



GI ON DEMAND
— GastroGIF —

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

- Registered Dietitians
- GI Psychologists
- GI Sub-Specialists
- APP Patient GI
- Genetic Testing
- Telehealth Features
- Education Resources

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

1



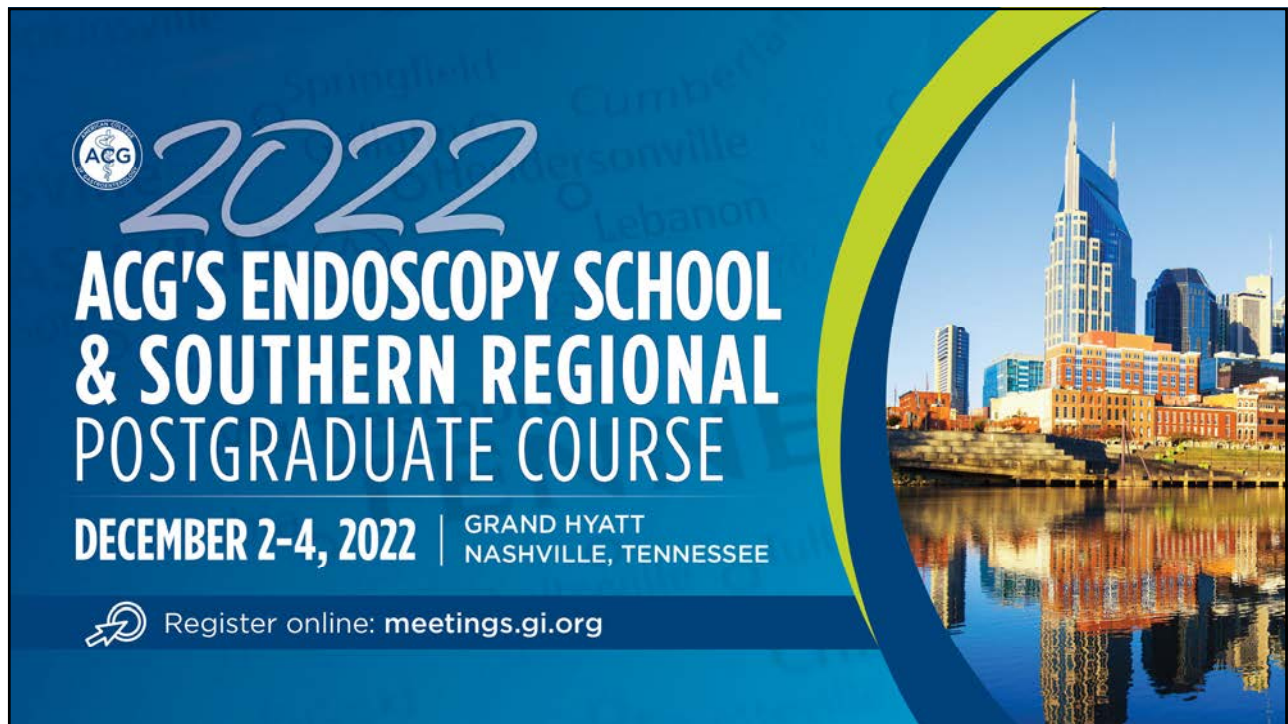
ACG ²⁰²²
OCTOBER 21-26, 2022 | CHARLOTTE, NC


**REGISTRATION
IS OPEN!**

REGISTER ONLINE:
[ACGMEETINGS.GI.ORG](https://acgmeetings.gi.org)

ACG THE AMERICAN COLLEGE OF GASTROENTEROLOGY

2



 **2022**
**ACG'S ENDOSCOPY SCHOOL
& SOUTHERN REGIONAL
POSTGRADUATE COURSE**
DECEMBER 2-4, 2022 | GRAND HYATT
NASHVILLE, TENNESSEE
Register online: meetings.gi.org

The banner features a dark blue background with a large, stylized '2022' in white. To the right, a circular inset shows a cityscape with a prominent skyscraper (the AT&T Building) reflected in water. The ACG logo is in the top left corner.

3



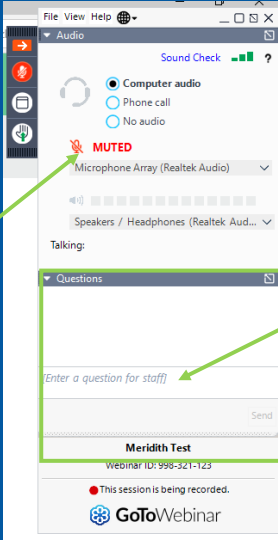
2023 **ACG HEPATOLOGY
SCHOOL & WESTERN
REGIONAL POSTGRADUATE COURSE**
JANUARY 27-29, 2023 | CAESARS PALACE
LAS VEGAS, NEVADA
Register online: meetings.gi.org

The banner has a white background with a large, stylized '2023' in orange. To the right, a circular inset shows a cityscape with a prominent tower (the Flamingo Las Vegas) and a fountain. The ACG logo is in the bottom left corner.

