
Phathom
PHARMACEUTICALS
CHANGING THE LANDSCAPE IN GI
Going beyond to advance treatments for patients with acid-related disorders
INVESTOR DAY
DECEMBER 14, 2020

Safe harbor statement

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our future results of operations and financial position, business strategy, prospective products, product approvals, research and development costs, timing and likelihood of success, plans and objectives of management for future operations, and future results of current and anticipated products, are forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as “may,” “will,” “should,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplates,” “believes,” “estimates,” “predicts,” “potential” or “continue” or the negative of these terms or other similar expressions. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. These risks, uncertainties and other factors include, without limitation: the impact of COVID-19 on our ongoing and future clinical trials is highly uncertain due to factors outside our control; potential delays in enrollment and completion of clinical trials; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the success of our clinical trials of vonoprazan, and the results of prior clinical trials and other investigator-initiated clinical trials of vonoprazan are not necessarily predictive of our future results and the FDA and comparable foreign regulatory authorities may not accept the data from such prior trials to support approval; regulatory developments in the United States and foreign countries; unexpected adverse side effects or inadequate efficacy of vonoprazan that may limit its development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; our ability to obtain and maintain intellectual property protection for vonoprazan; our ability to comply with our license agreement with Takeda; our ability to maintain undisrupted business operations due to the ongoing spread of COVID-19, including delaying or otherwise disrupting our clinical trials, manufacturing and supply chain, and other risks described in our filings with the Securities and Exchange Commission (SEC), including our Annual Report on Form 10-K and any subsequent filings with the SEC. You are cautioned to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to revise or update this presentation to reflect events or circumstances after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.


Phathom
PHARMACEUTICALS
CHANGING THE LANDSCAPE IN GI
Going beyond to advance treatments for patients with acid-related disorders
Terrie Curran

Today's speakers

Terrie Curran
President & Chief Executive Officer

Azmi Nabulsi, MD
Chief Operating Officer

Martin Gilligan
Chief Commercial Officer

Todd Branning
Chief Financial Officer

Key Opinion Leaders

Stuart Spechler
MD

Colin Howden
MD

Ronnie Fass
MD

Phathom PHARMACEUTICALS

Going Beyond

to advance treatments for patients with acid related disorders

HEADQUARTERS
Florham Park, NJ

RAISED $209M | OCT 2019
Gross Proceeds in IPO

FORMED IN 2019
Listed on NASDAQ: PHAT

Vonoprazan: First innovative therapy for acid related disorders in more than 25 years

P-CAB

Potassium competitive acid blocker

Topline data from two pivotal phase 3 trials in **2021**

US / Europe / Canada rights licensed from **TAKEDA**

Approved in

14 COUNTRIES

across Asia and Latin America

>$725M

net sales in Japan for the 12 months ended Sept 30, 2020[1]

+17% YoY

volume-driven sales growth in the 6th year on the market[2]

[1] US dollars based on September 30, 2020 conversion rate of 0.0095 dollars to one yen
[2] Growth based on prior comparable 12-month period

Phathom pipeline: promising late stage opportunities for unmet GI needs

	Target Indications	Phase 1[1]	Phase 2[1]	Phase 3	Expected Milestones
Vonoprazan	**GERD** Healing of Erosive Esophagitis (EE) and relief of heartburn			pHalcon ee A research study for *Erosive Esophagitis*	*Enrollment complete* ***Topline results 2H21***
	Maintenance of healing of Erosive Esophagitis (EE) and relief of heartburn				
Vonoprazan + antibiotics	***H. pylori* treatment** Dual therapy (vonoprazan + amoxicillin)			pHalcon hp A research study for *H. pylori Infection*	*Phase 3 LSI Jan 2021* ***Topline results 2Q21***
	Triple therapy (vonoprazan + amoxicillin + clarithromycin)				

Phathom has development and commercialization rights to vonoprazan in the United States, Europe, and Canada
[1]Phase 1 and 2 studies in healing of Erosive Esophagitis, maintenance of Erosive Esophagitis, and *H. pylori* treatment conducted by Takeda

Phathom pipeline: promising late stage opportunities for unmet GI needs

	Target Indications	Phase 1[1]	Phase 2[1]	Phase 3	Expected Milestones
Vonoprazan	**GERD**			pHalcon-ee	
	Healing of Erosive Esophagitis (EE) and relief of heartburn				*Enrollment complete*
	Maintenance of healing of Erosive Esophagitis (EE) and relief of heartburn				***Topline results 2H21***
	Treatment of heartburn associated with Non-erosive Reflux Disease (NERD)				*Phase 2 FSI mid-21*
Vonoprazan + antibiotics	***H. pylori* treatment**			pHalcon-hp	
	Dual therapy (vonoprazan + amoxicillin)				*Phase 3 LSI Jan 2021*
	Triple therapy (vonoprazan + amoxicillin + clarithromycin)				***Topline results 2Q21***

Phathom has development and commercialization rights to vonoprazan in the United States, Europe, and Canada

[1]Phase 1 and 2 studies in healing of Erosive Esophagitis, maintenance of Erosive Esophagitis, and *H. pylori* treatment conducted by Takeda

Building a leading biopharma company

ADVANCING THE PIPELINE

- Nov 2020, completed enrollment in Ph3 PHALCON-EE; Topline results expected 2H21
- Complete enrollment in PHALCON-HP expected in Jan 2021; Topline results expected 2Q21
- Launching NERD development program; Phase 2 initiation expected mid-2021

REGULATORY PROGRESS

- FDA Fast Track and QIDP designations in combination with certain antibiotics – *H. pylori*
- Target NDA submissions: *H. pylori* – 2H21; Erosive Esophagitis – 2022
- Received agreement from FDA on proposed initial pediatric study plans

PREPARING FOR LAUNCH

- Assembled an experienced and proven Executive Management team
- Key leadership appointments in commercial, medical, and finance
- Established commercial supply chain and multiple manufacturing sources

WELL CAPITALIZED

- Raised $209M gross proceeds in IPO in Oct 2019
- Filed S-3 shelf registration in Nov 2020
- Initiated “At the Market” facility in Nov 2020

What we will cover today

Vonoprazan clinical profile and MOA, phase 3 studies, planned indication expansion

GERD classifications and prevalence, QoL impacts, acid control and healing

H. pylori treatment limitations and vonoprazan's potential to deliver

NERD unmet needs and vonoprazan's pharmacological profile

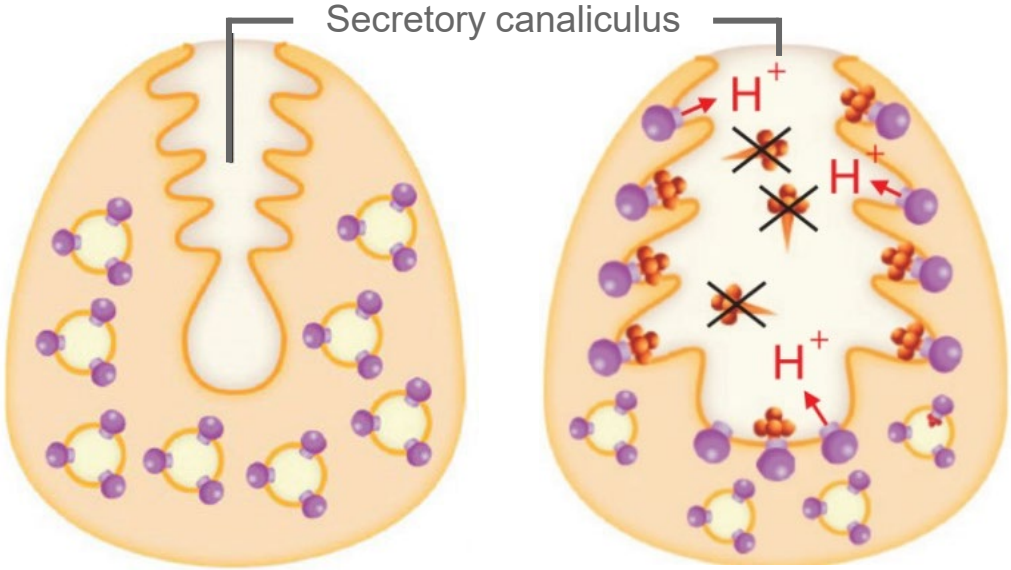
US market opportunity and commercialization strategy

Access to capital and a strong balance sheet


VONOPRAZAN
INNOVATIVE MECHANISM OF ACTION FOR ACID RELATED DISORDERS
Azmi Nabulsi, MD
Phathom
PHARMACEUTICALS

PPIs: mechanism limits effectiveness

GASTRIC PARIETAL CELL



PPI:
COVALENTLY BINDING PRODRUG

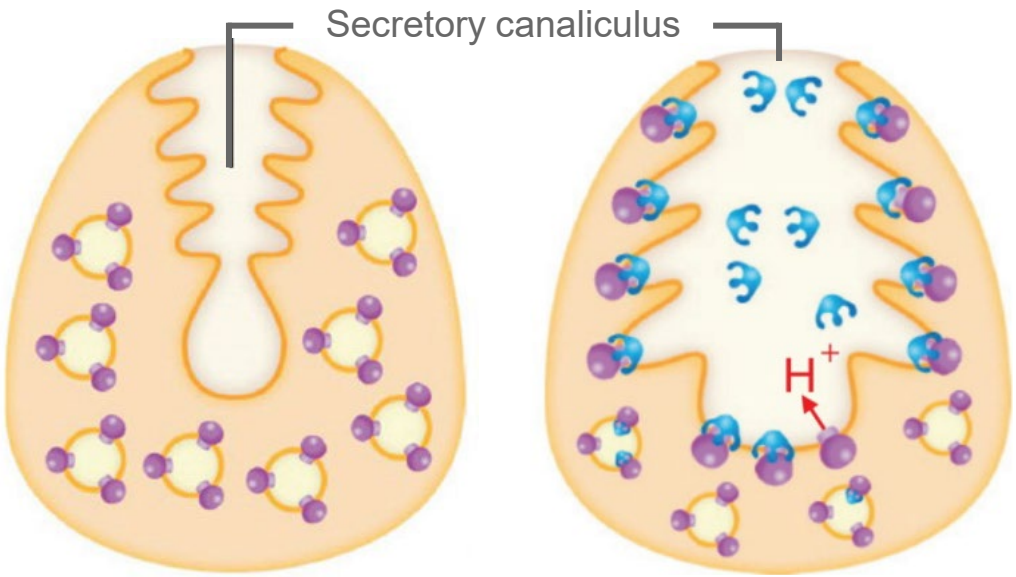
- Short plasma half-life
- Acid needed for activation but unstable in presence of acid
- Meal required to stimulate pumps
- Primarily metabolized via CYP2C19

- ✕ **Slow** onset of action
- ✕ **Limited** potency
- ✕ **Limited** duration of activity

Oshima et al, J Neurogastroenterol Motil, 2018

Vonoprazan: distinct mechanism designed to address PPI shortcomings

GASTRIC PARIETAL CELL



Quiescent phase *Active phase after meal*

Tubulovesicle Proton pump (H^+, K^+ -ATPase)

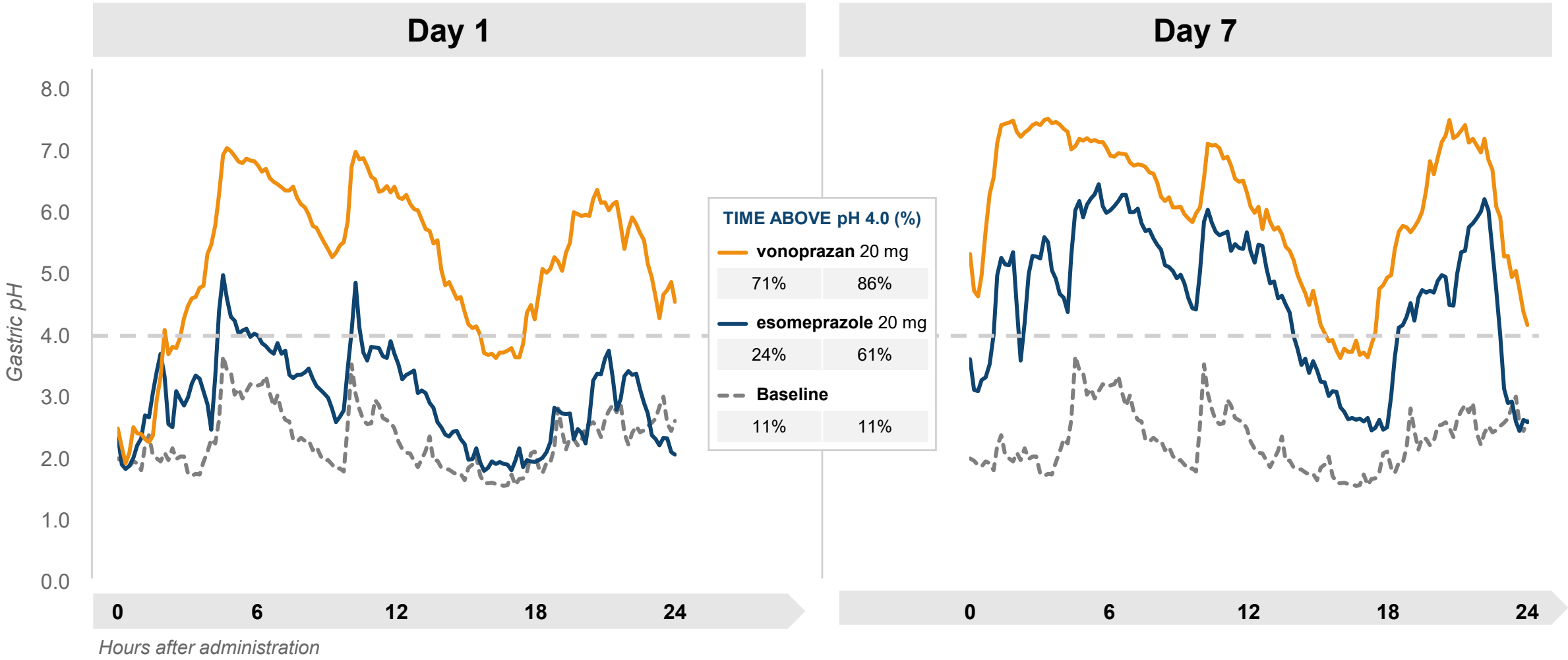
Vonoprazan:
COMPETITIVE ENZYME INHIBITOR

- Long plasma half-life
- Stable in acid
- High accumulation in canaliculus
- Very slow dissociation rate
- Primarily metabolized via CYP3A4/5

- ✔ **Rapid** onset of action
- ✔ **Potent** acid control
- ✔ **Durable** 24-hr activity

Oshima et al, J Neurogastroenterol Motil, 2018

Vonoprazan demonstrated faster, more potent, and more durable acid control vs. PPI



Sakurai et al, Alimentary Pharmacology and Therapeutics, 2015; Study evaluating efficacy, rapidity and duration of acid-inhibitory effects of vonoprazan vs. two control PPIs, esomeprazole and rabeprazole, in 20 healthy Japanese adult male volunteers

Vonoprazan safety profile similar to PPIs

>7,000 patients have received vonoprazan in clinical studies

No dose-related increase in adverse events observed in clinical studies

>25 million patients have received vonoprazan since launch

ADVERSE EVENTS IN CLINICAL DEVELOPMENT REFLECTED IN JAPANESE PRESCRIBING INFORMATION

Incidence of 0.1-5.0%

Diarrhea[1]	Elevated liver enzymes
Constipation	Rash
Nausea	Eosinophilia

HEPATIC EVENTS OF SPECIFIC INTEREST IN LIGHT OF FIRST-GENERATION PCABs

Pooled data across head-to-head Phase 2 and 3 studies	**vonoprazan** 10 and 20mg	**lansoprazole** 15 and 30mg
ALT or AST >3X ULN or Bilirubin >2X ULN	1.0%	0.8%

[1]10.6% in combination with antibiotics for treatment of *H. pylori*
Ashida et al, World J Gastro 2018; Data on file


VONOPRAZAN
FOR GERD
Phathom
PHARMACEUTICALS

Vonoprazan for GERD

~65M US

~50M EU5

People with GERD

~6.8B US

PPI doses prescribed[1]

~15-45%

Inadequately treated with PPIs

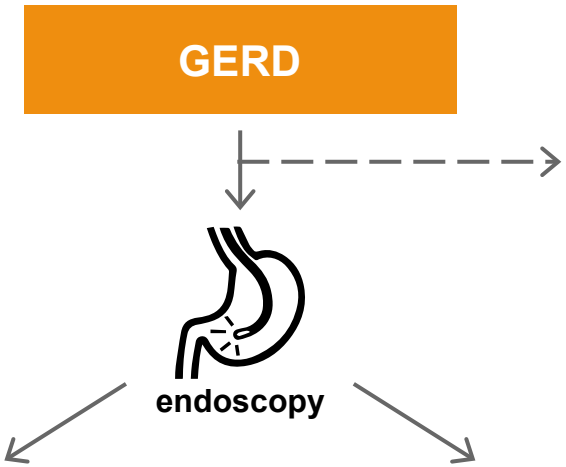
Many patients experience breakthrough heartburn and recurrence of erosions while on PPIs

Vonoprazan may offer more rapid, potent and durable healing and symptom control

[1] For the 12 months ended October 31, 2020

El-Serag APT 2010; El-Serag Gut 2014; IQVIA data Oct 2020

Key unmet needs within GERD classifications



Frequently treated as symptomatic GERD without endoscopic evaluation

KEY UNMET NEEDS

Erosive Esophagitis (EE)

> **Improved efficacy**: healing/maintenance of healing of erosions and symptom control (rapid and durable)

