Access GI Expertise, Educational Resources and Support for You and Your Patients

A Free ACG Member Benefit Designed to Help You and Your Patients!
Learn More and Join Today at GIONDEMAND.COM

ACG 2022
OCTOBER 21–26, 2022 | CHARLOTTE, NC

REGISTRATION IS OPEN!
REGISTER ONLINE: ACGMEETINGS.GI.ORG
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, 2022 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, 2023 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 41 – Thursday, October 13, 2022
C. diff Infection Treatment: What is New?
Faculty: Monika Fischer, MD, MS, FACG
Moderator: Colleen R. Kelly, MD, FACG
Thursday, October 13th at Noon Eastern and NEW! 8pm Eastern!

There will be no ACG Virtual Grand Rounds October 20th or 27th. Join us in Charlotte, NC for ACG 2022 – Annual Scientific Meeting & Postgraduate Course – October 21 – 26, 2022

Week 44 – Thursday, November 3, 2022
Obscure Bleeding: Are There Options After Endoscopy?
Faculty: Kathy P. Bull-Henry, MD, MBA, FACG
Moderator: John R. Saltzman, MD, FACG
Thursday, November 3rd at Noon Eastern and NEW! 8pm Eastern!

Visit gi.org/ACGVGR to Register
Disclosures

Nimish Vakil, MD, FACP
AstraZeneca: Speaker
Isothrive: Consultant, Advisory Board
Merck: Author
Phathom: Consultant, Advisory Board
Redhill Biopharma: Consultant, Advisory Board

Nalini M. Guda, MD, FACP
Boston Scientific Corporation: Consultant
Hemostasis LLC: Consultant
Lupin, India: Honorarium for non-product related presentations
Zydus, India: Honorarium for non-product related presentations

*All of the relevant financial relationships listed for these individuals have been mitigated
Refactory, Recurrent Ulcer Disease and Persistent Gastritis: New Management Strategies

Nimish Vakil MD FACG
University of Wisconsin School of Medicine and Public Health
Madison WI

Definitions

• A refractory peptic ulcer is defined as an endoscopically proven ulcer greater than 5 mm in diameter that does not heal after 8 to 12 weeks of treatment with a proton pump inhibitor.
• A recurrent ulcer is one that recurs after it has healed completely
• A giant gastric ulcer is one that is larger than 3 cm in diameter
• Atrophic gastritis is defined as the loss of gastric glands with or without intestinal metaplasia in the setting of chronic inflammation
Clean based gastric ulcer not healed at 8 weeks

Questions to ask:

- Were the edges of the ulcer biopsied?
- Was testing for H pylori performed and was it treated?
- Were NSAIDs and aspirin stopped?
- Is the ulcer smaller than before?

90% of refractory ulcers will heal after an additional 8 weeks of twice daily PPI therapy

Vakil N. Refractory and recurrent peptic ulcers
Uptodate accessed July 4, 2002

https://www.uptodate.com
Still Unhealed: Consider other drugs known to cause peptic ulcer disease

- Corticosteroids and bleeding peptic ulcer
  - Recent study from the Taiwan National Health Insurance Database:
    - Hazard ratio
      \[
      \frac{1.37 (95\% \text{ CI}: 1.12-1.68, P = 0.003)}{1.66 (95\% \text{ CI}: 1.38-2.00, P < 0.001)} \text{ for the 7-day window,} \\
      \frac{1.84 (95\% \text{ CI}: 1.57-2.16, P < 0.001)}{1.84 (95\% \text{ CI}: 1.57-2.16, P < 0.001)} \text{ for the 14-day window and} \\
      \frac{1.84 (95\% \text{ CI}: 1.57-2.16, P < 0.001)}{1.84 (95\% \text{ CI}: 1.57-2.16, P < 0.001)} \text{ for the 28-day window.}
      \]
  - SSRIs, Spironolactone, Alendronate and clopidogrel
    - Confounded by concomitant aspirin and NSAID use

Surreptitious NSAID use is a major cause of refractory ulcer

- Consecutive patients undergoing esophagogastroduodenoscopy with ulcers
- No exposure to antibiotics, or antulcer therapy within the past 6 months.
- Before endoscopy, patients were interviewed regarding the use of NSAID or aspirin.
- During endoscopy, antral biopsies were obtained for urease test and histology.
- Serum thromboxane B2 levels were compared with those of healthy volunteers.