4

ACG Virtual Grand Rounds universe.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.

Meridith Test
Webinar ID: 998-321-123
This session is being recorded.
GoToWebinar

5

ACG Virtual Grand Rounds universe.gi.org

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.

6

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.

7

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, FACP

Moderator: Colleen R. Kelly, MD, FACP

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, FACP

Moderator: John R. Saltzman, MD, FACP

Thursday, November 3rd at Noon Eastern and **NEW! 8pm Eastern!**



Visit gi.org/ACGVGR to Register

8

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

REGISTRATION IS OPEN!

REGISTER ONLINE:
[ACGMEETINGS.GI.ORG](https://acgmeetings.gi.org)

ACG THE AMERICAN COLLEGE OF GASTROENTEROLOGY

9

ACG Virtual Grand Rounds universe.gi.org

Disclosures



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



Nalini M. Guda, MD, FACG
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

10

Refractory, Recurrent Ulcer Disease and Persistent Gastritis: New Management Strategies



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

11

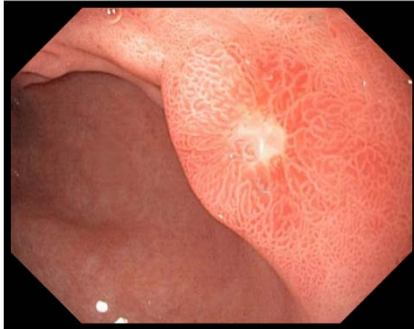
Definitions

- 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

12

Clean based gastric ulcer not healed at 8 weeks

Gastric ulcer



Note the clean white base in the ulcer crater with no evidence of active bleeding.

Courtesy of Nimish Vakil, MD.

UpToDate®

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

Uptodate.com accessed July 4, 2002

13

Causes of refractory gastric/duodenal ulcers

Persisting <i>H. pylori</i> infection
Poor compliance with treatment
Resistant organism
Inadequate <i>H. pylori</i> regimen
Unrecognized <i>H. pylori</i> infection:
False negative <i>H. pylori</i> testing
Skipped or inadequate testing
Ulcers related to nonsteroidal anti-inflammatory drugs (NSAIDs)
Continued NSAID use
Undiscovered NSAID use
Poor response to co-therapy with a proton pump inhibitor (PPI) or histamine 2 receptor antagonist (H2RA)
Other mechanisms
Impaired healing:
Cigarette smoking
Inadequate inhibition of acid secretion:
Poor compliance with treatment
Pharmacologic resistance or tolerance to H2RAs
Pharmacologic resistance to PPIs
Rapid metabolism (inactivation) of PPIs
Hypersecretory states:
Gastrinoma
Antral G cell hyperfunction
Idiopathic hypersecretory duodenal ulcer
Co-therapies:
Glucocorticoids (especially when given with NSAIDs)
Cytotoxic drugs
Other drugs, such as methamphetamine or cocaine use
Uncommon causes:
Cancer
Crohn disease
Infections other than <i>H. pylori</i>
Eosinophilic, inflammatory, infiltrative conditions, mesenteric ischemia

H. pylori: Helicobacter pylori.

UpToDate®

Vakil N. Refractory and recurrent peptic ulcers
 Uptodate accessed July 4, 2022
<https://www.uptodate.com>

14

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
 - 1.37 (95% CI: 1.12-1.68, P = 0.003) for the 7-day window,
 - 1.66 (95% CI: 1.38-2.00, P < 0.001) for the 14-day window and
 - 1.84 (95% CI: 1.57-2.16, P < 0.001) for the 28-day window.
- SSRIs, Spironolactone, Alendronate and clopidogrel
 - Confounded by concomitant aspirin and NSAID use

Aliment Pharmacol Ther 2015 Sep;42(5):599-606.

15

Surreptitious NSAID use is a major cause of refractory ulcer

- Consecutive patients undergoing esophagogastroduodenoscopy with ulcers
- No exposure to antibiotics, or antiulcer 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.

J Clin Gastroenterol 2006 Oct;40(9):795-800.