Non-erosive Reflux Disease (NERD)

> **Improved symptom control**: speed and durability of relief

> **On-demand dosing**: speed and durability of symptom relief with flexible dosing

Opportunity in Erosive Esophagitis

GERD

Frequently treated as symptomatic GERD without endoscopic evaluation

endoscopy

Erosive Esophagitis (EE)

> **Improved efficacy**: healing/maintenance of healing of erosions and symptom control (rapid and durable)

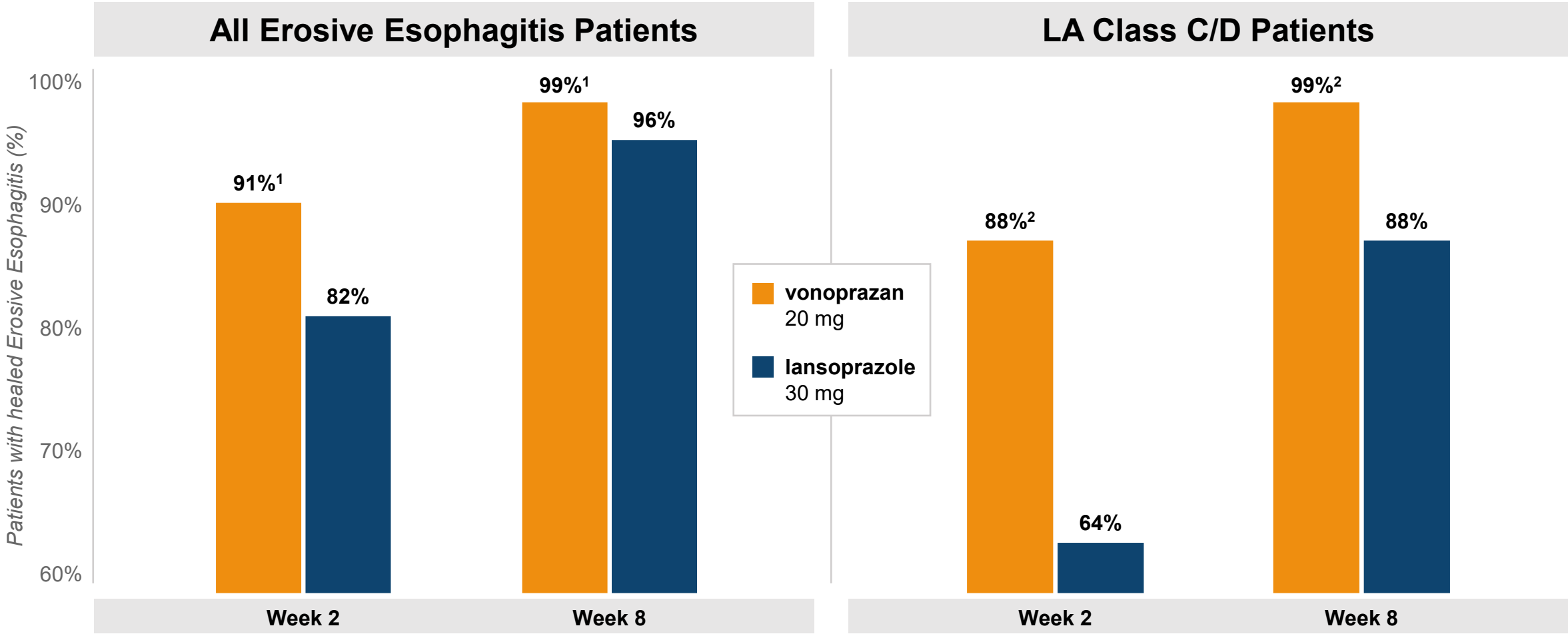
Non-erosive Reflux Disease (NERD)

> **Improved symptom control**: speed and durability of relief

> **On-demand dosing**: speed and durability of symptom relief with flexible dosing

KEY UNMET NEEDS

Japan Erosive Esophagitis phase 3: faster and improved healing vs. PPI

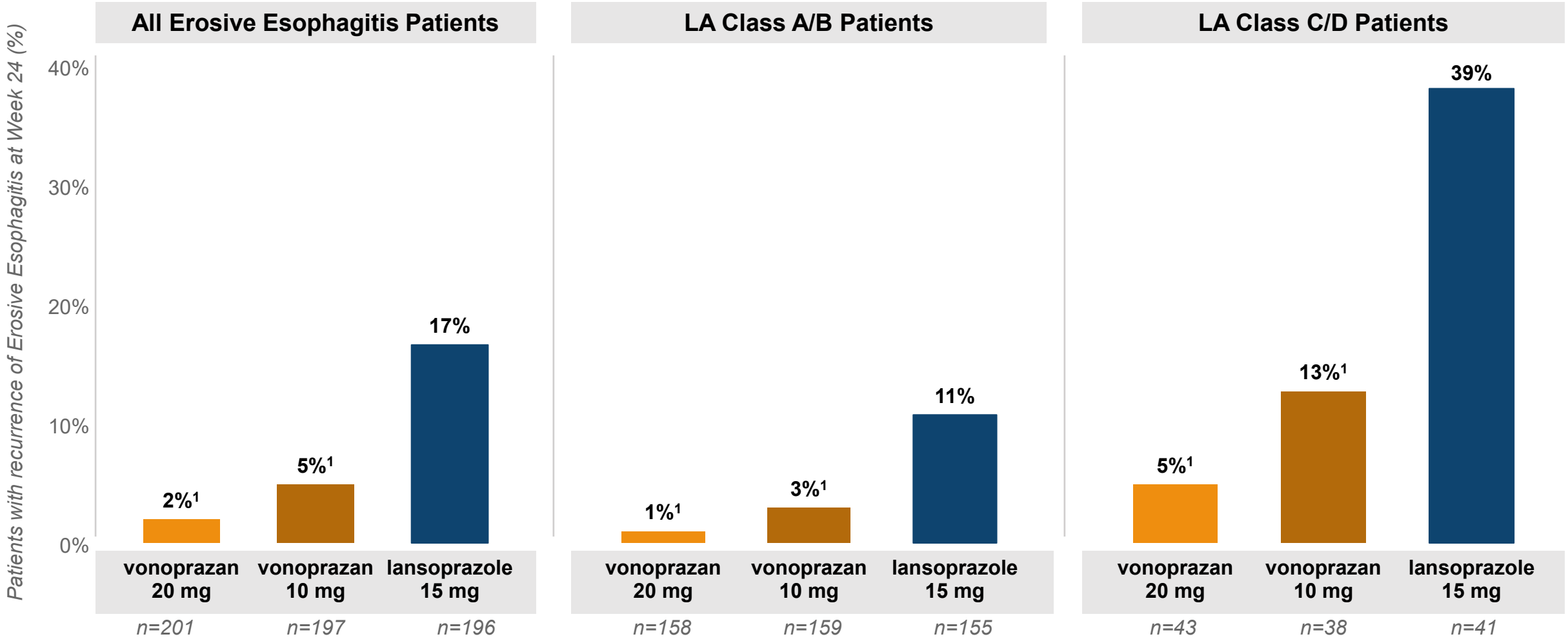


n=404, [1]Statistically significant ($p < 0.05$) for superiority versus lansoprazole

n=147, [2]Statistically significant ($p < 0.05$) for superiority versus lansoprazole

Ashida et al, Aliment Pharmacol Ther 2016;
Note: clinical trial met prespecified non-inferiority endpoint and post hoc superiority test

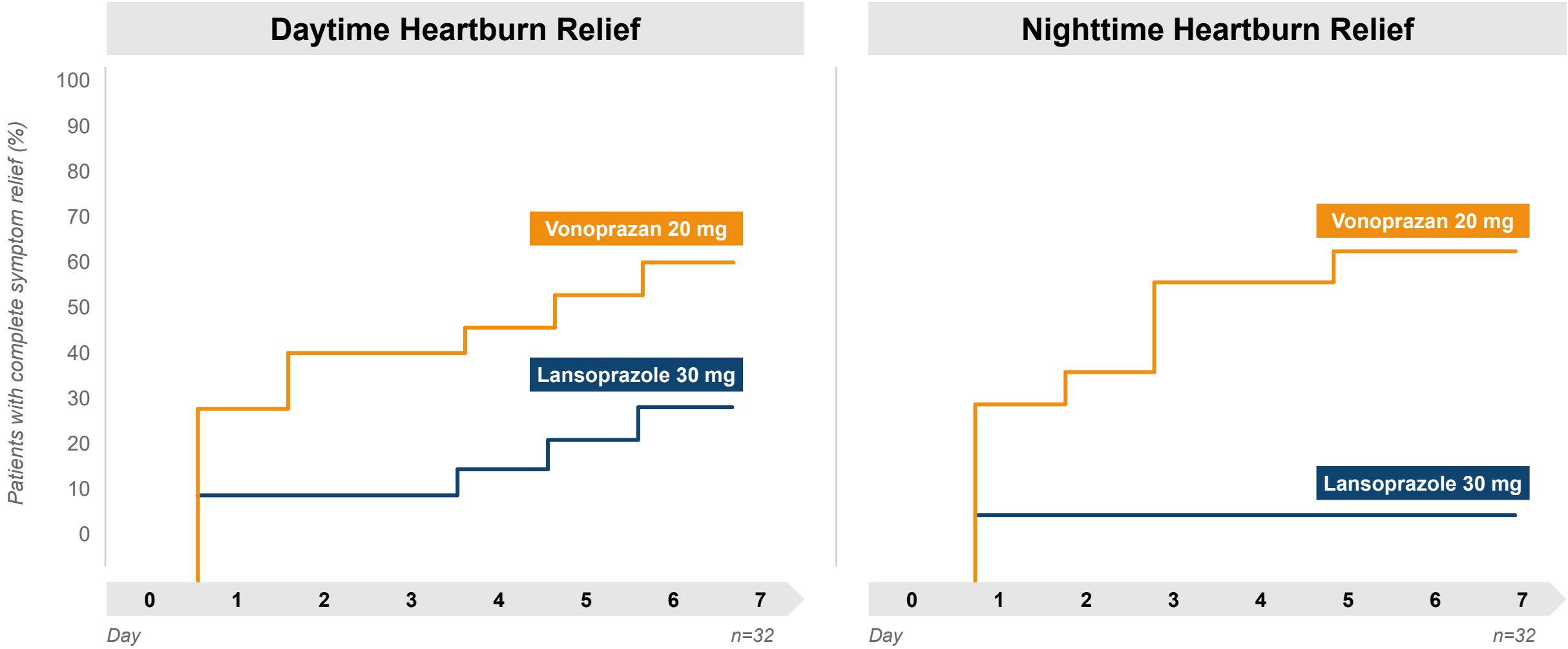
Japan Erosive Esophagitis phase 3: lower 6-month recurrence rates vs. PPI



[1] $p < 0.05$ for superiority of vonoprazan 20 mg and vonoprazan 10 mg versus lansoprazole

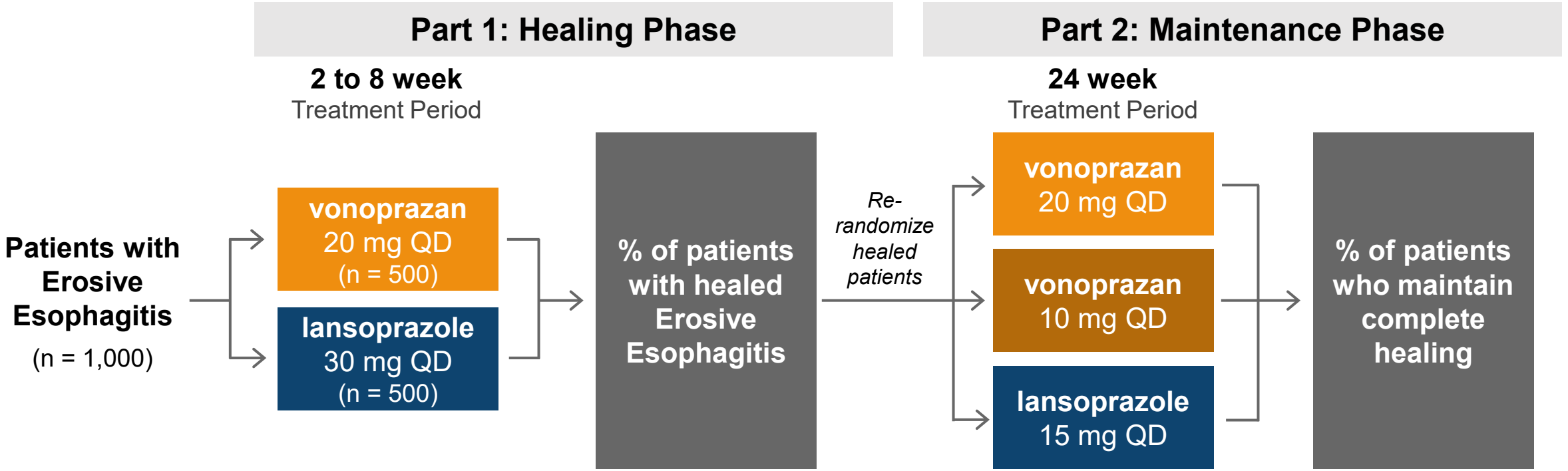
Ashida et al, Aliment Pharmacol Ther 2018;
Note: clinical trial met prespecified non-inferiority endpoint and post hoc superiority test

Faster and more complete heartburn relief vs. PPI



Oshima et al, AP&T 2018

Phathom US/Europe Erosive Esophagitis phase 3 study design



Nov 2020 Enrollment completed; **2H21** Topline results expected

Study EE-301 healing phase testing hierarchy

Primary Endpoint
Noninferiority Test (10% margin):
% healed by Week 8

Power:
>90%

Key secondary endpoints to support labeling

Key Secondary Endpoint Testing Hierarchy[1]

1. ***Noninferiority Test: Power >90%***
   % of 24-hour heartburn-free days over the Healing Period
2. ***Superiority Test: Power 80%***
   % of Grades C/D subjects who have healed at Week 2
3. ***Superiority Test: Power 80%***
   % with onset of sustained resolution of heartburn by Day 3

[1] Additional secondary endpoints include testing healing for all grades at Week 8 and Week 2

Study EE-301 maintenance phase testing hierarchy

Primary Endpoint for Both Vonoprazan Doses
Noninferiority Test (10% margin):
% who maintained healing through Week 24[1]

Power:
>90%

Key secondary endpoints to support labeling

Secondary Endpoint Testing Hierarchy

1. ***Superiority Test:*** **Vonoprazan 20 mg**
   % of Grades C/D maintaining healing through Week 24
2. ***Superiority Test:*** **Vonoprazan 20 mg**
   % of All Grades maintaining healing through Week 24
3. ***Noninferiority Test:*** **Vonoprazan 20 mg**
   % of 24-hour heartburn-free days through Week 24

Power >90% for each test

Vonoprazan 10 mg dose to be tested for same endpoints in same order if all 3 vonoprazan 20 mg endpoints are met

[1] Hochberg family testing for both 20 mg and 10 mg vonoprazan doses. If both doses meet primary endpoint, secondary endpoint hierarchical testing will be conducted in the order indicated

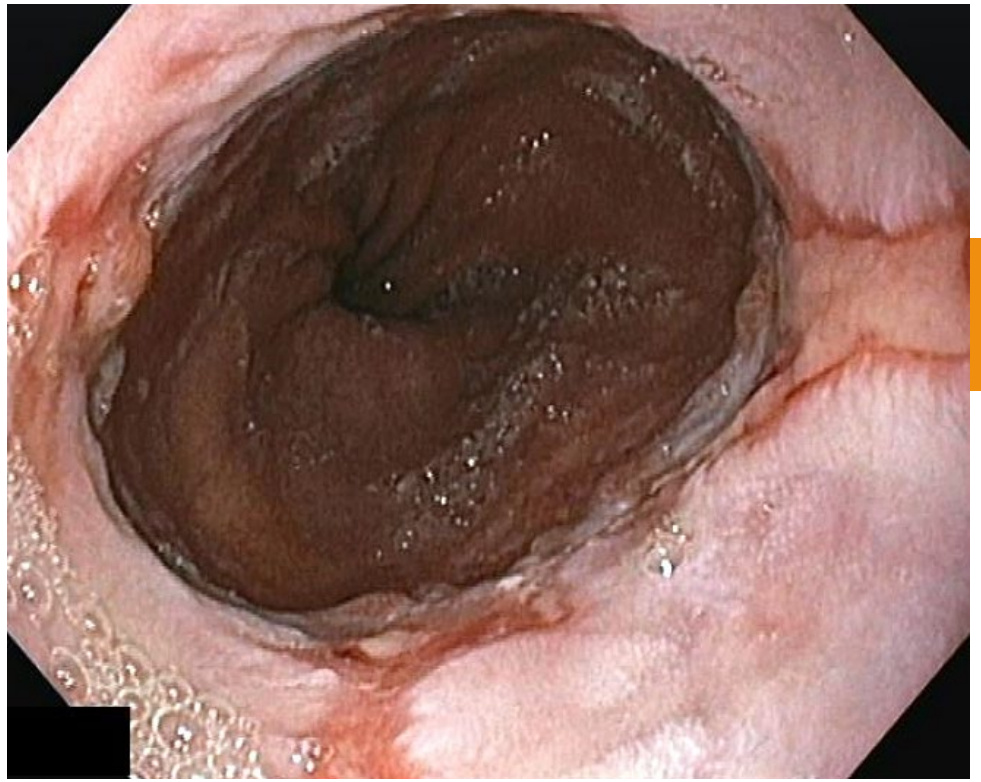
EROSIVE ESOPHAGITIS & GERD

Stuart J. Spechler, M.D.

