
<td>High (long-term under evaluation)</td>
<td>Very high</td>
</tr>
<tr>
<td>Cost</td>
<td>Low</td>
<td>Variable (insurance coverage)</td>
<td>High up-front (Multiple EGDs)</td>
</tr>
</tbody>
</table>

Importance of shared decision making in selection of initial therapy for an individual patient

New Therapeutic Options for Eosinophilic Gastrointestinal Disease

- What’s wrong with symptom-based management in EoE?
- What’s new with the “old” therapeutic options for EoE?
- How do we manage refractory EoE?
- How do we treat EGIDs outside of the esophagus?
Case Presentation

A 48-year-old woman with asthma, allergic rhinitis and 20-year history of progressive dysphagia

Initial ER food impaction 10 years ago. Endoscopy demonstrated a high-grade stricture not traversed. Disimpaction complicated by severe chest pain with pneumomediastinum. Biopsies obtained showed 75 eos/hpf. She was started on fluticasone 880 mcg swallowed BID.

A repeat EGD on Flovent showed a persistent high grade stricture requiring use of a pediatric endoscope. Savary dilation was performed to 36 Fr with severe chest pain requiring hospitalization. Biopsies showed 65 eos/hpf.

Novel Targeted Therapeutics in EoE

2020 AGA/JTF Allergy/Immunology Guidelines: Management of EoE

Biologic Therapies: **Anti-IgE**
Recommendation: In patients with EoE the AGA/JTF suggests against the use of anti-IgE therapy (conditional recommendation; very low-quality evidence)

Biologic Therapies: **Anti-IL-5**
Recommendation: In patients with EoE the AGA/JTF recommends to use anti-IL-5 therapy only in the context of a clinical trial (no recommendation; knowledge gap).

Biologic Therapies: **Anti-IL-13**
Recommendation: In patients with EoE the AGA/JTF recommends to use anti-IL-13 or anti-IL-4 receptor alpha therapy only in the context of a clinical trial (no recommendation; knowledge gap).

Misc Therapies: **Montelukast, Cromolyn, Immunomodulator, Anti-TNF**
Recommendation: In patients with EoE the AGA/JTF suggest using montelukast, cromolyn sodium, immunomodulators, and anti-TNF only in the context of a clinical trial (no recommendation; knowledge gap).

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**RPC4046: Anti-IL-13 Antibody**

- Recombinant, humanised monoclonal (IgG1κ) antibody, highly selective for IL-13
- Inhibits binding of IL-13 to the IL-13Rα1 and IL-13Rα2 receptors
- Administered as a weekly subcutaneous injection
RPC4046 Anti-IL-13 mAb reduced eosinophilic inflammation
Randomized, double blind, placebo-controlled trial; 99 patients; ages 18-65
16-week treatment: RPC4046 (SC)180 mg or 360 mg versus placebo
Primary Endpoint: Change in mean esophageal eosinophil count

Secondary Endpoint: Mean Change in Symptom Score (Daily Symptom Diary)
**Dupilumab EoE Phase 2 Trial**

*Anti-IL-4 receptor α mAB inhibits signaling of IL-4 and IL-13*

- Phase 2, multicenter, double-blind, randomized, placebo-controlled study in patients with active EoE

**Screening period** (1–35 days)

**Randomization** (1:1)  
*N = 47*

**Dupilumab SC 300 mg every week with 600 mg loading dose**  
n = 23

**Placebo**  
n = 24

**12-week treatment period**

16-week follow-up period

**PRO**, patient-reported outcome; SC, subcutaneous. ClinicalTrials.gov Identifier: NCT02379052.

**Dupilumab (Anti-IL4R) reduced dysphagia, esophageal eosinophilia and endoscopic activity in a phase 2 study in adults with EoE**

**Symptoms**

Week 10

- Placebo  
  (n/N = 14/24)
- Dupilumab 300 mg every week  
  (n/N = 17/23)

**Pathology**

Week 12

- Placebo  
  (n/N = 17/24)
- Dupilumab 300 mg every week  
  (n/N = 15/23)

**Endoscopy**

Week 12

- Placebo  
  (n/N = 16/24)
- Dupilumab 300 mg every week  
  (n/N = 18/23)

**LS**=Least Squares; **SDI**=Straumann Dysphagia Index; **EoE**=Eosinophilic Esophagitis Endoscopic Reference Score; **SE**=Standard Error.
Exploratory Endpoint
Dupilumab significantly improved esophageal distensibility plateau at Week 12

LS mean (± SE) % change from baseline in distensibility plateau

Placebo (n/N = 12/24)
Dupilumab 300 mg every week (n/N = 12/23)

P < 0.0001

Hirano Dellon Gastroenterology 2020;158:111–122

A Phase 3, Randomized, 3-Part Study to Investigate the Efficacy and Safety of Dupilumab in Adult and Adolescent Patients With Eosinophilic Esophagitis: Results From Part A