- 600 patients with ulcers
  - *Helicobacter pylori* negative in 212 patients (35.3%)
  - *H. pylori* negative ulcers were related to NSAID use in 68.9% of cases.
  - On the basis of serum thromboxane B2 levels, 30.8% of the patients with "non-*H. pylori* non-NSAID"
    - were considered to have consumed NSAIDs.
Lack of Adherence with H. pylori treatment due to side effects causes non-healing/recurrence

250 patients at tertiary hospitals in Asia
Resistant H. pylori infection is an important cause for failed eradication in the USA

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Pooled prevalence</th>
<th>95% Confidence intervals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarithromycin</td>
<td>29.5 %</td>
<td>25.4-34.5 %</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>38.7 %</td>
<td>31.4-46.6 %</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0.85 %</td>
<td>0.3-2.8 %</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>34%</td>
<td>23.9-45.8 %</td>
</tr>
</tbody>
</table>

Ho J Am J Gastroenterol 2022;117:1221

Rifabutin resistance

Table 2. Susceptibility Testing Results for Helicobacter pylori at Baseline

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Group</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin MIC</td>
<td>168 (16.5%)</td>
<td>326 (17)</td>
</tr>
<tr>
<td>Clarithromycin MIC</td>
<td>171 (17)</td>
<td>341 (17)</td>
</tr>
<tr>
<td>Metronidazole MIC</td>
<td>171 (17)</td>
<td>341 (17)</td>
</tr>
<tr>
<td>Rifabutin MIC</td>
<td>171 (17)</td>
<td>341 (17)</td>
</tr>
</tbody>
</table>

First and second-line treatment regimens for H pylori

<table>
<thead>
<tr>
<th>Drug combinations</th>
<th>Regimen</th>
<th>Recommended duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple therapy</td>
<td>PPI plus amoxicillin plus clarithromycin</td>
<td>Double dose of PPI every 12 h, 1000 mg amoxicillin every 12 h, 500 mg clarithromycin every 12 h</td>
</tr>
<tr>
<td>Quadruple non-bismuth-based concurrent therapy</td>
<td>PPI plus amoxicillin plus clarithromycin plus metronidazole</td>
<td>Standard dose of PPI every 12 h, 1000 mg amoxicillin every 12 h, 500 mg clarithromycin every 12 h, 500 mg metronidazole every 12 h</td>
</tr>
<tr>
<td>Bismuth-based quadruple therapy</td>
<td>PPI plus bismuth plus clarithromycin plus metronidazole</td>
<td>Standard dose of PPI every 12 h, 120 mg bismuth subcitrate every 6 h, 500 mg metronidazole every 12 h</td>
</tr>
<tr>
<td>Fluoroquinolone-based triple therapy</td>
<td>PPI plus amoxicillin plus levofloxacin with or without bismuth</td>
<td>Standard dose of PPI every 12 h, 1000 mg amoxicillin every 12 h, 500 mg levofloxacin every 24 h, 240 mg bismuth every 12 h</td>
</tr>
<tr>
<td>Ribavirin-based triple therapy</td>
<td>PPI plus amoxicillin plus ribavirin</td>
<td>Standard dose of PPI every 12 h, 1000 mg amoxicillin every 12 h, 125 mg ribavirin every 12 h</td>
</tr>
</tbody>
</table>

Lancet 2017; 390: 613–24

Inadequate Treatment Regimens are Widely Prescribed

- 68.6% of GIs and 79.8% of FPs or GPs selected clarithromycin, amoxicillin, and PPI triple therapy as their ideal first-line treatment.
- Clarithromycin-based regimens also comprised 50% of those selected for second-line treatment.
Inadequate Treatment Regimens are Widely Prescribed

- 24% of physicians would repeat clarithromycin triple therapy after PrevPac
- 43% would follow nonbranded clarithromycin triple therapy with another clarithromycin-based therapy (31% clarithromycin, metronidazole, and any PPI and 12% PrevPac)