Chief, Division of Gastroenterology; Co-Director, Center for Esophageal Diseases; Baylor University Medical Center at Dallas; Co-Director, Center for Esophageal Research; Baylor Scott & White Research Institute

Phathom PHARMACEUTICALS

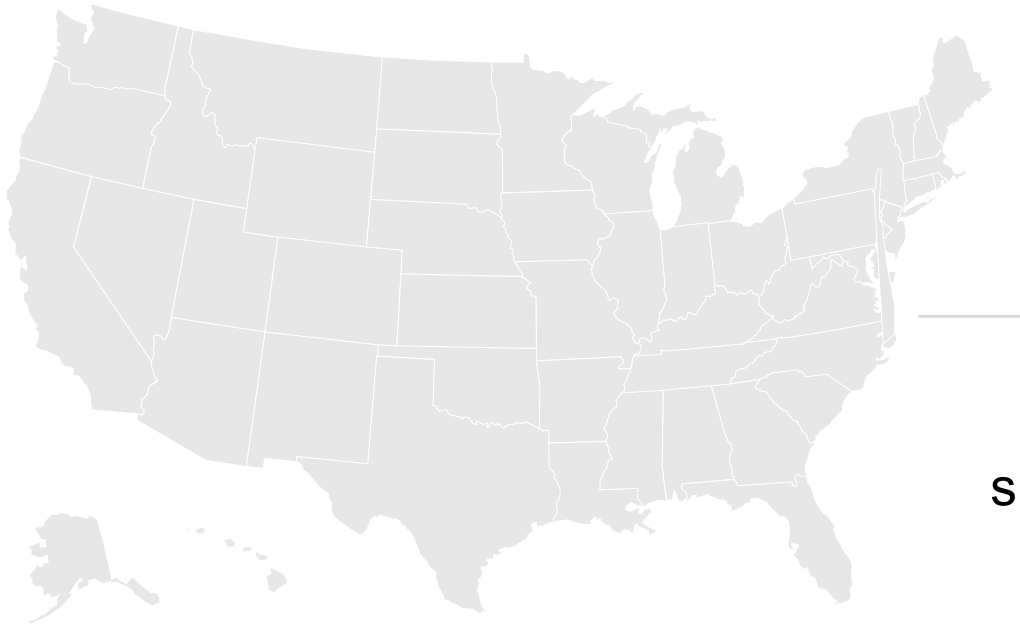
Gastroesophageal Reflux Disease (GERD)



Typical GERD Symptoms

- Heartburn
- Regurgitation

Gastroesophageal Reflux Disease (GERD) in the United States

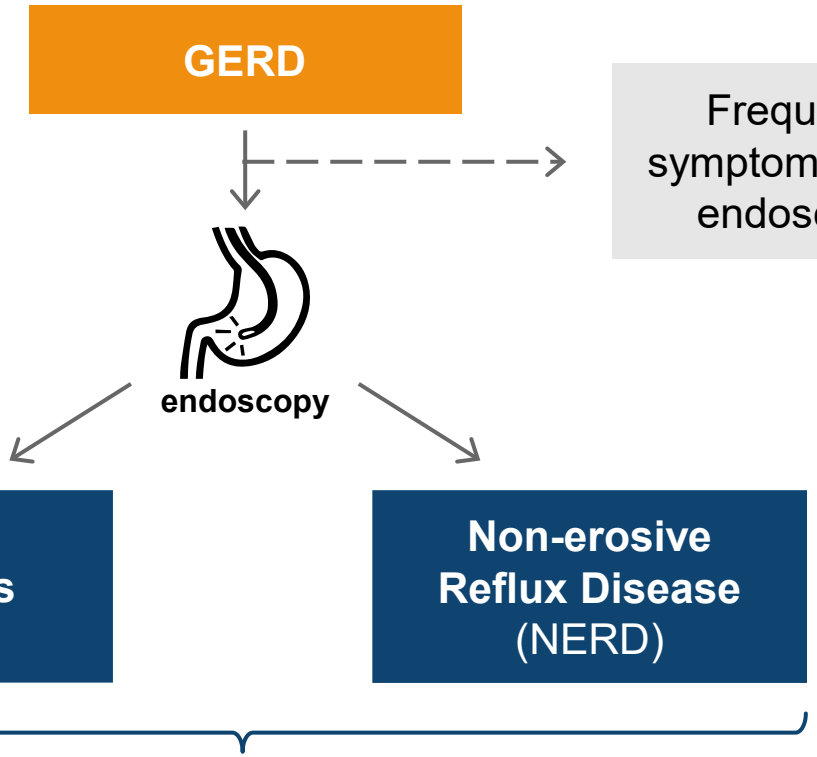


20%
of adults have heartburn
≥1 time/week

>$12 Billion
spent each year for evaluation
and treatment of GERD

Park, J Neurogastroenterol Motil, 2020 Apr 30; 26(2): 169–170
Dickman, et al., J Neurogastroenterol Motil, 2015 Jul; 21(3): 309–319

Flow of patients with GERD

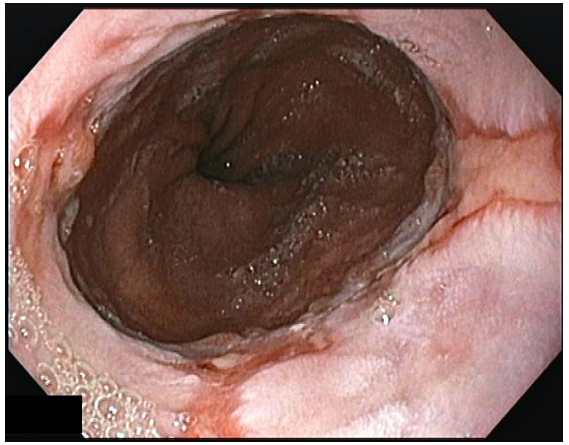


MONTREAL DEFINITION

GERD is "a condition that develops when the reflux of stomach contents into the esophagus causes troublesome symptoms and/or complications"

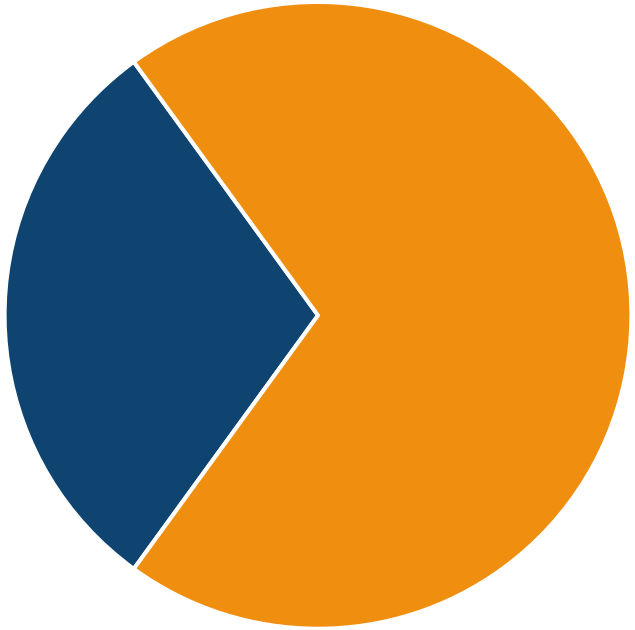
Results of endoscopy in patients with typical GERD symptoms

Reflux Esophagitis



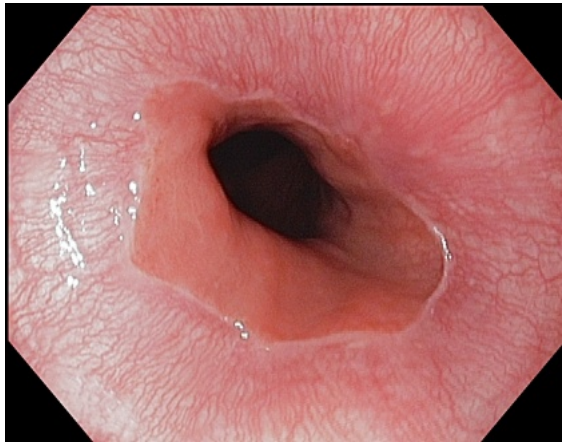
EE

30%



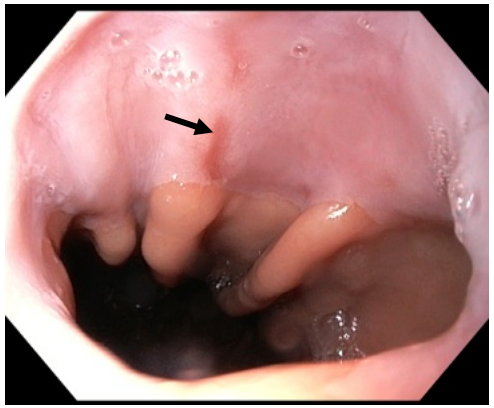
70%

No Reflux Esophagitis



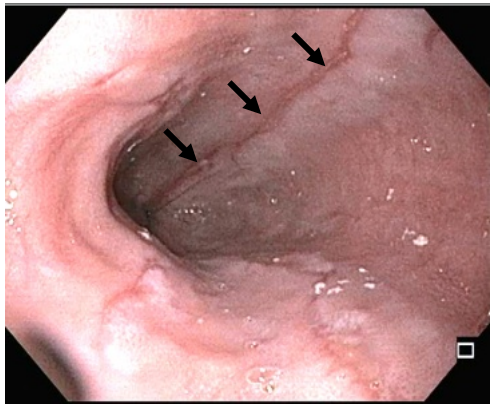
NERD

Reflux esophagitis (Erosive Esophagitis) – Los Angeles Grading System



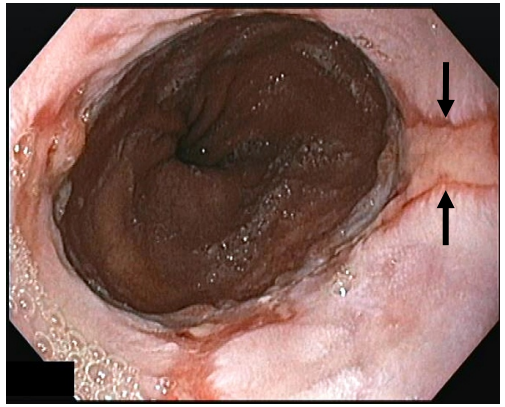
LA-A

≥1 mucosal break, ≤5 mm, does not extend between mucosal folds



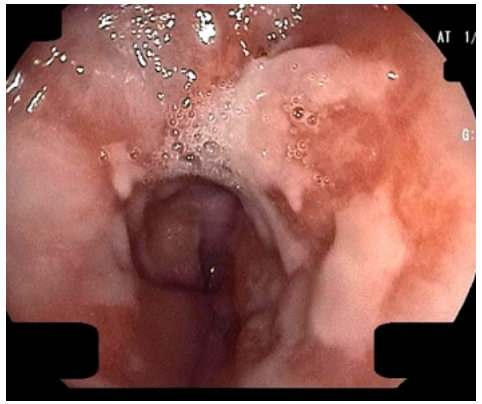
LA-B

≥1 mucosal break, >5 mm, does not extend between mucosal folds



LA-C

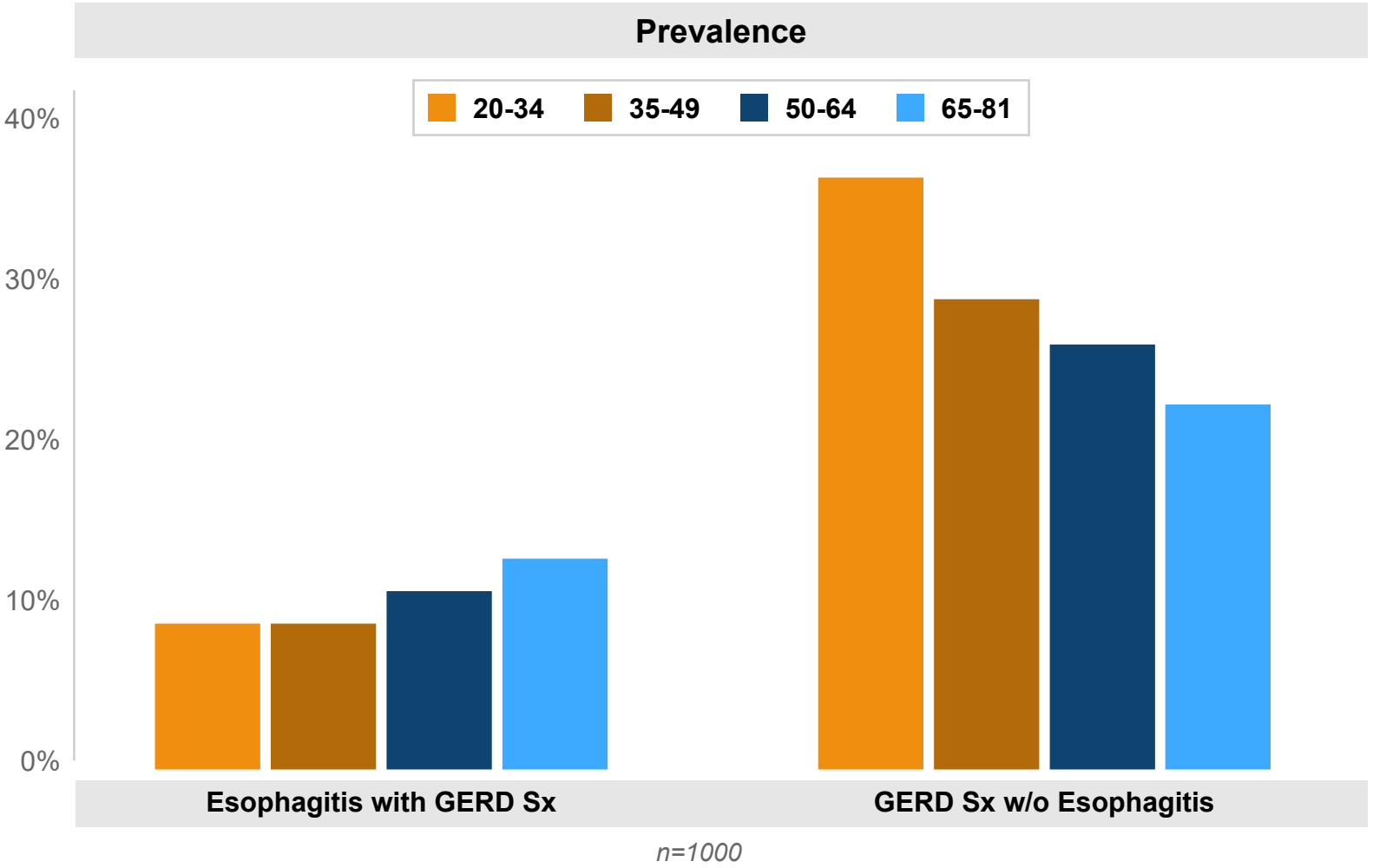
≥1 mucosal break, extends between mucosal folds, involves <75% of circumference



LA-D

≥1 mucosal break, involves >75% of circumference

Erosive Esophagitis and GERD symptoms in random sample of Swedish population



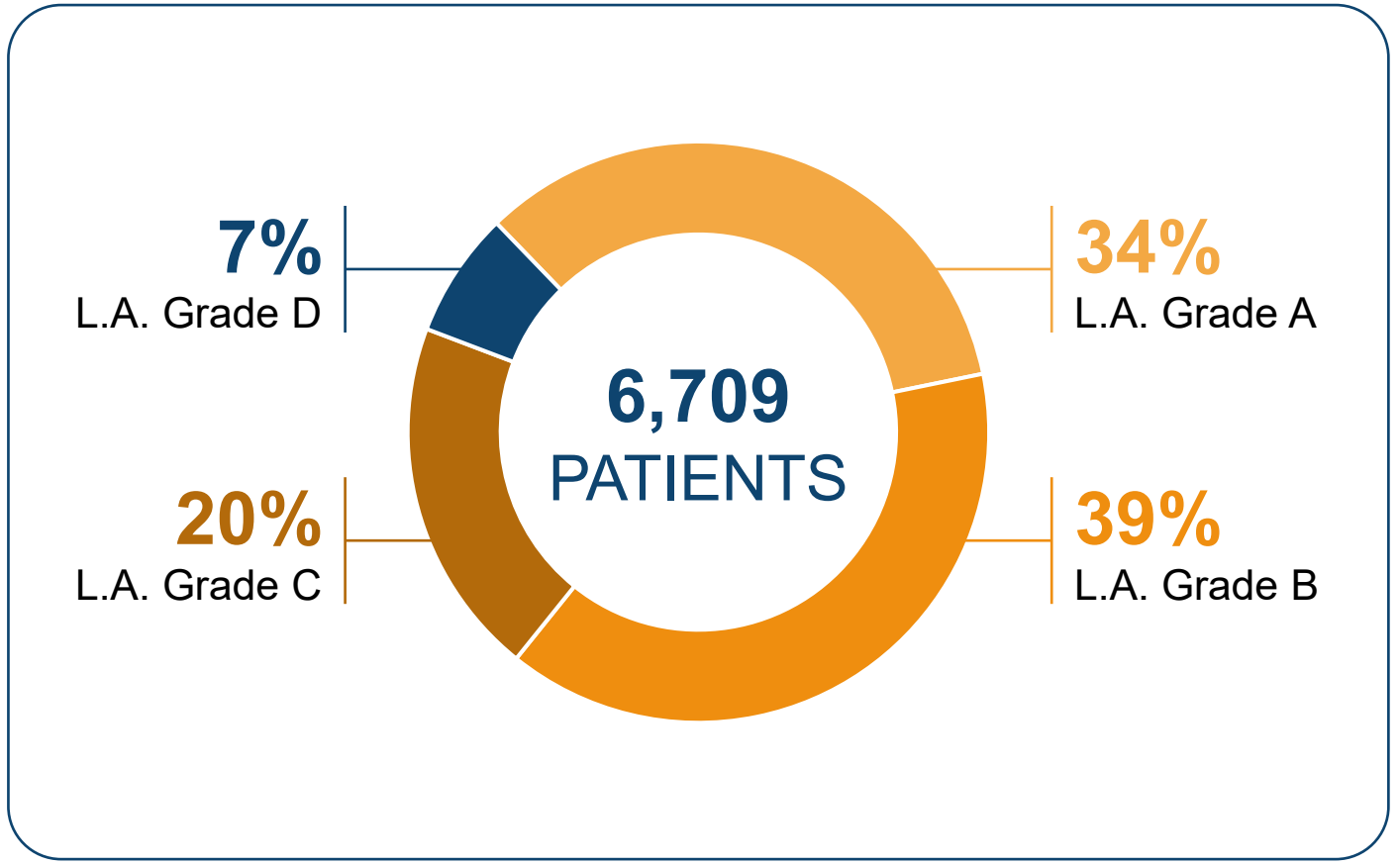
~20%
of population had weekly GERD symptoms