16

Causes of recurrent peptic ulcer disease

Persisting <i>H. pylori</i> infection
Poor compliance with treatment
Resistant organism
Inadequate <i>H. pylori</i> regimen
Unrecognized <i>H. pylori</i> infection:
False negative <i>H. pylori</i> testing
Skipped or inadequate testing
Ulcers related to nonsteroidal anti-inflammatory drugs (NSAIDs)
Continued NSAID use
Undiscovered NSAID use
Poor response to co-therapy with a proton pump inhibitor (PPI) or histamine 2 receptor antagonist (H2RA)
Other mechanisms
Hypersecretory states:
Gastrinoma
Antral G cell hyperfunction
Idiopathic hypersecretory duodenal ulcer
Co-therapies:
Glucocorticoids (especially when given with NSAIDs)
Cytotoxic drugs
Other drugs, such as methamphetamine or cocaine use
Uncommon causes:
Cancer
Crohn disease
Infections other than <i>H. pylori</i>
Eosinophilic, inflammatory, infiltrative conditions

H. pylori: *Helicobacter pylori*.

UpToDate®

Vakil N. Refractory and recurrent peptic ulcers
 Uptodate accessed July 4, 2022
<https://www.uptodate.com>

17

Lack of Adherence with *H. pylori* treatment due to side effects causes non-healing/recurrence

250 patients at tertiary hospitals in Asia

Adverse effect	Treatment compliance		Total	p-Value	Odds ratio with 95% confidence interval
	Yes	No			
No	114 (99.1%)	1 (0.9%)	115 (46.0%)	<0.001	62.9 (8.5-464.7)
Yes	87 (64.4%)	48 (35.6%)	135 (54.0%)		
Total	201 (80.4%)	49 (19.6%)	250		

TABLE 2: Association of adverse effects with treatment compliance

PPI: proton pump inhibitor

Cureus 2021 May 6;13(5):e14872.
 doi: 10.7759/cureus.14872.

18

Resistant *H. pylori* infection is an important cause for failed eradication in the USA

Antibiotic	Pooled prevalence	95% Confidence intervals
Clarithromycin	29.5 %	25-34.5 %
Metronidazole	38.7 %	31.4-46.6 %
Tetracycline	0.85 %	0.3-2.8 %
Levofloxacin	34%	23.9-45.8 %

Ho J Am J Gastroenterol 2022;117:1221

19

Rifabutin resistance

Table 2. Susceptibility Testing Results for *Helicobacter pylori* at Baseline

Antibiotic	RHB-105 Group	Active Comparator Group	Overall
Amoxicillin MIC			
Participants with MIC data*, n	174	171	345
≤0.125 µg/mL (susceptible), n (%)	161 (92.5)	162 (94.7)	323 (93.6)
>0.125 µg/mL (resistant), n (%)	13 (7.5)	9 (5.3)	22 (6.4)
Clarithromycin MIC			
Participants with MIC data*, n	174	171	345
≤0.25 µg/mL (susceptible), n (%)	149 (85.6)	136 (79.5)	285 (82.8)
0.5 µg/mL (intermediate), n (%)	0	0	0
>0.5 µg/mL (resistant), n (%)	25 (14.4)	35 (20.5)	60 (17.4)
Metronidazole MIC			
Participants with MIC data*, n	174	170	344
≤8 µg/mL (susceptible), n (%)	103 (59.2)	91 (53.5)	194 (56.4)
>8 µg/mL (resistant), n (%)	71 (40.8)	79 (46.5)	150 (43.6)
Rifabutin MIC			
Participants with MIC data*, n	174	171	345
≤0.125 µg/mL (susceptible), n (%)	174 (100)	171 (100)	345 (100)
>0.125 µg/mL (resistant), n (%)	0	0	0

Ann Intern Med. 2020;172:795-802.

20

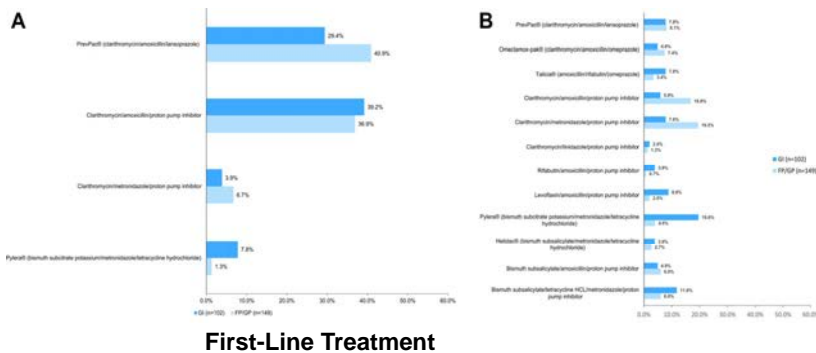
First and second-line treatment regimens for H pylori