Evan S. Dellon, MD1, Marc E. Rothenberg, MD, PhD2, Margaret H. Collins, MD2, Ikuo Hirano, MD3, Mirna Chehade, MD, MPH4, Albert J. Bredenoord, MD, PhD5, Alfredo J. Lucendo, MD, PhD6, Jonathan M. Spergel, MD, PhD7, Qiong Zhao, PhD8, Jennifer D. Hamilton, PhD8, Bethany Beazley, PhD8, Isabelle Guillemin, PhD8, Siddhesh Kamat, MS8, Leda Mannent, MD9, Marcella Ruddy, MD9, Elizabeth Laws, PhD10, Bolanle Akinlade, MD9, Nikhil Amin, MD9, Allen Radin, MD9, Brad Shumel, MD10, Jennifer Maloney, MD10
*co-last authors

1University of North Carolina School of Medicine, Chapel Hill, NC, USA; 2Cincinnati Children’s Hospital Medical Center and University of Cincinnati College of Medicine, Cincinnati, OH, USA; 3Northwestern University Feinberg School of Medicine, Chicago, IL, USA; 4Mount Sinai Center for Eosinophilic Disorders, Icahn School of Medicine at Mount Sinai, New York, NY, USA; 5Amsterdam University Medical Center, Amsterdam, Netherlands; 6Hospital General de Tomelloso, Tomelloso, Spain; 7Children’s Hospital of Philadelphia, PA, USA; 8Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; 9Sanofi, Chilly-Mazarin, France; 10Sanofi, Bridgewater, NJ, USA
Phase 3 Part A Randomized Trial of Dupilumab in Eosinophilic Esophagitis

Co-primary endpoints: Dupilumab significantly reduced dysphagia and intraepithelial eosinophil counts at Week 24 (n=81)

![Graph showing absolute change in DSQ total score from baseline and proportion of patients achieving peak esophageal intraepithelial eosinophil counts of ≤6 eos/hpf at Week 24.](image)

**Absolute change in DSQ total score from baseline**

<table>
<thead>
<tr>
<th>Week</th>
<th>Placebo</th>
<th>Dupilumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>39/0</td>
<td>42/0</td>
</tr>
<tr>
<td>1</td>
<td>37/2</td>
<td>42/0</td>
</tr>
<tr>
<td>2</td>
<td>36/4</td>
<td>40/2</td>
</tr>
<tr>
<td>3</td>
<td>34/5</td>
<td>41/1</td>
</tr>
<tr>
<td>4</td>
<td>33/6</td>
<td>40/2</td>
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<tr>
<td>5</td>
<td>33/6</td>
<td>40/2</td>
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<tr>
<td>6</td>
<td>32/9</td>
<td>40/2</td>
</tr>
<tr>
<td>7</td>
<td>32/10</td>
<td>38/4</td>
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<tr>
<td>8</td>
<td>32/10</td>
<td>38/4</td>
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<tr>
<td>9</td>
<td>32/10</td>
<td>38/4</td>
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<td>38/4</td>
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<td>11</td>
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<td>23</td>
<td>36/4</td>
<td>40/2</td>
</tr>
<tr>
<td>24</td>
<td>36/4</td>
<td>40/2</td>
</tr>
</tbody>
</table>

**Responders (%)**

- Placebo: 70%
- Dupilumab: 59.5%

**Number of patients/imputed patients**

- Placebo: 39/0
- Dupilumab: 42/0

*P < 0.05, **P < 0.01, ***P < 0.001.

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New Therapeutic Options for Eosinophilic Gastrointestinal Disease

- What’s wrong with symptom-based management in EoE?
- What’s new with the “old” therapeutic options for EoE?
- How do we manage refractory EoE?
- How do we treat EGIDs outside of the esophagus?
Eosinophilic Gastroenteritis

Eosinophilic gastroenteritis (EGE) is a rare, inflammatory condition of the stomach and/or intestine characterized by symptoms/signs referable to GI inflammation combined with histologic features of eosinophil-predominant mucosal inflammation.

Therapeutic Choices for Eosinophilic Gastroenteritis

Medications

- **Systemic corticosteroids**
- Proton pump inhibition
- Swallowed topical corticosteroids (budesonide)
- Antihistamine (ketotifen)
- Cromolyn sodium
- Immunomodulators (azathioprine)
- Omalizumab (Anti-IgE) (Foroughi et al. J Allergy Clin Immunol 2007;120:594-601)
- Mepolizumab (Anti-IL-5) (Prussin J Allergy Clin Immunol 2013; 11 abs)
- Vedolizumab (Anti-α4β7 integrin)

Diet therapy
Prospective Study of **Elemental diet In Eosinophilic gastroenteritis Nutrition Trial (ELEMENT)**

- **15 adults (18-65 years) with histologically active EG/EGE (≥ 30 eos/hpf) in stomach and/or duodenum**
- GI symptoms ≤ 1 month prior to enrollment
- Treated with elemental diet for 6 weeks
- **Primary endpoint:** % of participants with complete histologic remission at end of treatment