~15%
of population had Erosive Esophagitis

GERD Sx shown are over past 3 months; 20% of overall group had weekly GERD Sx; 5.0-6.7% of each age groups had esophagitis w/o GERD Sx
Ronkainen J et al. Scand J Gastroenterol 2005;40:275

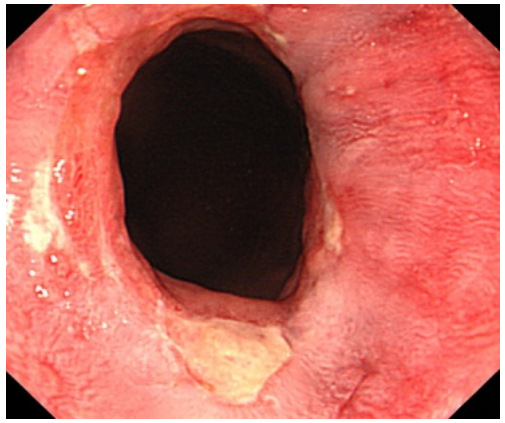
Erosive Esophagitis: distribution of grades

Classification of a large real-world sample of Erosive Esophagitis patients who underwent an endoscopy

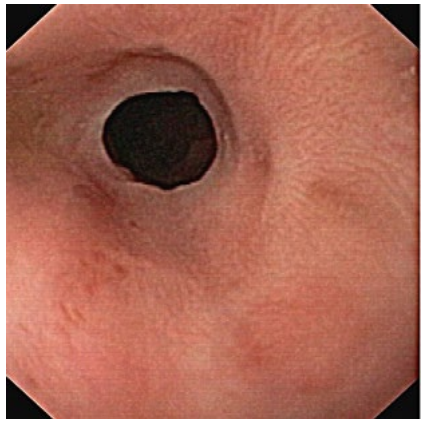


El-Serag, Johanson. Scand J Gastro 2002;37:899

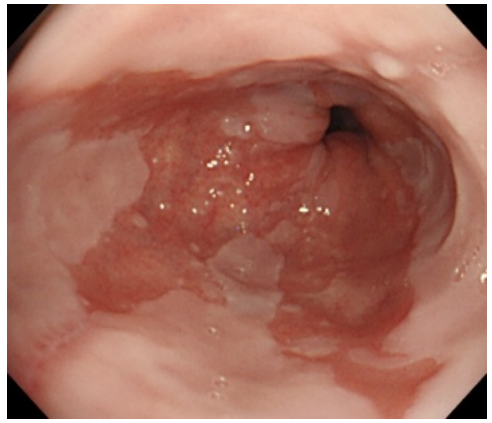
Esophageal complications of GERD



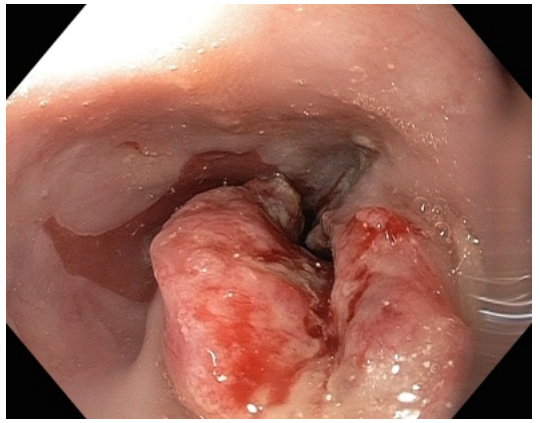
Ulcer



Stricture



Barrett's Esophagus



Cancer

Proton pump inhibitors (PPIs)

- **omeprazole** (Prilosec, Zegerid)
- **lansoprazole** (Prevacid)
- **rabeprazole** (Aciphex)
- **pantoprazole** (Protonix)
- **esomeprazole** (Nexium)
- **dexlansoprazole** (Dexilant)

First PPI (omeprazole) introduced in
1989

First-line therapy for severe **GERD**

Some available **OTC**

Incomplete symptom response to PPIs in Erosive Esophagitis

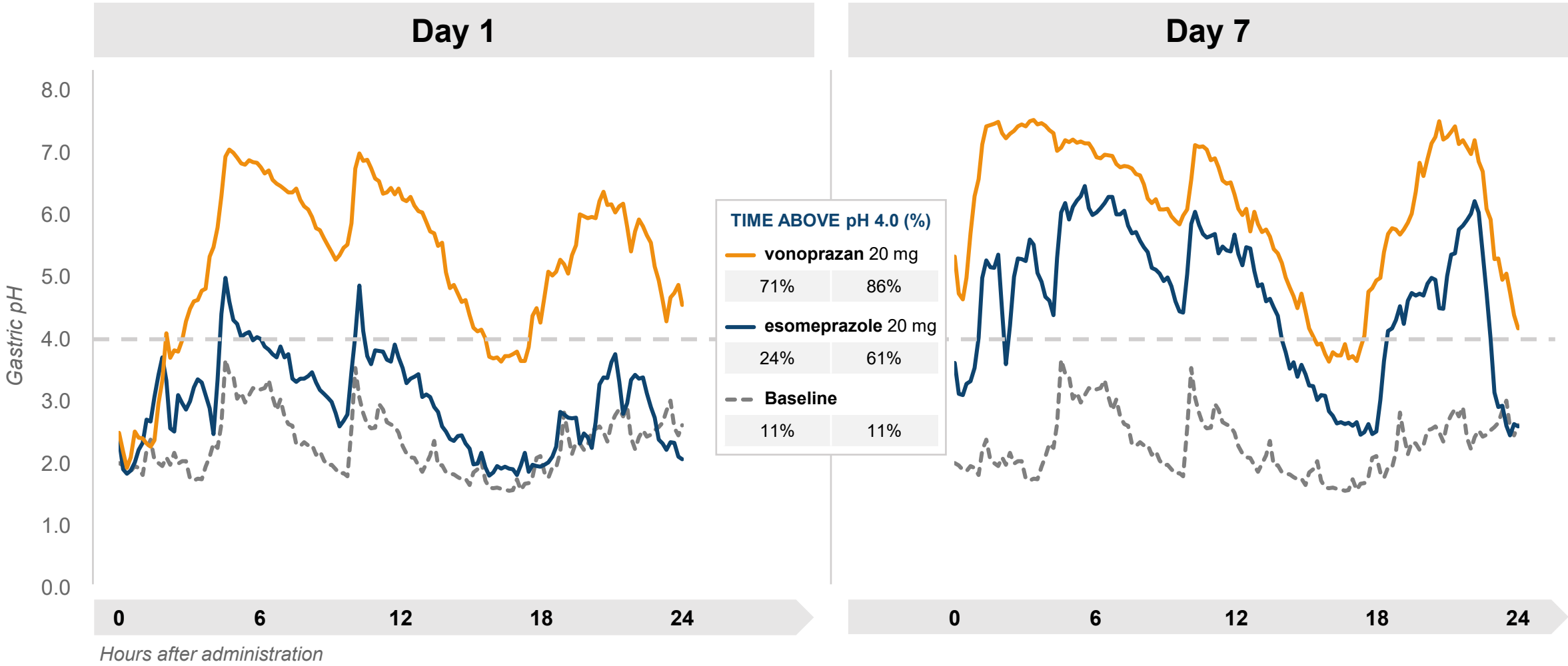
	esomeprazole 40 mg QD	lansoprazole 30 mg QD
Incomplete GERD symptom relief at 4 weeks	37.1%	39.8%
Days with heartburn, weeks 1–4	27.5%	29.1%
Nights with heartburn, weeks 1–4	12.9%	14.2%

Castell DO, et al, Am J Gastroenterol. 2002;97:575-83

Limitations of PPIs

- Endoscopic/symptomatic relapse despite maintenance treatment
- Incomplete symptom control
- Breakthrough of nighttime heartburn
- Required to be dosed before meals
- Metabolism subject to genetic variants
  - CYP P450 2C19
- Incomplete EE healing, especially in severe grades

Vonoprazan demonstrated faster, more potent, and more durable acid control vs. PPI



Sakurai et al, Alimentary Pharmacology and Therapeutics, 2015; Study evaluating efficacy, rapidity and duration of acid-inhibitory effects of vonoprazan vs. two control PPIs, esomeprazole and rabeprazole, in 20 healthy Japanese adult male volunteers

Summary
Potential advantages of P-CABs

Compared to PPIs, vonoprazan:

- Exerts more rapid and profound control of stomach acid secretion
- Does not need to be dosed around meals
- Is not subject to variable metabolism
- May provide:
  - More rapid healing of EE – especially severe grades
  - Superior maintenance of healing


VONOPRAZAN FOR
H. PYLORI
Azmi Nabulsi, MD
Phathom
PHARMACEUTICALS

Vonoprazan for *H. pylori* infection

~115M US
People with *H. pylori*

~2.5M US
Patients treated annually

H. pylori designated as a **Class I carcinogen by WHO and Qualifying Pathogen under FDA GAIN Act**

Eradication rates in the US have fallen to **<80%** **due to increasing antibiotic resistance**

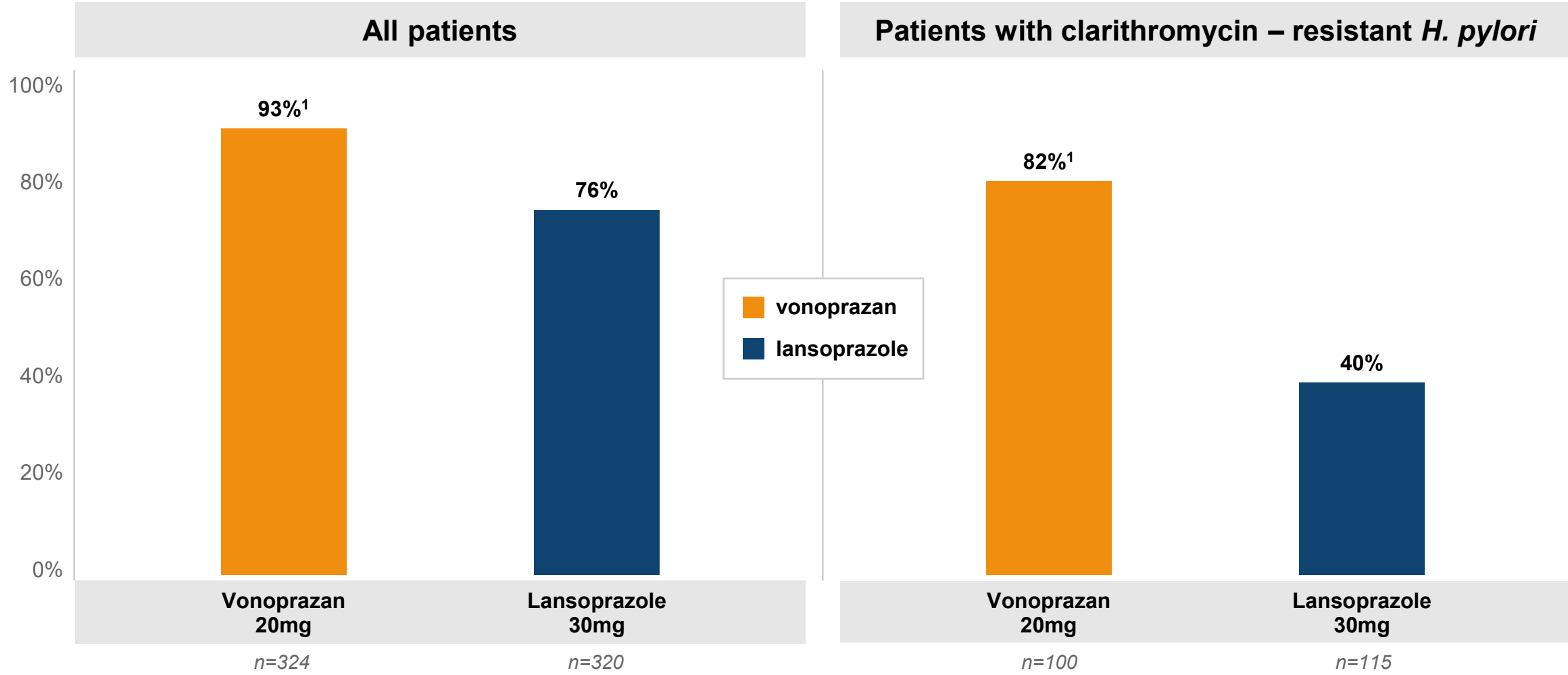
Antibiotic potency increases at higher pH

Vonoprazan-based regimens may restore eradication rates above 90% in the US and Europe

Hooi Gastroenterology 2017; Graham et al 2018; Erah et al 1997

Japan phase 3: vonoprazan triple therapy demonstrated superiority to PPI therapy

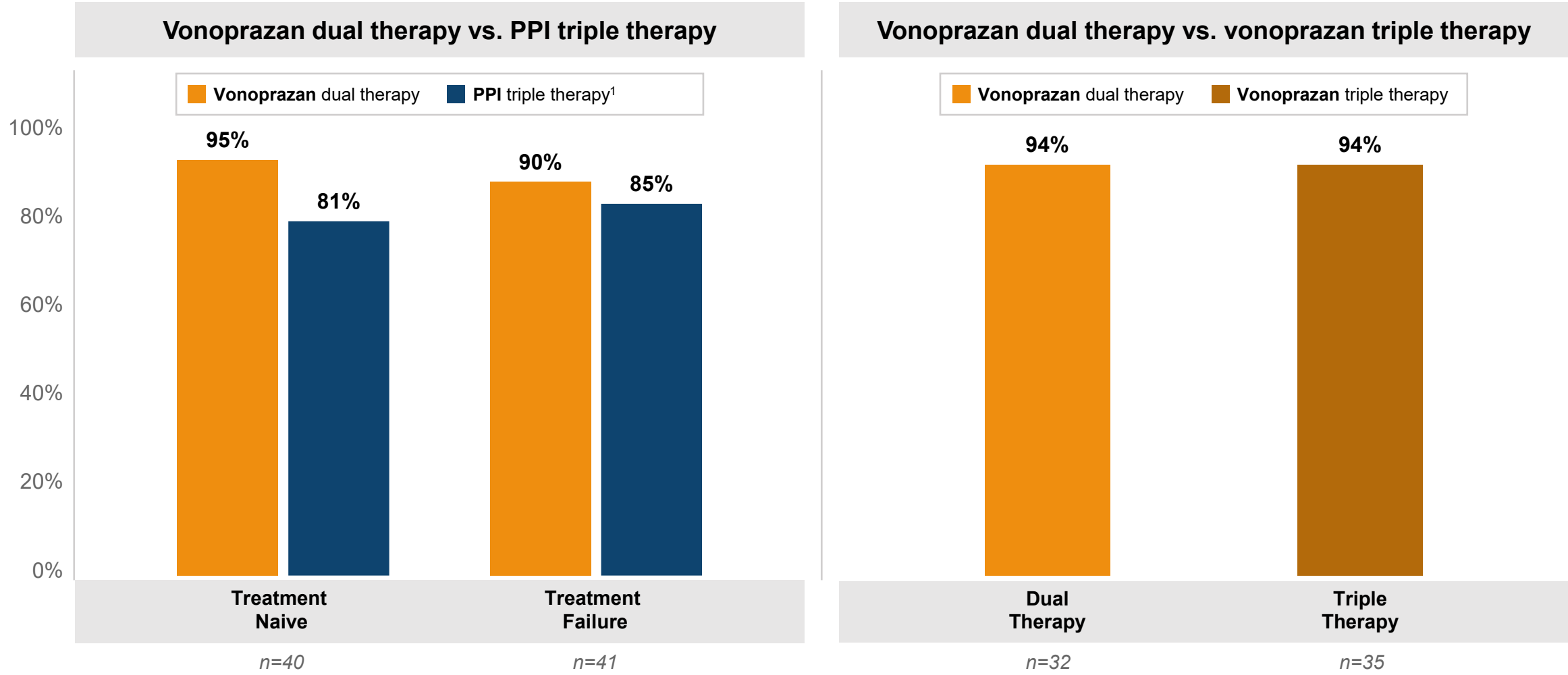
First-line triple therapy eradication rates of *H. pylori,* (combo with amoxicillin/clarithromycin)



[1] *p < 0.0001 for superiority of vonoprazan-based triple therapy to lansoprazole-based triple therapy*