	Drug combinations	Regimen	Recommended duration
Triple therapy	PPI plus amoxicillin* plus clarithromycin	Double dose† of PPI every 12 h 1000 mg amoxicillin every 12 h 500 mg clarithromycin every 12 h	14 days
Quadruple non-bismuth-based concomitant therapy	PPI plus amoxicillin plus clarithromycin plus metronidazole	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	14 days
Bismuth-based quadruple therapy	PPI plus bismuth subcitrate plus tetracycline plus metronidazole	Standard dose of PPI every 12 h 120 mg bismuth subcitrate every 6 h 500 mg tetracycline every 6 h 500 mg metronidazole every 8 h	14 days
Fluoroquinolone-based triple therapy‡	PPI plus amoxicillin plus levofloxacin with or without bismuth	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	14 days
Rifabutin-based triple therapy§	PPI plus amoxicillin plus rifabutin	Standard dose of PPI every 12 h 1000 mg amoxicillin every 12 h 150 mg rifabutin every 12 h	10 days

Lancet 2017; 390: 613–24

21

Inadequate Treatment Regimens are Widely Prescribed

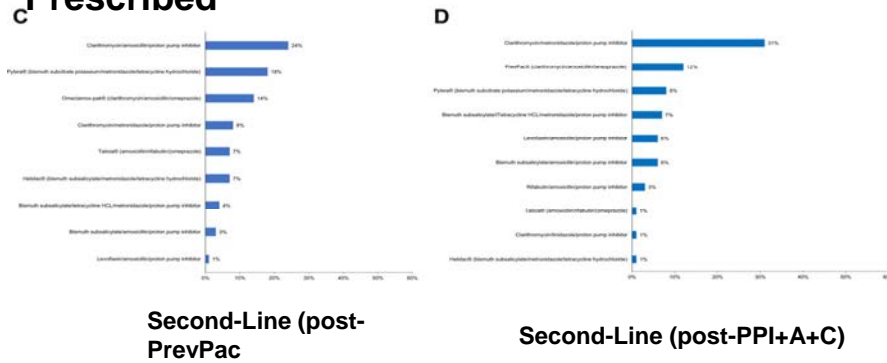


- 68.6% of GIs and 79.8% of FPs or GPs selected clarithromycin, amoxicillin, and PPI triple therapy as their ideal first-line treatment.
- Clarithromycin-based regimens also comprised 50% of those selected for second-line treatment.

Gastro Hep Advances 2022;1:231–240

22

Inadequate Treatment Regimens are Widely Prescribed

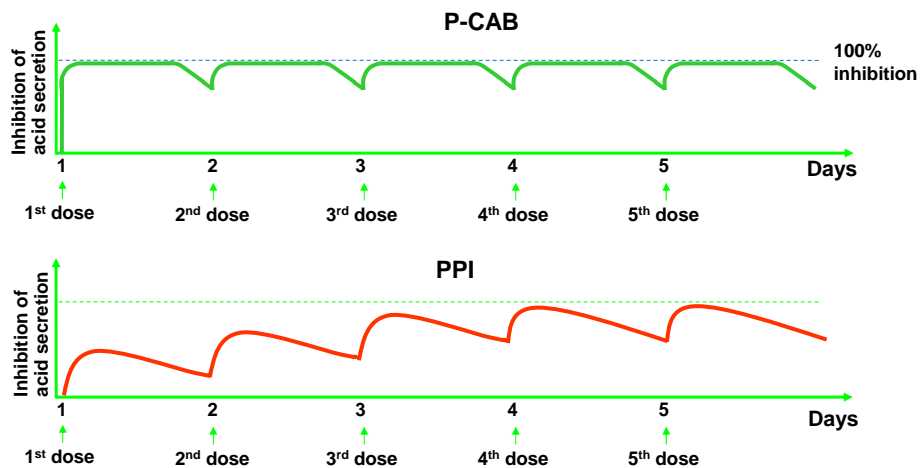


- 24% of physicians would repeat clarithromycin triple therapy after PrevPac
- 43% would follow nonbranded clarithromycin triple therapy with another clarithromycin-based therapy (31% clarithromycin, metronidazole, and any PPI and 12% PrevPac)

Gastro Hep Advances 2021;1231-240

23

Potassium competitive acid blockers and acid inhibition



24

PCAB based dual and triple therapy: recently approved

	VOQUEZNA TRIPLE PAK % (n)	VOQUEZNA DUAL PAK % (n)	LAC % (n)
Patients with <i>H. pylori</i> infection who did not have a clarithromycin or amoxicillin resistant strain at baseline^a	84.7 (222)	78.5 (208)	78.8 (201)
Treatment Difference from LAC (95% CI)	5.9 ^b (-0.8, 12.6)	-0.3 ^c (-7.4, 6.8)	
All randomized patients with <i>H. pylori</i> infection at baseline	80.8 (273)	77.2 (250)	68.5 (226)
Treatment Difference from LAC (95% CI)	12.3 ^d (5.7, 18.8)	8.7 ^e (1.9, 15.4)	