Potassium competitive acid blockers and acid inhibition

- P-CAB
- PPI
PCAB based dual and triple therapy: recently approved

<table>
<thead>
<tr>
<th>Patients with <em>H. pylori</em> infection who did not have a clarithromycin or amoxicillin resistant strain at baseline</th>
<th>VOQUEZNA TRIPLE PAK % (n)</th>
<th>VOQUEZNA DUAL PAK % (n)</th>
<th>LAC % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>84.7 (222)</td>
<td>78.5 (208)</td>
<td>78.8 (201)</td>
<td></td>
</tr>
</tbody>
</table>

| Treatment Difference from LAC (95% CI) | 5.9b (-0.8, 12.6) |

| All randomized patients with *H. pylori* infection at baseline | 80.8 (273) | 77.2 (250) | 68.5 (226) |

| Treatment Difference from LAC (95% CI) | 12.3d (5.7, 18.8) |

Voquenaza package insert

Rifabutin triple therapy

<table>
<thead>
<tr>
<th>Analysis</th>
<th>RHB-105 Group</th>
<th>Active Comparator Group</th>
<th>Treatment Difference</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITT analysis on the primary efficacy end point†</td>
<td>83.8 (191/228)</td>
<td>57.7 (131/227)</td>
<td>26.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>95% CI, %</td>
<td>78.4 to 88.0</td>
<td>51.2 to 64.0</td>
<td>18.0 to 34.1</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antimicrobial Resistance Status at Baseline</th>
<th>Responders*</th>
<th>Treatment Difference†</th>
<th>P Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>RHB-105 Group (n = 228)</td>
<td>56.1 (55/98)</td>
<td>25.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>95% CI, %</td>
<td>46.3 to 65.3</td>
<td>12.2 to 37.9</td>
<td></td>
</tr>
</tbody>
</table>

Ann Intern Med. 2020;172:795-802
Test for Cure after H. pylori eradication

- All current guidelines recommend testing for cure after H. pylori treatment
- Test 1 month after completion of eradication therapy
- Patient should not be on acid inhibitors or antibiotics
  - Most common cause for a false negative test:
    - Continued use of PPIs
    - Test done too soon after completing treatment

Persistent Ulcer, non-specific pathology: Consider Idiopathic acid hypersecretion and Zollinger-Ellison syndrome

Suspect Zollinger Ellison Syndrome when
Diarrhea is a symptom
There is a family history of gastrinoma or MEN type 1
Gastric folds are hypertrophied at endoscopy
Gastrin levels are >1000 pg/ml
Multiple ulcers are present
Basal acid output >15mEq/hr
Hypercalcemia and high PTH levels suggest MEN 1

Suspect Idiopathic acid hypersecretion Syndrome when
Diarrhea can be a symptom
Gastrin levels are <100 pg/ml
Basal acid output >10mEq/hr
Idiopathic ulcer disease unrelated to H pylori, NSAIDs or gastric hypersecretion

- Described worldwide
- Elderly, white males in western countries
- Propensity for recurrence (35%)
- Recurrent hemorrhage is high in patients presenting with bleeding (13.5%)
- Smoking and stress may be factors
- High incidence soon after earthquakes in Japan

The Korean Journal of Internal Medicine Vol. 30, No. 5, September 2015

Cameron ulcers

- Within a large hiatus hernia; 10–20 % for hiatal hernias larger than 5cm; acute GI bleeding or chronic anemia; older women most affected

Checkpoint inhibitor ulcers: pembrolizumab

A monoclonal antibody targeting programmed cell death (PD-1) receptor on T cells
Used in melanoma, head and neck, non small cell lung cancer

Prednisone 1mg/kg/day for 4 weeks with pantoprazole and discontinuation of pembrolizumab

Ulcerated raised lesions: multiple ulcers, thickened folds: lymphoma


Ulcerated raised lesions: malignancy

• An ulcerated mass protruding into the lumen
• Folds surrounding the ulcer crater that are nodular, clubbed, fused, or stop short of the ulcer margin
• Overhanging, irregular, or thickened ulcer margins