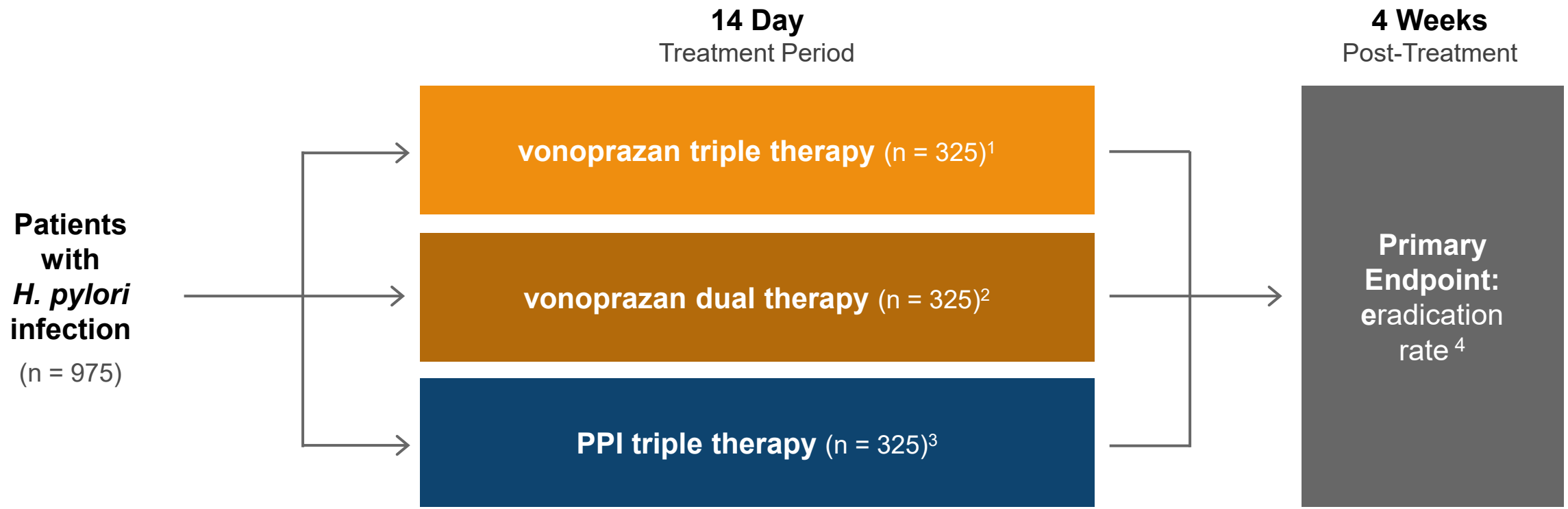
Murakami et al, Gut 2016.
Note: clinical trial met prespecified non-inferiority endpoint and post hoc superiority test

Vonoprazan demonstrated eradication rates >90% in dual therapy with amoxicillin



[1] Triple therapy includes PPI + Amoxicillin + Clarithromycin
Furuta, DDW 2016; Furuta, DDW 2018

Phathom US/Europe *H. pylori* phase 3 study design



Jan 2021 Enrollment expected to be completed; **2Q21** Topline results expected

[1]Vonoprazan 20 mg BID + amoxicillin 1 g BID + clarithromycin 500 mg BID
[2]Vonoprazan 20 mg BID + amoxicillin 1 g TID (partially blinded)
[3]Lansoprazole 20 mg BID + amoxicillin 1 g BID + clarithromycin 500 mg BID

Note: Diagnosis of infection and test of cure confirmed by 13C-urea breath test
[4] Primary analysis of non-inferiority excluding patients with infection resistant to clarithromycin and amoxicillin; key secondary analyses of superiority in patients with clarithromycin resistant infection and in all comers

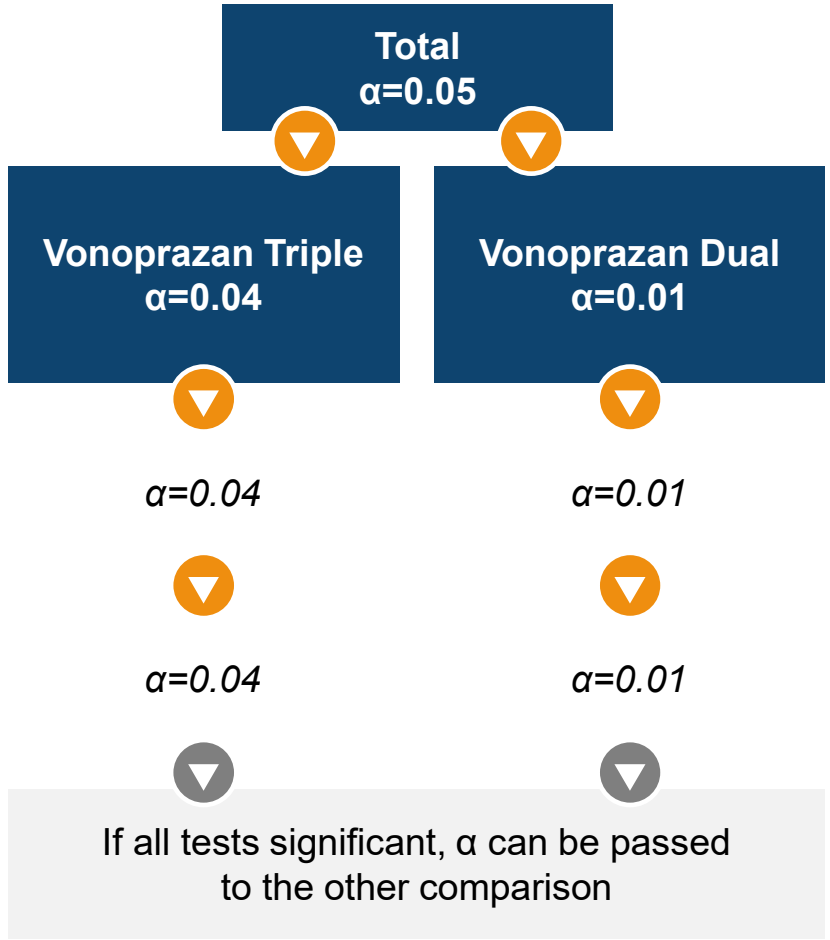
Study HP-301 statistical testing hierarchy

Primary Endpoint
Noninferiority Test (10% margin):
HP eradication rate excluding amoxicillin or clarithromycin resistant strains

Power
>90%[1]

Secondary Endpoint Testing Hierarchy - Weighted Bonferroni

1. ***Superiority Test: Power >90%[1]***
   HP eradication rate in clarithromycin resistant strains
2. ***Superiority Test: >90%[1]***
   HP eradication rate in all subjects



[1] Power for dual therapy not calculated due to limited historical data

H. PYLORI

Colin W. Howden, MD, FRCP, FACP, AGAF, FACG
Hyman Professor of Medicine and Chief, Division of Gastroenterology
University of Tennessee Health Science Center

H. pylori

Most **common chronic** bacterial infection of mankind

Most infections acquired in childhood

May be **asymptomatic**

Approximately 20% of persons infected with *H. pylori* develop related gastroduodenal disorders during their lifetime

Consensus conference concluded that ***H. pylori* infection causes gastric cancer**

Up to 36%

US adults are infected

Hooi et al, Gastroenterology 2017; 152: 420-9;
Talley, et al., American Journal of Gastroenterology. 103(3):510–514, MARCH 2008

H. pylori eradication may prevent gastric cancer

Study	Method	Results
Il Ju Choi et al 2018	***Prospective, double-blind, placebo-controlled, randomized*** trial, HP eradication therapy vs placebo, median follow up 5,9 years, South Korea	Metachronous gastric cancer in 7.2% in the treatment group vs 13.4% in the placebo group (hazard ratio in the treatment group, 0.50; 95% confidence interval, 0.26 to 0.94; P=0.03).
Il Ju Choi et al 2020	***Prospective, double-blind, placebo-controlled*** trial, first degree relatives of gastric cancer patients, n= 1838, randomized to Eradication therapy or Placebo, median follow-up of 9.2 years, South Korea	Gastric cancer in 1.2% in the treatment group and in 2.7% in the placebo group (hazard ratio, 0.45; 95% confidence interval [CI], 0.21 to 0.94; P = 0.03).
S Kumar et al 2020	Retrospective Veterans Health Administration cohort, n= 371,813 patients (median age 62 years; 92.3% male) who received a diagnosis of *H. pylori* infection from January 1, 1994, through December 31, 2018, USA	Confirmed *H. pylori* eradication after treatment reduced risk of gastric cancer (SHR, 0.24; 95% CI, 0.15-0.41; P <.001).

Under diagnosis and inadequate treatment

VA study found that not all patients with *H. pylori* were treated[1]

AMONG THOSE WHO WERE TREATED, ONLY

20%

were re-tested

- Study from Cleveland, OH also found substantial problems with establishing diagnosis, providing appropriate treatment and following up after treatment[2]
- ACG 2017 guideline recommended treating all patients who are infected and re-testing all after treatment[3]

[1] Kumar et al, Gastroenterology 2020; 158: 527
[2] Vakil et al, Gastroenterology 2019; 156: Su1266
[3] Chey et al, Am J Gastroenterol 2017; 112: 212

Indications for testing ACG Practice Guidelines 2017

Test for – and treat – *H. pylori* infection

- Active peptic ulcer disease (PUD)
- Confirmed history of PUD
- Low grade gastric MALT lymphoma
- Post-resection of early gastric cancer
- Dyspepsia
- Long-term, low-dose aspirin
- Prior to chronic NSAID therapy
- Unexplained iron deficiency
- ITP

Chey et al, Am J Gastroenterol 2017; 112: 212

Recent success rates with different regimens

Retrospective study of Rhode Island patient population evaluating the cure rate of various *H. pylori* regimens

Regimen	N	Cure Rate
Bi-based quadruple with tetracycline, 14 days	585	87%
PPI-clarithromycin-amoxicillin, 14 days	161	79%
Bi-based quadruple with doxycycline, 14 days	48	70%

Alsamman et al, Dig Dis Sci 2019; 64: 2893

Recent resistance rates from US and Europe

Author/ years of study	Resistance Rate (%)					
	Clarithromycin	Metronidazole	Amoxicillin	Tetracycline	Levofloxacin	Rifabutin
Chey 2009-11 	16	20	<2	<2	31	<2
Kumar 2009-19 	43	42	N/A	N/A	69	N/A
Graham 2017-18 	17	44	6	N/A	N/A	0
Nyssen 2013-17 	23	32	N/A	N/A	N/A	N/A

Chey et al, Am J Gastroenterol 2017; 112: 212
Kumar et al, GastroHep 2020; 2: 6
Graham et al, Ann Intern Med 2020; 172: 795
Nyssen et al Gut 2020; Epub ahead of print

Life and death of *H. pylori*

- pH is an important factor for effective eradication of *H. pylori*
  - Amoxicillin and clarithromycin are more stable at higher pH, leading to higher exposure
  - Higher pH also increases *H. pylori* replication rate

***H. pylori* MIC[1] Values as a Function of pH**			
	MIC_{90} (mg/L)		
Agent	**pH 7.5**	**pH 6.0**	**pH 5.5**
Penicillin	0.03	0.5	0.5
Ampicillin	0.06	0.25	0.5
Cephalexin	2	16	32
Erythromycin	0.06	2	8
Clarithromycin	0.03	0.06	0.25
Ciprofloxacin	0.12	0.5	2
Tetracycline	0.12	0.25	0.5

[1] MIC: minimum inhibitory concentration
Erah et al., 1997

Unmet need: problems with current treatment regimens

Growing antimicrobial resistance

- Clarithromycin especially

Complexity

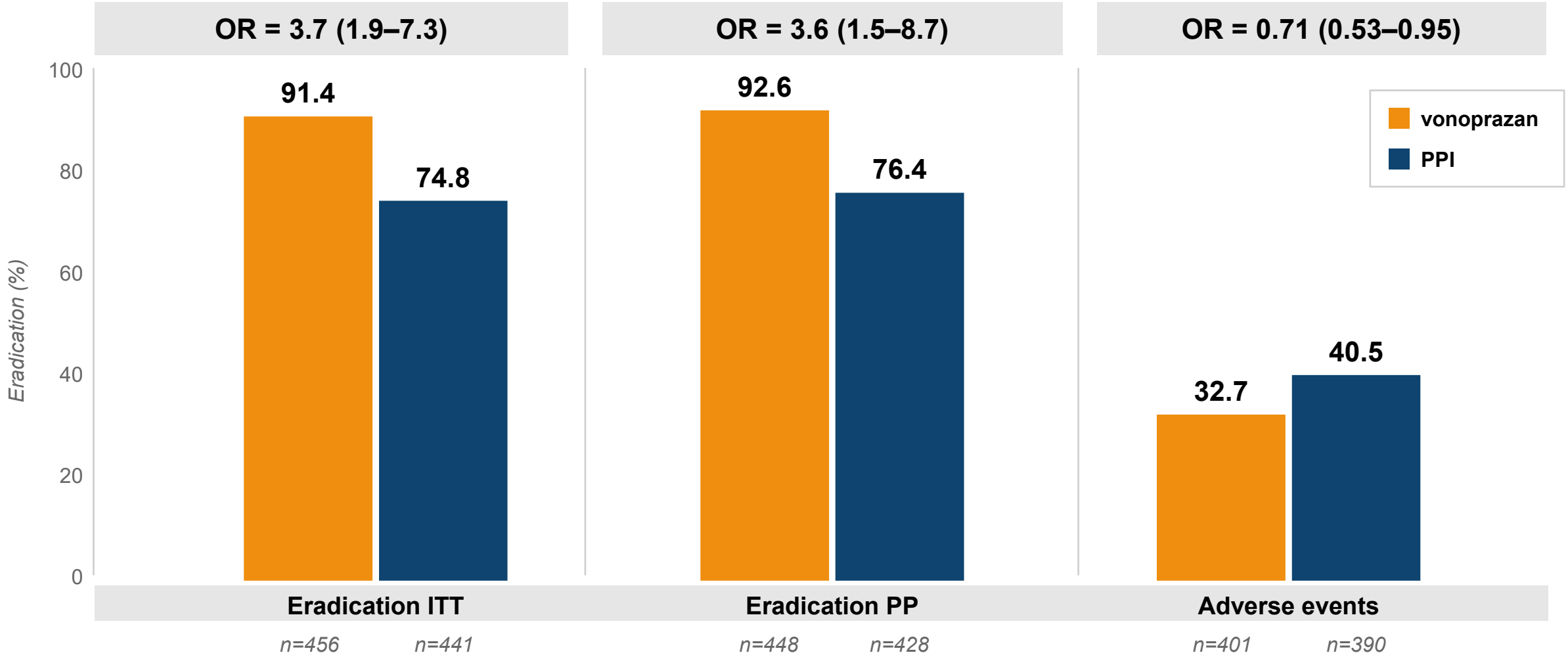
- 3 or 4 medicines
- Multiple tablets daily

Adverse effects

- Diarrhea, taste disturbance, nausea
- *C. difficile* infection

Vonoprazan vs. PPI as triple therapy for *H. pylori*

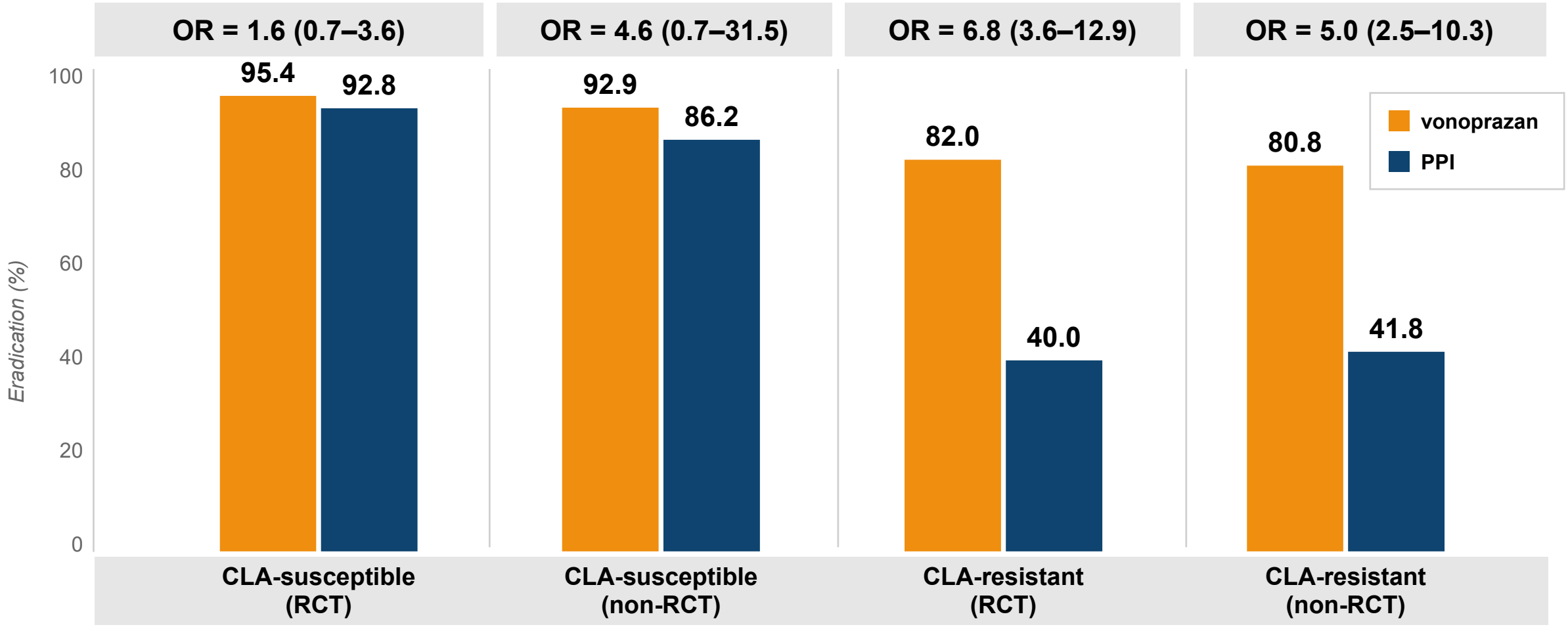
Meta-analysis of 3 RCTs (vonoprazan 20 mg vs. PPI bid, Amoxicillin/Clarithromycin x 7 Days; 897 patients)