**Histologic Improvement Post-Diet**

- Stomach: P=0.001
- Duodenum: P=0.002


Benralizumab (Anti-IL5Rα) for PDGFRA-Negative Hypereosinophilic Syndrome

- **Randomized, double-blind, placebo-controlled, phase 2 trial**
- **20 patients with HES; Primary endpoint:** ≥50% reduction in peripheral eosinophil count achieved (90% active vs 30% placebo) at week 12
- **Gastrointestinal mucosal biopsies < 1 eos/hpf in 7/7 patients with GI involvement during OLE**

Anti-Siglec-8 Antibody for Eosinophilic Gastritis and Duodenitis

Evan S. Dellon, M.D., M.P.H., Kathryn A. Peterson, M.D., Joseph A. Murray, M.D., Gary W. Falk, M.D., Nirmala Gonsalves, M.D., Mima Chehade, M.D., M.P.H., Robert M. Genta, M.D., John Leung, M.D., Paneez Khoury, M.D., Amy D. Klon, M.D., Sabine Hazan, M.D., Michael Vaezi, M.D., Adam C. Bledsoe, M.D., Sandy R. Durran, M.D., Chao Wang, Ph.D., Camilla Shaw, B.S.N., R.N., Alan T. Chang, B.S., Bhupinder Singh, M.D., Arnol P. Kamboj, M.D., Henrik S. Rasmussen, M.D., Ph.D., Marc E. Rothenberg, M.D., Ph.D., and Ikuo Hirano, M.D.

- Randomized, double-blind, placebo-controlled trial
- 65 adults with moderately severe UGI symptoms and active histology (gastric ≥30 eos/hpf in 5 hpf; duodenal ≥30 eos/hpf in 3 hpf)
- Anti-Siglec-8 mAb at 2 doses (1 mg/kg, 3 mg/kg) vs placebo
- 4 monthly doses with endpoints assessed 2 weeks after last dose

Table 2. Primary and Secondary Efficacy End Points.

<table>
<thead>
<tr>
<th>End Point</th>
<th>Low-Dose AK002 (N=22)</th>
<th>High-Dose AK002 (N=21)</th>
<th>Combined AK002 (N=43)</th>
<th>Placebo (N=22)</th>
<th>Low-Dose AK002 (N=19)</th>
<th>High-Dose AK002 (N=20)</th>
<th>Combined AK002 (N=39)</th>
<th>Placebo (N=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean change in gastrointestinal eosinophil count (95% CI) — %</td>
<td>-79 (-95 to -59)</td>
<td>-92 (-100 to -81)</td>
<td>-86 (-94 to -71)</td>
<td>9 (-15 to 31)</td>
<td>-92 (-100 to -70)</td>
<td>-97 (-100 to -89)</td>
<td>-92 (-100 to -83)</td>
<td>10 (-14 to 40)</td>
</tr>
<tr>
<td>Least-squares mean difference from placebo</td>
<td>-95 (-122 to -68)</td>
<td>-102 (-128 to -76)</td>
<td>-98 (-121 to -76)</td>
<td>-98 (-130 to -77)</td>
<td>-103 (-133 to -81)</td>
<td>-107 (-100 to -83)</td>
<td>-105 (-128 to -83)</td>
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<tr>
<td>P value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<td>&lt;0.001</td>
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Anti-Siglec-8 Antibody for Eosinophilic Gastritis and Duodenitis: Secondary Endpoint: Symptom Efficacy

![Graph showing change in total symptom score over time for different doses and placebo.](image)

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Weeks</th>
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<tbody>
<tr>
<td>Placebo</td>
<td>20</td>
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<td>20</td>
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</table>


Pharmaceutical pipeline for eosinophilic GI disease in 2020

*More products moving forward than in past decade*

![Diagram showing timeline of drug development phases for various medications.](image)

Drug Name
- Budesonide oral suspension
- Budesonide orodispersible tablet
- Fiuticasone ODT
- Mepolizumab
- Reslizumab
- Beznalizumab
- QAX576
- RPC4046
- Dupilumab
- Omalizumab
- OC000459
- AK002
- Losartan

Why consider biologic therapy?

- Corticosteroid-refractory patients
- Avoid possible long-term adverse effects of corticosteroids (esp for eosinophilic gastroenteritis)
- Concept of therapy targeting specific allergic pathways
- Systemic treatment of multiple forms of atopy
- Potential benefits for esophageal remodeling as well as inflammation
- Potential benefits of intermittent rather than daily therapy

Novel Therapeutics on the Horizon for EGID

- Therapeutic goals of EoE therapy include symptoms, pathology, and remodeling consequences
- Regulatory approval of formulations of swallowed topical corticosteroids optimized for esophageal delivery will improve the management of EoE
- Emerging data on biologic therapies for EoE and EGE are promising
Questions?

Speaker: Ikuo Hirano, MD, FACG

Moderator: Christine Y. Hachem, MD, FACG

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