Voquenaza package insert

25

Rifabutin triple therapy

Table 3. *Helicobacter pylori* Eradication Rate, by Treatment Group

Analysis	RHB-105 Group	Active Comparator Group	Treatment Difference	P Value*
ITT analysis on the primary efficacy end point†				
Eradication rate, % (n/N)	83.8 (191/228)	57.7 (131/227)	26.1	<0.001
95% CI, %	78.4 to 88.0	51.2 to 64.0	18.0 to 34.1	

Table 4. *Helicobacter pylori* Eradication Rate, by Antimicrobial Resistance Status at Baseline

Antimicrobial Resistance Status at Baseline	Responders*		Treatment Difference†	P Value‡
	RHB-105 Group (n = 228)	Active Comparator Group (n = 227)		
Resistance to any antibiotic§				
Eradication rate, % (n/N)	81.2 (69/85)	56.1 (55/98)	25.1	<0.001
95% CI, %	71.6 to 88.1	46.3 to 65.5	12.2 to 37.9	

Ann Intern Med. 2020;172:795-802

26

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

27

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

28

Idiopathic ulcer disease unrelated to H pylori, NSAIDs or gastric hypersecretion

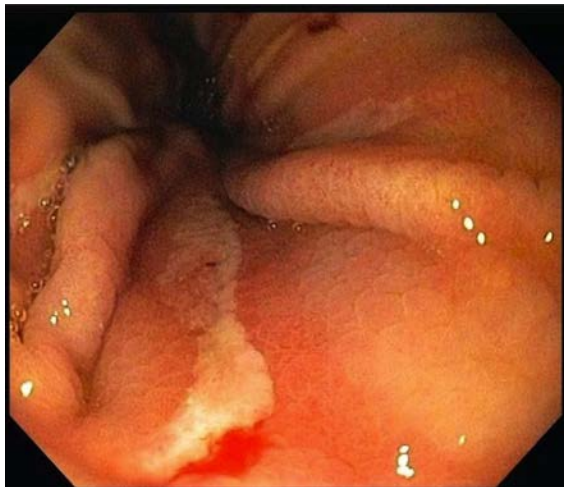
- Described worldwide
- Elderly, white males in western countries
- Propensity for recurrence (35%)
- Recurrent hemorrhage is high in patients presenting with bleeding (13.5%)
- Smoking and stress may be factors
- High incidence soon after earthquakes in Japan

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

29

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

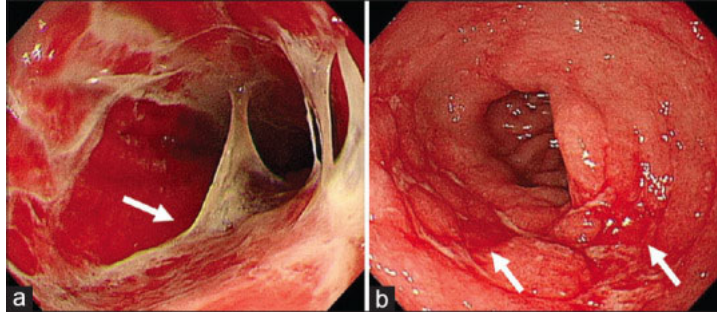


Endoscopy. 2013; 45(5): 397–400.

30

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

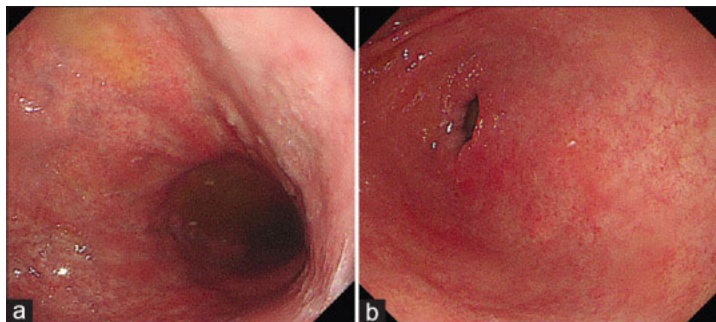


J Postgrad Med. 2022 Jan-Mar; 68(1): 38–40.

31

Checkpoint inhibitor ulcers: pembrolizumab

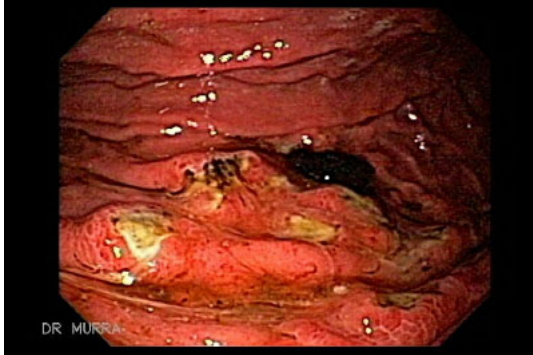
Prednisone 1mg/kg/day for 4 weeks with pantoprazole and discontinuation of pembrolizumab



J Postgrad Med. 2022 Jan-Mar; 68(1): 38–40.