Lyu et al, Biomed Res Int 2019; 978: 1212

H. pylori eradication by clarithromycin susceptibility

Meta-analysis of 5 Studies (2 RCTs) of vonoprazan vs. PPI as triple therapy (n=1599 patients)



Li et al, Helicobacter 2018: 23: e12495

Dual *H. pylori* therapy

Potent acid inhibition of P-CABs may allow for dual therapy with amoxicillin

POTENTIAL ADVANTAGES

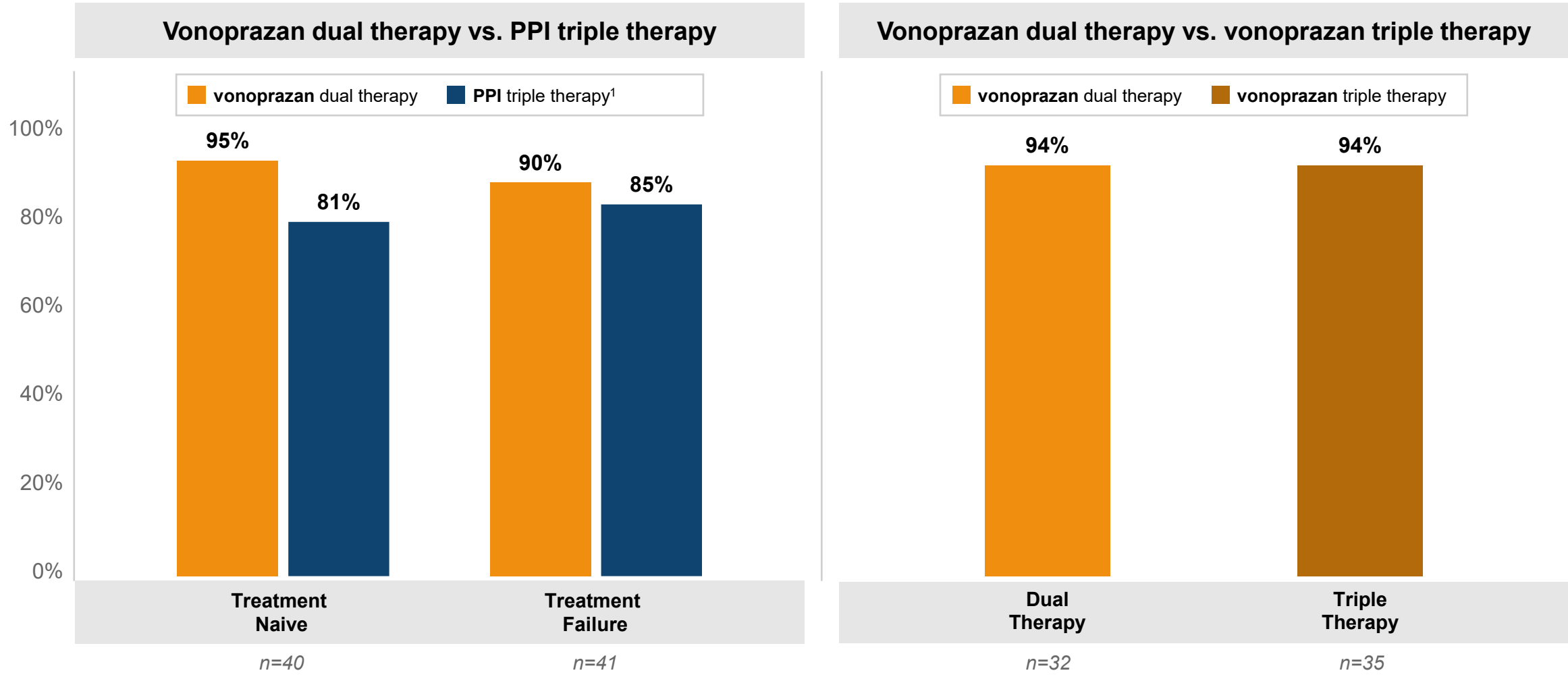
Obviates concern regarding antibiotic susceptibility (no clarithromycin)

Reduces number of antibiotics

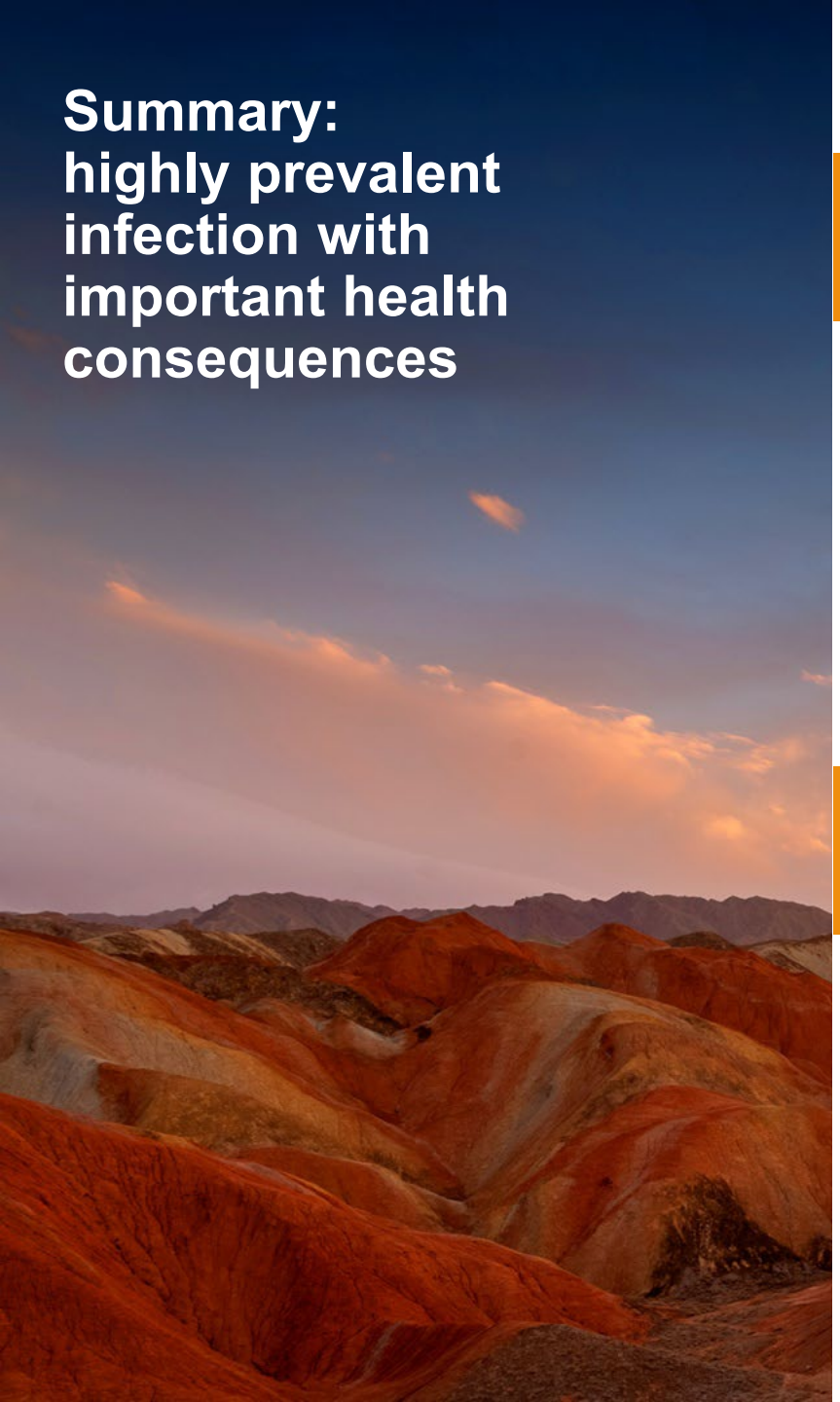
- Ease of regimen
- Antibiotic stewardship

Yang et al, Clin Gastroenterol Hepatol 2015; 13: 895

Vonoprazan demonstrated eradication rates >90% in dual therapy with amoxicillin



[1] Triple therapy includes PPI + Amoxicillin + Clarithromycin
Furuta, DDW 2016; Furuta, DDW 2018



Summary: highly prevalent infection with important health consequences

Treatment is suboptimal

- Largely still dependent on clarithromycin
- Lack of data on resistance
- Complicated regimens with 3 or 4 drugs

Prospect of simpler, efficacious vonoprazan-based regimens

- Triple therapy with high eradication rate in resistant population
- Dual combination with amoxicillin


VONOPRAZAN
FOR NERD
Azmi Nabulsi, MD
Phathom
PHARMACEUTICALS

Opportunity in Non-erosive Reflux Disease (NERD)

GERD

Frequently treated as symptomatic GERD without endoscopic evaluation

endoscopy

KEY UNMET NEEDS

Erosive Esophagitis (EE)

> **Improved efficacy**: healing/maintenance of healing of erosions and symptom control (rapid and durable)

Non-erosive Reflux Disease (NERD)

> **Improved symptom control**: speed and durability of relief

> **On-demand dosing**: speed and durability of symptom relief with flexible dosing

NERD development strategy

Clear rationale for further NERD evaluation

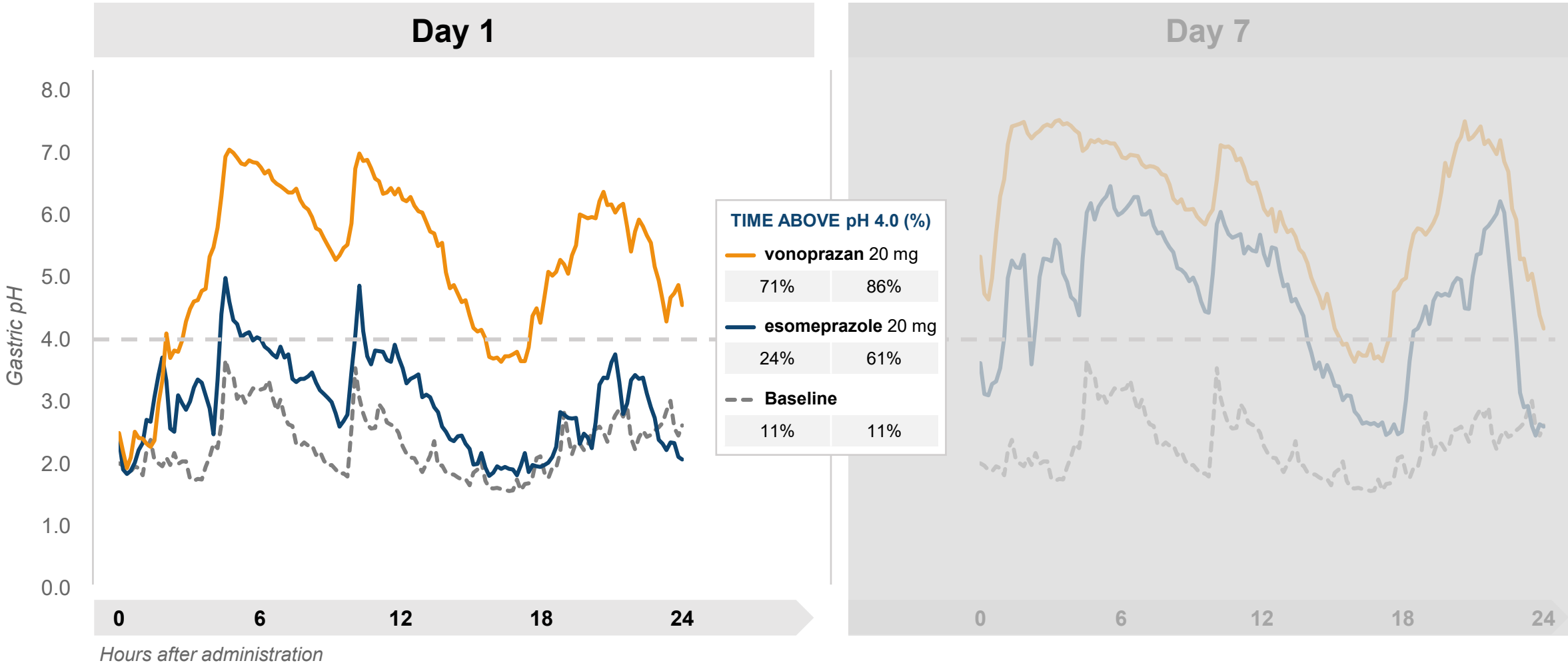
- Significant patient need for greater flexibility and convenience in management of symptoms
- Unapproved non-continuous regimens are widely used by US patients
- Pharmacological profile of vonoprazan supports potential for success
- Phathom intends to pursue:
  - a phase 2 on-demand study
  - followed by a phase 3 study evaluating both vonoprazan continuous and on-demand dosing regimens

Pharmacology of current products are not suitable for on-demand use

- PPI slow onset not well-suited to on-demand dosing
- Patients and physicians have concerns with sustained daily PPI dosing
- H2RAs have rapid onset but short duration and tachyphylaxis with repeat use

Vonoprazan pharmacologic profile (speed of onset, potency, and duration) has the potential to meet unmet needs

Vonoprazan pharmacological profile well-suited for NERD



Sakurai et al, Alimentary Pharmacology and Therapeutics, 2015; Study evaluating efficacy, rapidity and duration of acid-inhibitory effects of vonoprazan vs. two control PPIs, esomeprazole and rabeprazole, in 20 healthy Japanese adult male volunteers

Outcomes of vonoprazan NERD Japan studies

Two Japan studies with Vonoprazan:

- p=0.2310 [10mg]; p=0.0504 [20mg][1]
- p=0.0643[2]

Results trended in favor of vonoprazan

[1] Kinoshita (2016), n=827
[2] Kinoshita (2019), n=483

Enhance probability of success through specific design elements

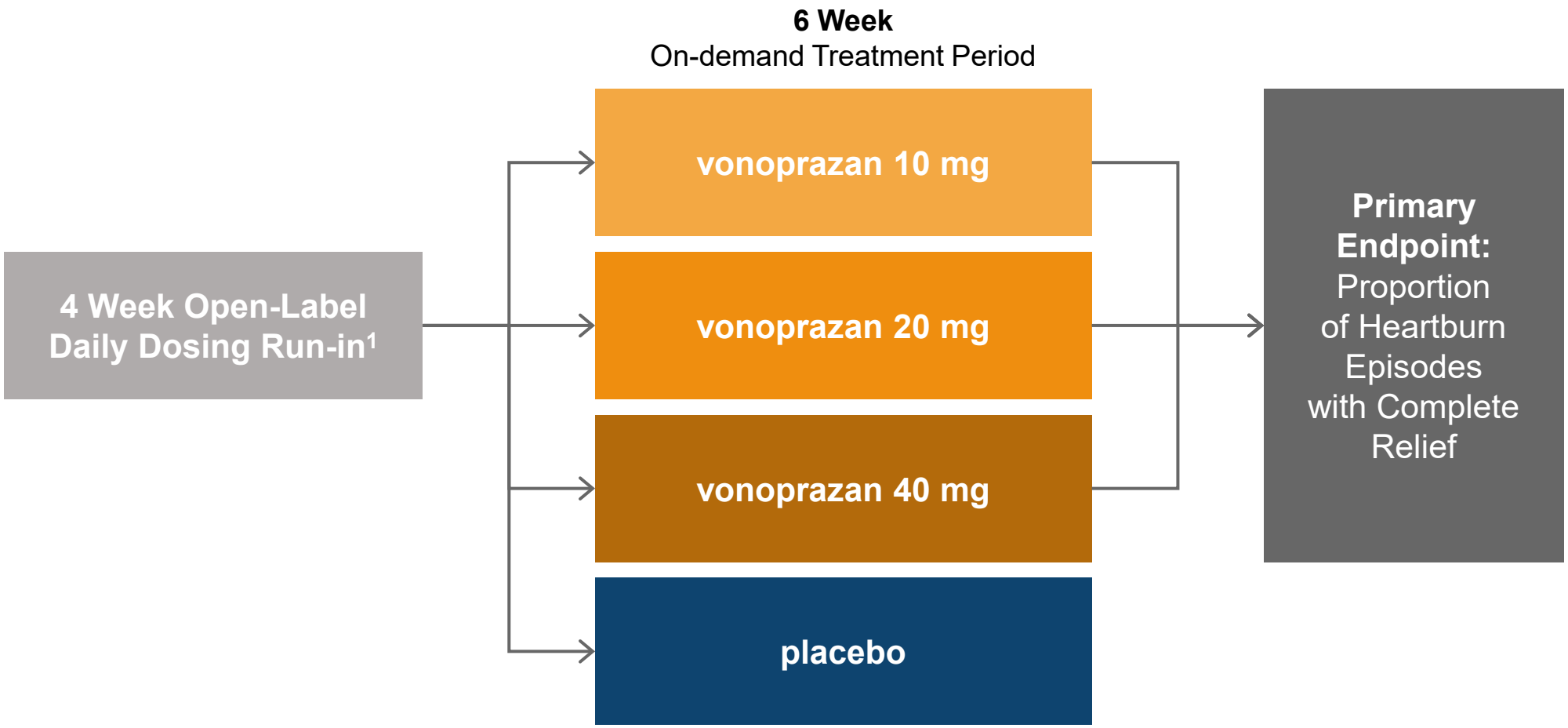
> Enroll patients at US-only trial sites where historically more consistent outcomes in NERD studies