Rare causes: Anisakiasis

*Anisakis pegreffii* can cause life-threatening allergic reactions and abdominal pain
Sushi, ceviche, raw marinated anchovies

Giant gastric ulcers

- A giant peptic ulcer is an ulcer larger than 3 cm in size.
Mortality
Malignant: 30 day: 12%, 12 month: 62%
Benign: 30 day: 10%, 12 month: 22%

Limitations
Retrospective study

Summary: Management of refractory persistent ulcer

Gastric Ulcer at 8 weeks after treatment

Healed

Confirm H pylori eradication

Discuss future NSAID use & prophylaxis if relevant

Abnormal Pathology

Manage based on diagnosis

Persistent ulcer at 8 weeks

Re-biopsy from edges of ulcer

No diagnostic pathology

Stop smoking

Confirm discontinuation of NSAIDs

Confirm adherence with treatment

Extend course of twice daily PPI for 8 weeks

Persistent ulcer at 16 weeks

Re-biopsy from edges of ulcer

No diagnostic pathology

Serum Gastrin and Calcium level

Gastrin >1000 pg/ml

Tests for gastrinoma

Low Gastrin & Calcium

Tests for MEN syndrome

Normal Gastrin <100 pg/ml

Idiopathic gastric hypersecretion

No diagnostic pathology

American College of Gastroenterology
Atrophic gastritis and gastric cancer

- Helicobacter pylori
- Acute gastritis
- Chronic gastritis
- Atrophic gastritis
- Intestinal metaplasia
- Gastritis with lymphoid follicular hyperplasia
- Gastritis with lymphoid follicular hyperplasia
- Duodenal ulcer
- Gastric ulcer
- Low-grade gastric MALT lymphoma
- Gastric cancer

Development of Gastric cancer

Baseline N = 1246 HP+ with Relative risk gastric cancer n=36

- Atrophy moderate 657 2.7% 1.7 (0.8-3.7)
- Atrophy severe 208 7.2% 4.9 (2.8-19.2)
- Intestinal metaplasia 464 6.5% 6.4 (2.6,16.1)

Histology Improves With H pylori Eradication

- 587 patients from China randomized to OAC (n=295) or to placebo (n=292)
- 226 patients with eradication were compared with 245 patients who remained infected at 1 year
- At 1 year, gastritis had improved significantly with eradication but intestinal metaplasia was not significantly different

OAC=omeprazole, amoxicillin, and clarithromycin.

Preventing Gastric Cancer: China

2423 healthy persons were recruited in 1994 from Changle County, China
Patients were then randomized eradication treatment or placebo
7 cancers (0.86%) in the treatment group and 11 (1.35%) in the placebo group (p=0.33)
Treatment of H. pylori was associated with a significant (P = 0.02) reduction in the incidence of gastric cancer in subjects without premalignant lesions but not in patients with pre-malignant lesions

Biopsy protocol and surveillance in suspected atrophic gastritis and intestinal metaplasia

- 5 biopsies: 2 antral (greater and lesser curve 2 cm from pylorus), 1 gastric incisura, corpus lesser curve 4 cm from incisura and corpus-mid 8 cm from the cardia
- No consensus and no clear evidence to guide decision-making regarding surveillance
- Current guidelines recommend repeat endoscopy and biopsy every 3 years
Summary: Atrophic gastritis

- Be alert for subtle signs of atrophy
- Test for H pylori including histology and immunostain (organisms may be few)
- Treating H pylori helps some but not all patients with regard to cancer progression
- Repeat endoscopy and biopsy every 3 years

Questions and Answers

Nimish Vakil, MD, FACG

Nalini M. Guda, MD, FACG
CONNECT AND COLLABORATE IN GI

ACG GI Circle
Connect and collaborate within GI

ACG & CCF IBD Circle
ACG Hepatology Circle
ACG Functional GI Health and Nutrition Circle
ACG Women in GI Circle

ACG’s Online Professional Networking Communities
LOGIN OR SIGN-UP NOW AT: acg-gi-circle.within3.com