32

Ulcerated raised lesions: multiple ulcers, thickened folds: lymphoma



https://www.gastrointestinalatlas.com/english/gastric_lymphoma.html

33

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

<https://www.olympus-europa.com/medical/en/Products-and-Solutions/Medical-Solutions/EndoAtlas/>

34

Rare causes: Anisakiasis

Anisakis pegreffii can cause life-threatening allergic reactions and abdominal pain

Sushi, ceviche, raw marinated anchovies



VIDEOGIE | VOL 84, ISSUE 3, P528, SEPTEMBER 01, 2016
[Emerg Infect Dis.](#) 2013 Mar; 19(3): 496–499.

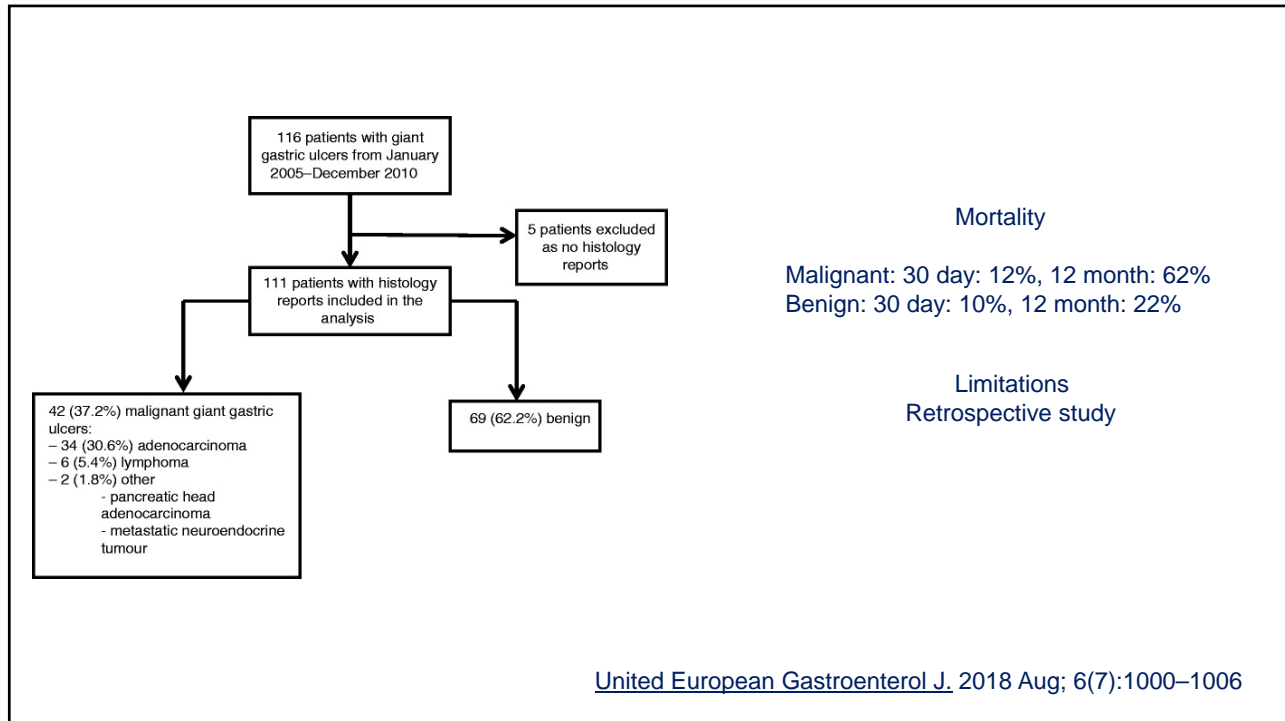
35

Giant gastric ulcers

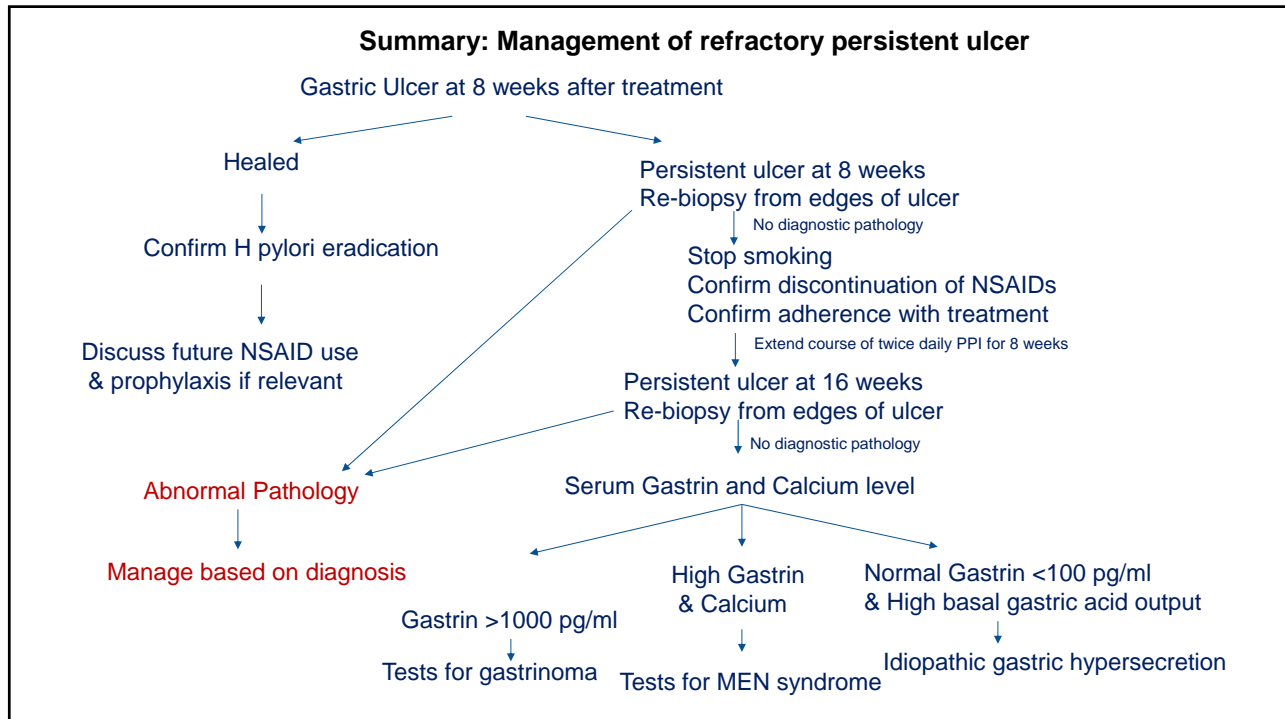
- A giant peptic ulcer is an ulcer larger than 3 cm in size.