> Focused training on identifying and excluding functional heartburn

> Use of pictograms to ensure true heartburn symptoms

> Utilize twice daily e-diary for consistent heartburn data capture

NERD phase 2 planned trial design – reviewed with FDA



Note: Trial initiation expected mid-2021

[1] Dosing initiated at onset of a heartburn episode; rescue antacid medication allowed after 3 hours of taking test medication

NERD ON-DEMAND

Ronnie Fass, MD, FACG
Professor of Medicine, Case Western Reserve University; Medical Director, Digestive Health Center; Chair, Division of Gastroenterology and Hepatology; Head, Esophageal and Swallowing Center; MetroHealth Medical Center

Phathom PHARMACEUTICALS

Non-erosive Reflux Disease – NERD

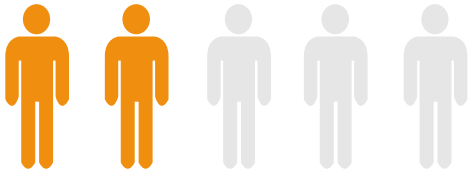
NERD

- Symptomatic reflux disease without erosions
- Episodic heartburn and regurgitation are core symptoms
  - However, symptoms can impair quality of life, particularly if nighttime heartburn is present
- Treatment focuses on relief and prevention of symptoms, thus on-demand regimens best suited

54% of GERD patients experience persistent symptoms despite daily PPI use

Results of a survey of 71,812 persons in the United States

Ever Had GERD Symptoms



Had GERD Symptoms in the Past Week

Of those taking a daily PPI:

Had Persistent GERD Symptoms

Sean D. Delshad et al. Gastroenterology 2020;158:1250–1261

Definitions of continuous vs. on-demand therapies in NERD

Continuous Therapy

Physician Driven

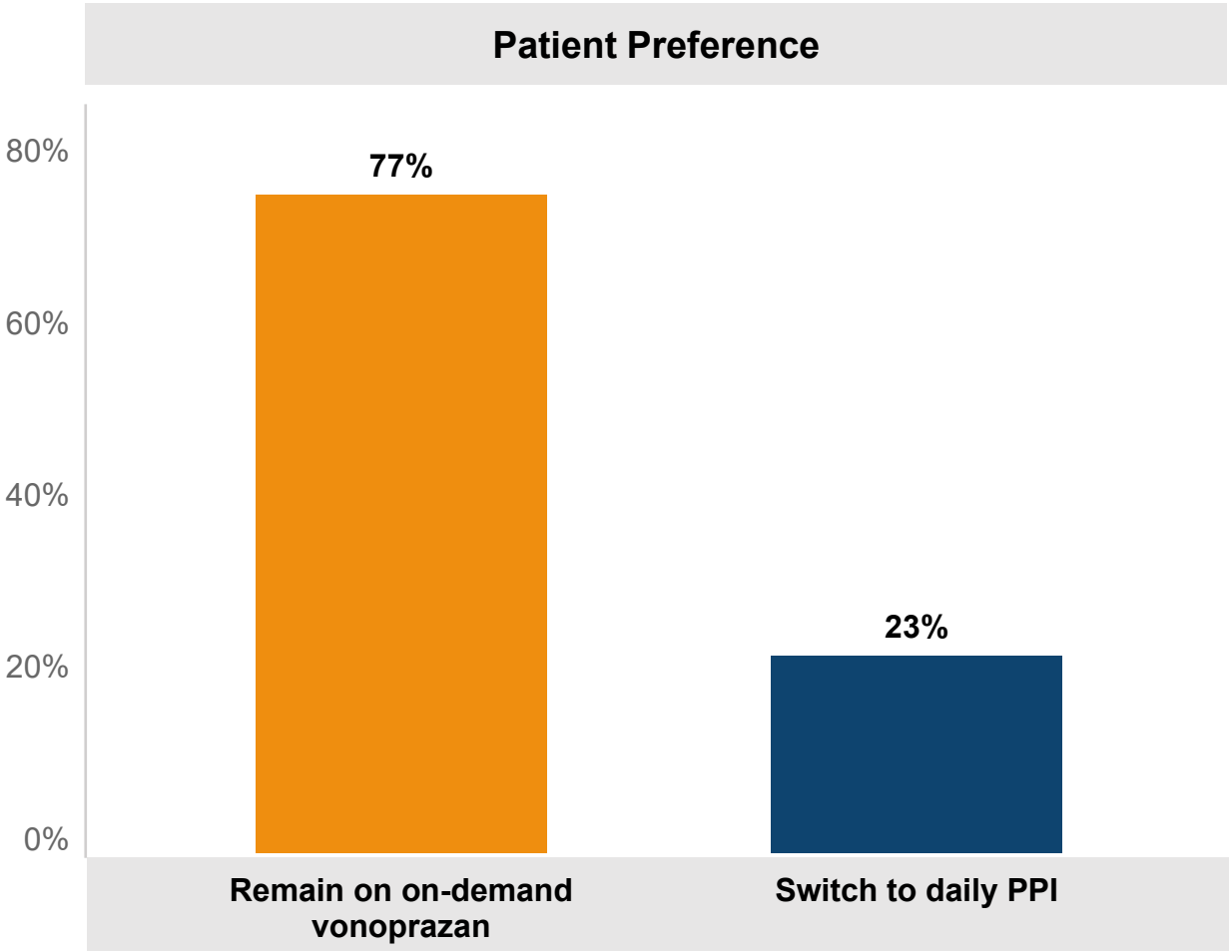
Daily therapy to prevent symptom occurrence

On-demand Therapy

Patient driven

As needed therapy to treat symptom occurrence

Higher patient preference for on-demand vonoprazan vs. daily PPI



Study Design

- Japanese study of 30 NERD patients
- Subjects identified as “Satisfied” or “Very Satisfied” with continuous daily PPI therapy
- All subjects switched to 20mg on-demand vonoprazan for 8 weeks
- Subjects were asked their preference for remaining with on-demand vonoprazan vs. switching back to daily PPI

Hoshikawa et al, Esophagus 2019

Non-continuous, off-label PPI regimens are commonly used despite being suboptimal

GERD Medication Frequency of Use (n = 9234)

Frequency of use	PPI (n = 4935)	Histamine-2 Receptor Blocker (n = 2286)	Antacids (n = 2370)
Every few months	170 (3.2)	138 (6.0)	160 (6.8)
Few times a month	266 (5.0)	225 (10.9)	375 (16.0)
Once a week	383 (7.4)	249 (10.7)	317 (12.0)
2-3 days/week	521 (9.6)	438 (18.9)	612 (29.6)
4-6 days/week	351 (6.5)	254 (11.3)	355 (13.5)
Daily	3,229 (68.1)	956 (41.0)	513 (20.3)
Unknown	15 (0.2)	26 (1.4)	38 (1.9)

31%

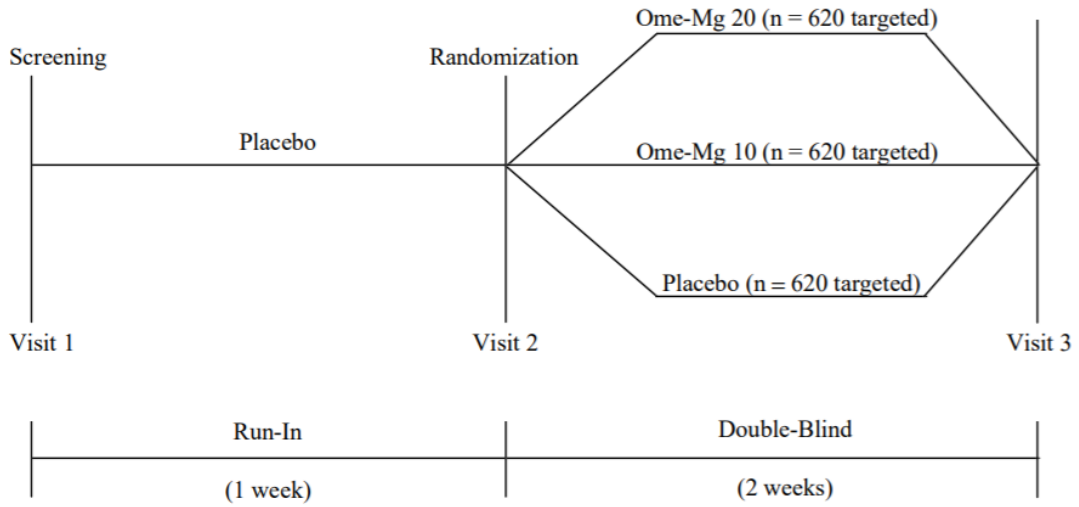
Sean D. Delshad et al. Gastroenterology 2020;158:1250–1261

PPIs are not suitable for on-demand treatment

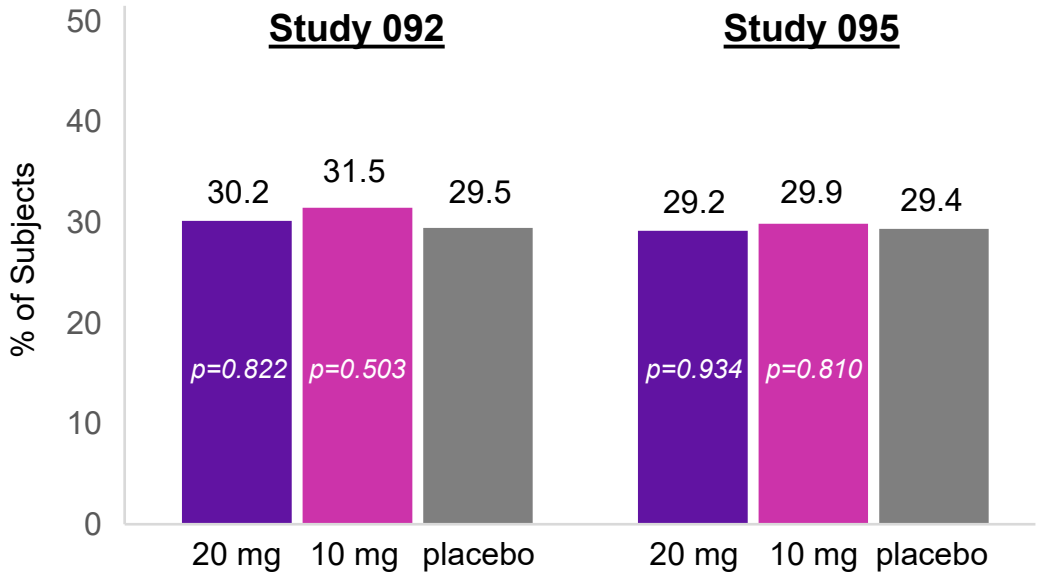
Two independent randomized trials with omeprazole in patients with episodic heartburn

- **Objective:** evaluate efficacy of omeprazole QD when dosed as needed vs placebo
- **Primary endpoint:** percentage of first episodes with sustained complete relief

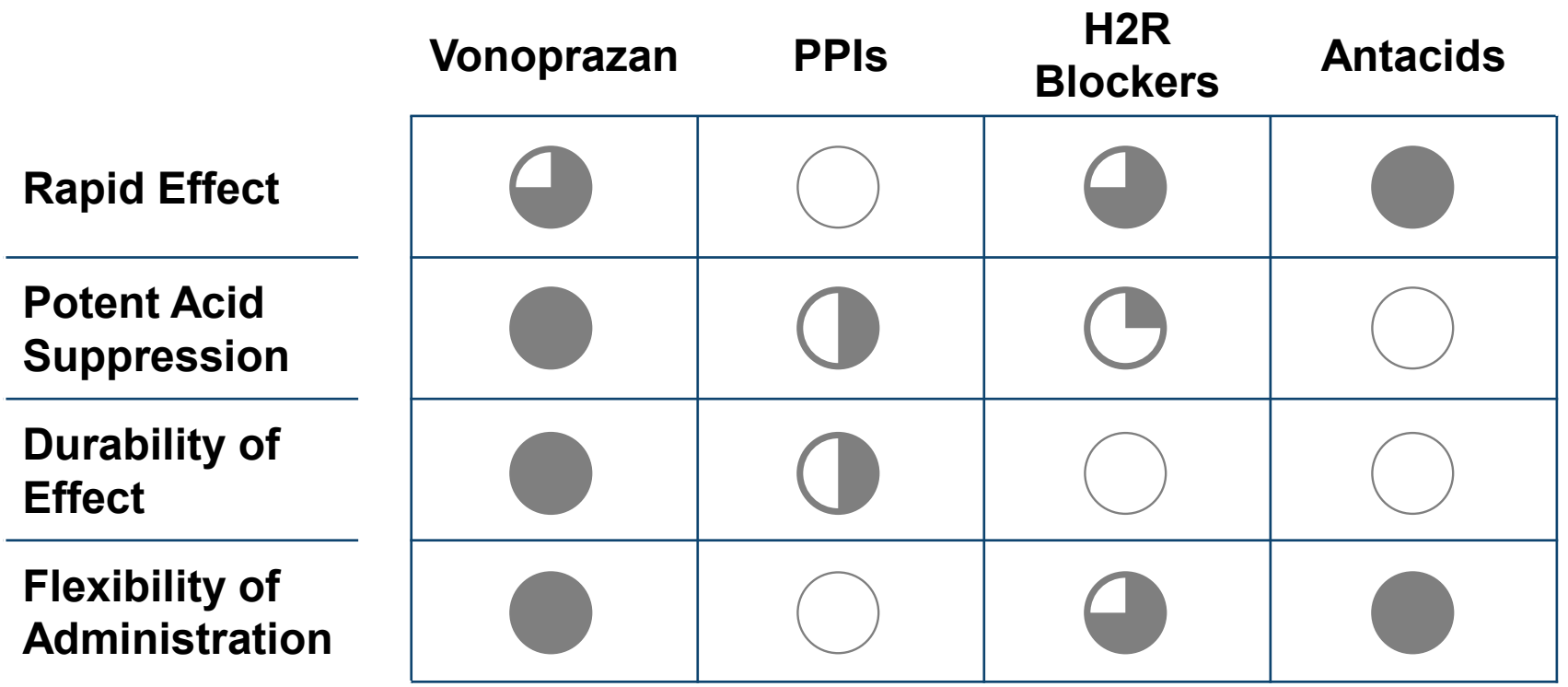
Study Design of Studies 092 and 095

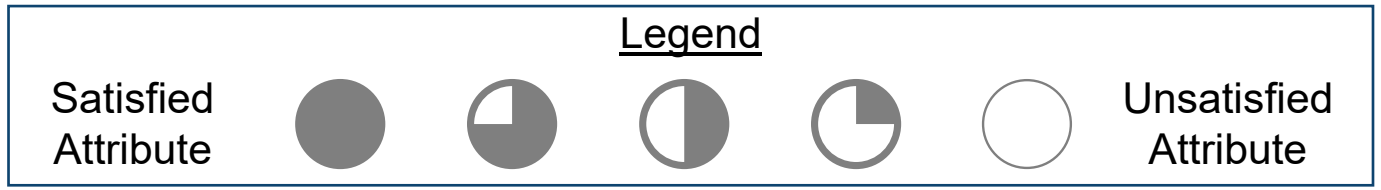


Percentage of episodes with sustained complete relief – first episode



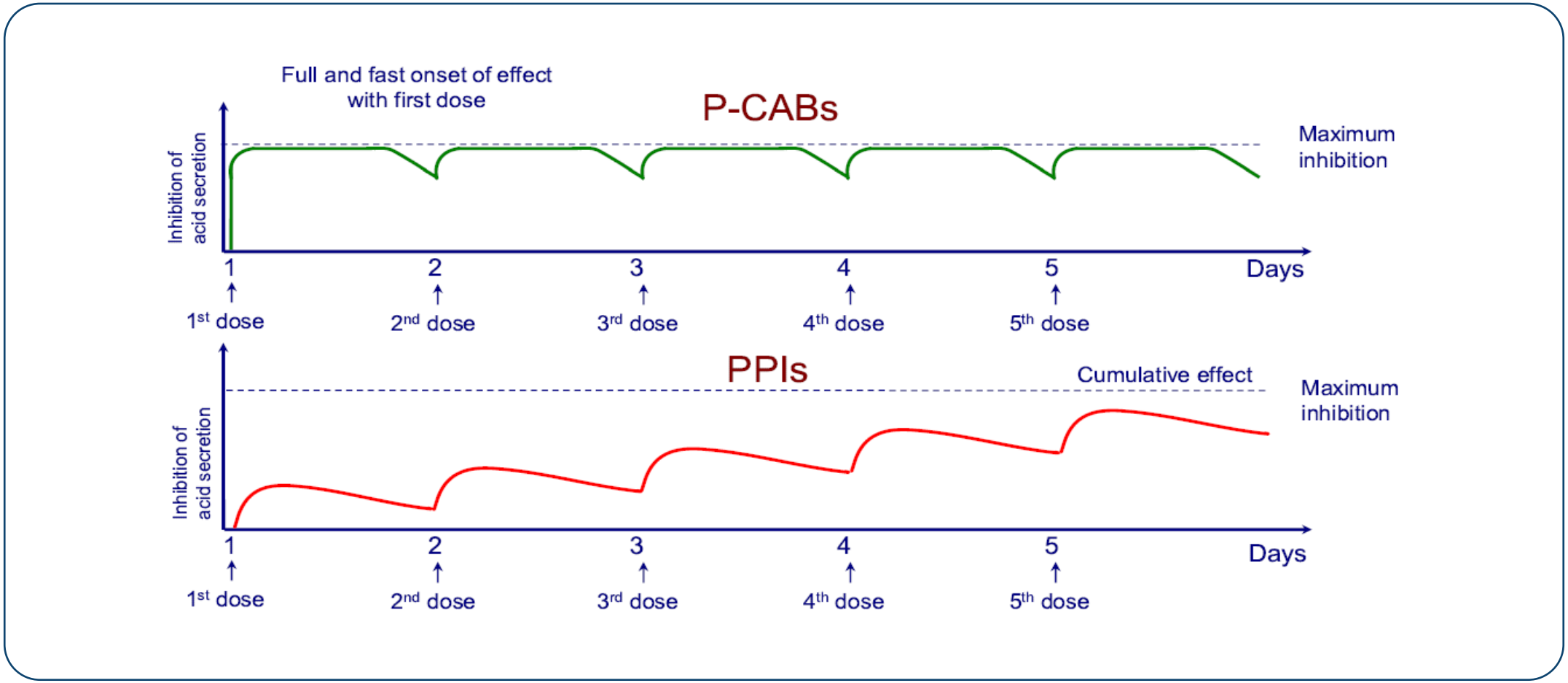
Vonoprazan's pharmacologic profile is well-suited for on-demand therapy





P-CABs: full effect at 1st dose, similar levels of acid inhibition with subsequent doses

Computer simulation



P-CAB: Potassium Competitive Acid Blocker; PPI: Proton Pump Inhibitor

Andersson K, et al. Pharmacol Ther. 2005;108;294:307

Hunt RH & Scarpignato C. Curr Treat Options Gastroenterol. 2018;16:570-590.