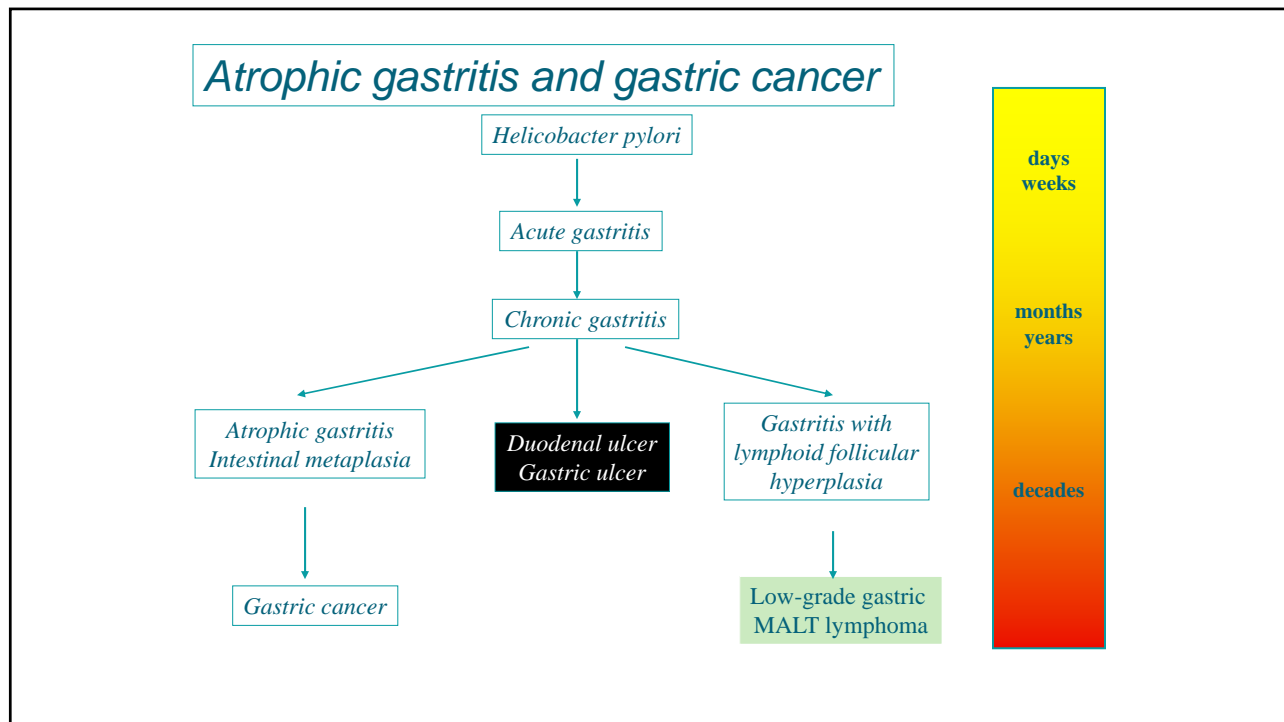
36



37



38



39

Development of Gastric cancer

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

Uemura N. New Engl J Med 2001;345:784-9

40

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.

Sung et al. *Gastroenterology*. 2000;119:7-14.

41

Preventing Gastric Cancer: China

2423 healthy persons were recruited in 1994 from Changle County, China

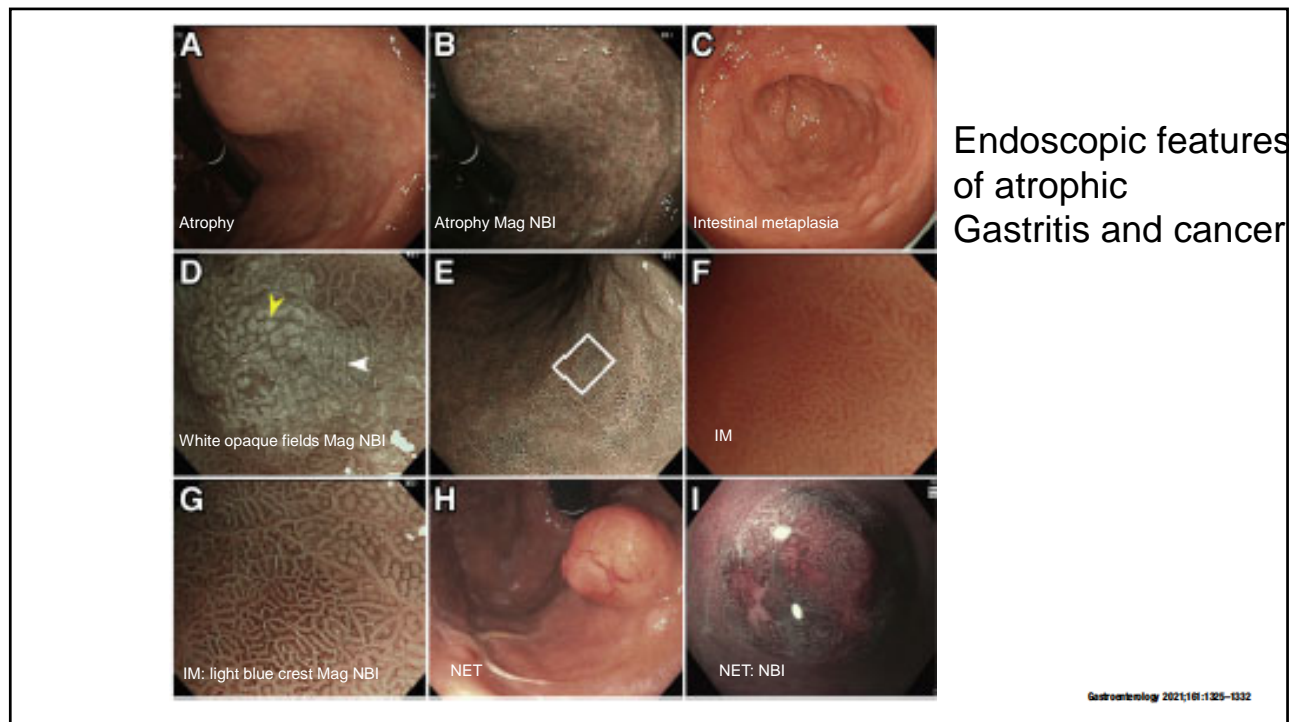
Patients were then randomized eradication treatment or placebo

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

Wong B. *JAMA*. 2004 Jan 14;291(2):187-94.

42



43

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

Gastroenterology 2021;161:1325-1332

44

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

45

 Virtual Grand Rounds universe.gi.org

Questions and Answers



Nimish Vakil, MD, FACC



Nalini M. Guda, MD, FACC

46

CONNECT AND COLLABORATE IN GI



ACG & CCF IBD Circle

ACG Hepatology Circle

ACG Functional GI Health and Nutrition Circle

ACG GI Circle
Connect and collaborate within GI

ACG Women in GI Circle

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



47