Summary: potential of vonoprazan for treatment of NERD

- Currently available options for on-demand treatment of NERD (antacids, H2 blockers) have limited clinical efficacy
- On-demand treatment with PPIs is not FDA approved
- The pharmacology of PPI's does not support an adequate on-demand treatment profile
- Vonoprazan pharmacology supports potential development as an effective on-demand treatment option for NERD patients


NERD DEVELOPMENT PROGRAM
Azmi Nabulsi, MD
Phathom PHARMACEUTICALS

Delivering on the potential of vonoprazan

	Target Indications	Phase 1[1]	Phase 2[1]	Phase 3	Expected Milestones
Vonoprazan	**GERD**			pHalcon ee (A research study for *Erosive Esophagitis*)	
	Healing of Erosive Esophagitis (EE) and relief of heartburn				*Enrollment complete*
	Maintenance of healing of Erosive Esophagitis (EE) and relief of heartburn				***Topline results 2H21***
	Treatment of heartburn associated with Non-erosive Reflux Disease (NERD)				*Phase 2 FSI mid-21*
Vonoprazan + antibiotics	***H. pylori* treatment**			pHalcon hp (A research study for *H. pylori Infection*)	
	Dual therapy (vonoprazan + amoxicillin)				*Phase 3 LSI Jan 2021*
	Triple therapy (vonoprazan + amoxicillin + clarithromycin)				***Topline results 2Q21***

Phathom has development and commercialization rights to vonoprazan in the United States, Europe, and Canada

[1]Phase 1 and 2 studies in healing of Erosive Esophagitis, maintenance of Erosive Esophagitis, and *H. pylori* treatment conducted by Takeda


COMMERCIAL
OPPORTUNITY
Martin Gilligan
Phathom
PHARMACEUTICALS

After 25 years: innovation that matches unmet needs

H2 ANTAGONISTS

Introduced in **1970s**

Tagamet

Zantac®

Pepcid®

> **~$3.5B** peak US sales

PPIs

Introduced in **1980s**

PREVACID® LANSOPRAZOLE

Prilosec

Nexium® esomeprazole

AcipHex®

PROTONIX® (pantoprazole sodium)

> **~$12.5b** peak US sales

25 YEARS

- > **Most GERD patients believe they can get better control over their symptoms**[1]
- > **GERD patients try 2 or more therapies to control symptoms**[1]
- > **2 out of 3 physicians are concerned about long-term use of PPIs**[2]

P-CABs

Introduced in Japan **2015**

Takecab® (vonoprazan)

> **>$725M** net sales in Japan for the 12 months ended Sep. 30, 2020[3]

[1] SRI, June 2020 | Qualitative patient interviews
[2] SRI, August 2020 | N= 83 US HCPs (41 GI & 42 PCP)
[3] US dollars based on the September 30, 2020 conversion rate of 0.0095 dollars to one yen

Japanese experience signals potential success for the US

Current US market has many similarities to the Japanese market at launch of Takecab

Heavily genericized market

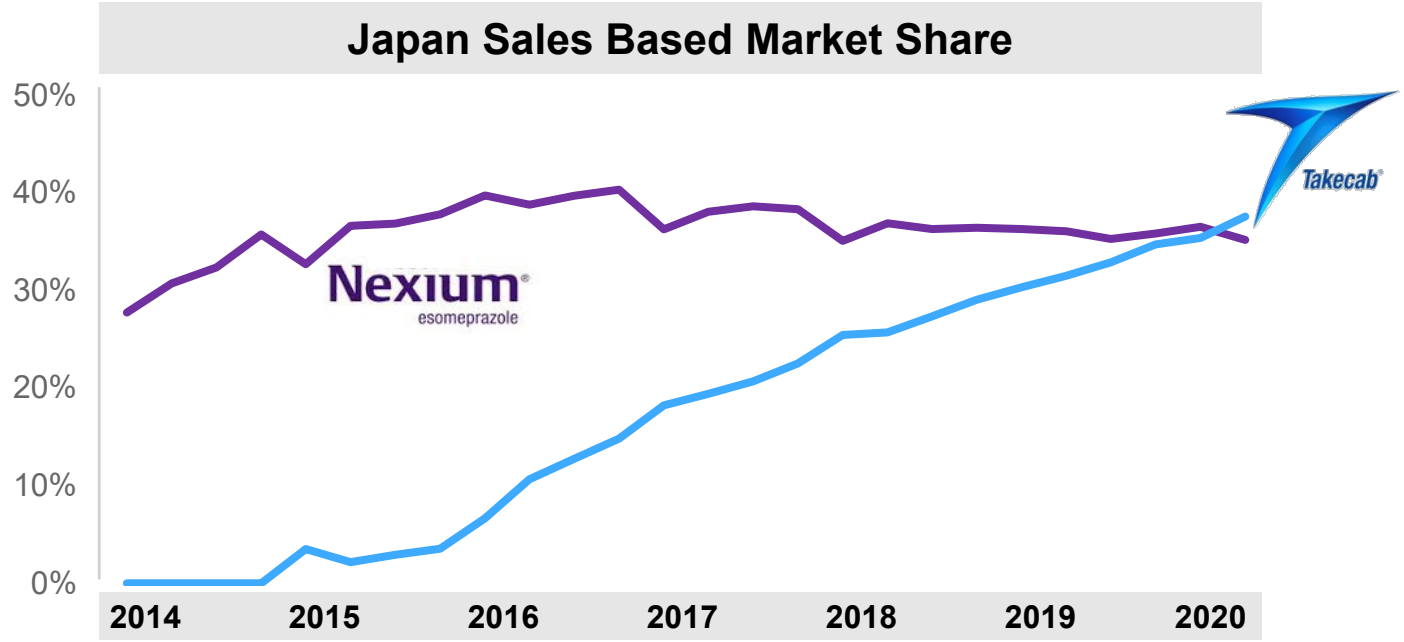
PPI dissatisfaction/patient switching

Declining *H. pylori* eradication rates

MARKET LEADER IN JAPAN

DOCUMENTED COST-EFFECTIVENESS

PREMIUM BRANDED PRICE



Japan Experience

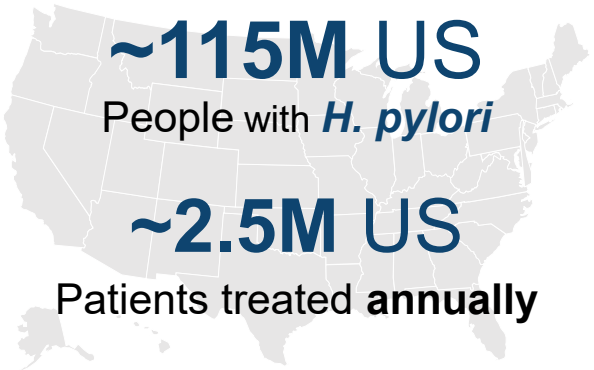
- Vonoprazan has achieved >$725M in net sales[1] and 38% value-based market share driven predominantly by volumetric gains from generic competitors
- Majority of vonoprazan sales are in GERD
- Vonoprazan-based regimens achieved ~80% *H. pylori* market share in 2nd full year

[1] Net sales for the 12 months ended September 30, 2020 and corresponding conversion rate of 0.0095 USD : 1 JPY; IQVIA Quarterly MIDAS data (as of 2Q20); Deguchi et al Digestion 2019

Significant opportunities to bring value to patients, physicians, and payors

> **"People want to get better fast. They want instant results. They want to see that something's working – it encourages them to take it, to be compliant if they see that they're feeling better." – PCP**

H. pylori

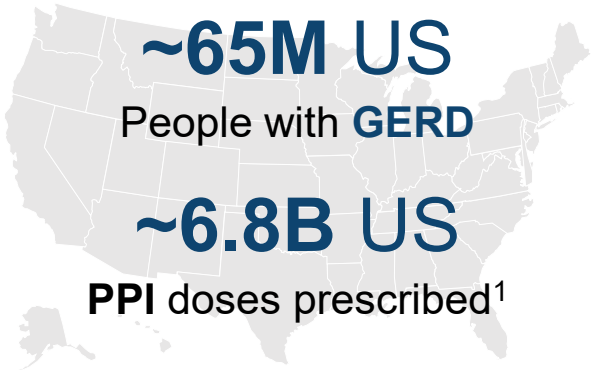


~115M US
People with ***H. pylori***

~2.5M US
Patients treated **annually**

- *H. pylori* designated as a Class I carcinogen by WHO and Qualifying Pathogen under FDA GAIN Act
- **<80%** eradication due to antibiotic resistance
- Antibiotic potency increases at higher pH

Erosive Esophagitis / GERD



~65M US
People with **GERD**

~6.8B US
PPI doses prescribed[1]

- **~15-45%** inadequately treated with PPIs
- Many patients experience breakthrough heartburn and recurrence of erosions while on PPIs

Hooi Gastroenterology 2017; Graham et al 2018; Erah et al 1997; El-Serag APT 2010; El-Serag Gut 2014; IQVIA data Oct 2020
[1]For the 12 months ended October 31, 2020

Minimal US branded competition anticipated across all potential indications

UNCONTESTED PIPELINE

> No products in late-stage development in the US or EU

LACK OF NOVEL SOLUTIONS

> Other products introduced in the US are variations of old regimens

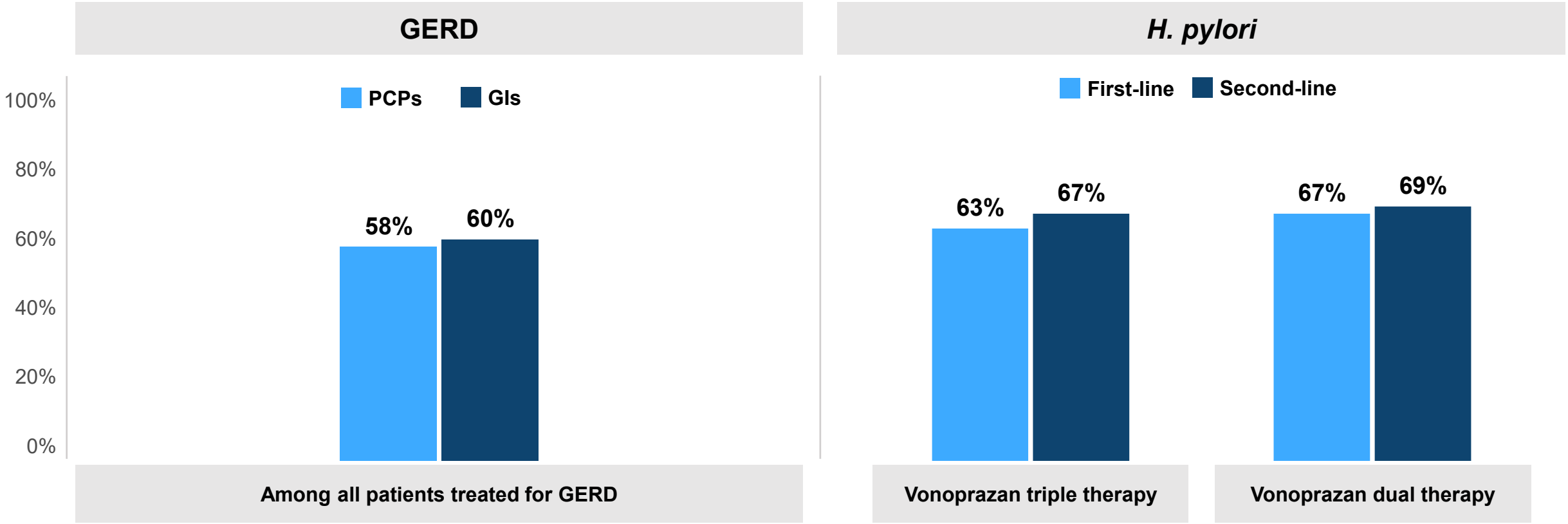
CATEGORY DIFFERENTIATION

> P-CABs in development in Asia have a clinical profile similar to PPIs and/or a short half-life and a different chemical structure compared to vonoprazan

Promotionally sensitive market with little to no branded competition + **Minimal competition for share of voice** + **Innovation starved market**

US physicians express strong preference to prescribe vonoprazan

US physician preference share, %

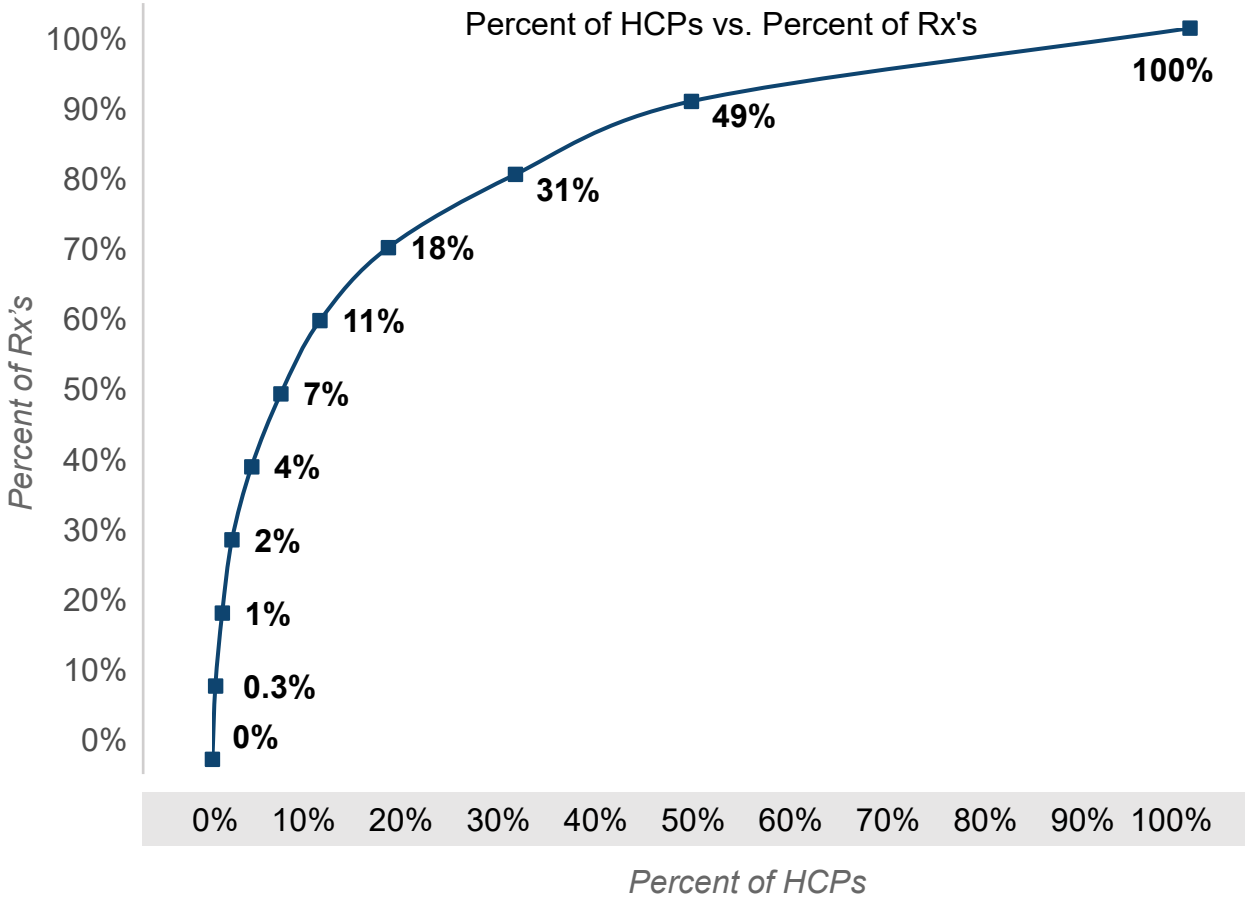


2019 US SURVEY OF 100 GASTROENTEROLOGISTS AND 100 PRIMARY CARE PHYSICIANS

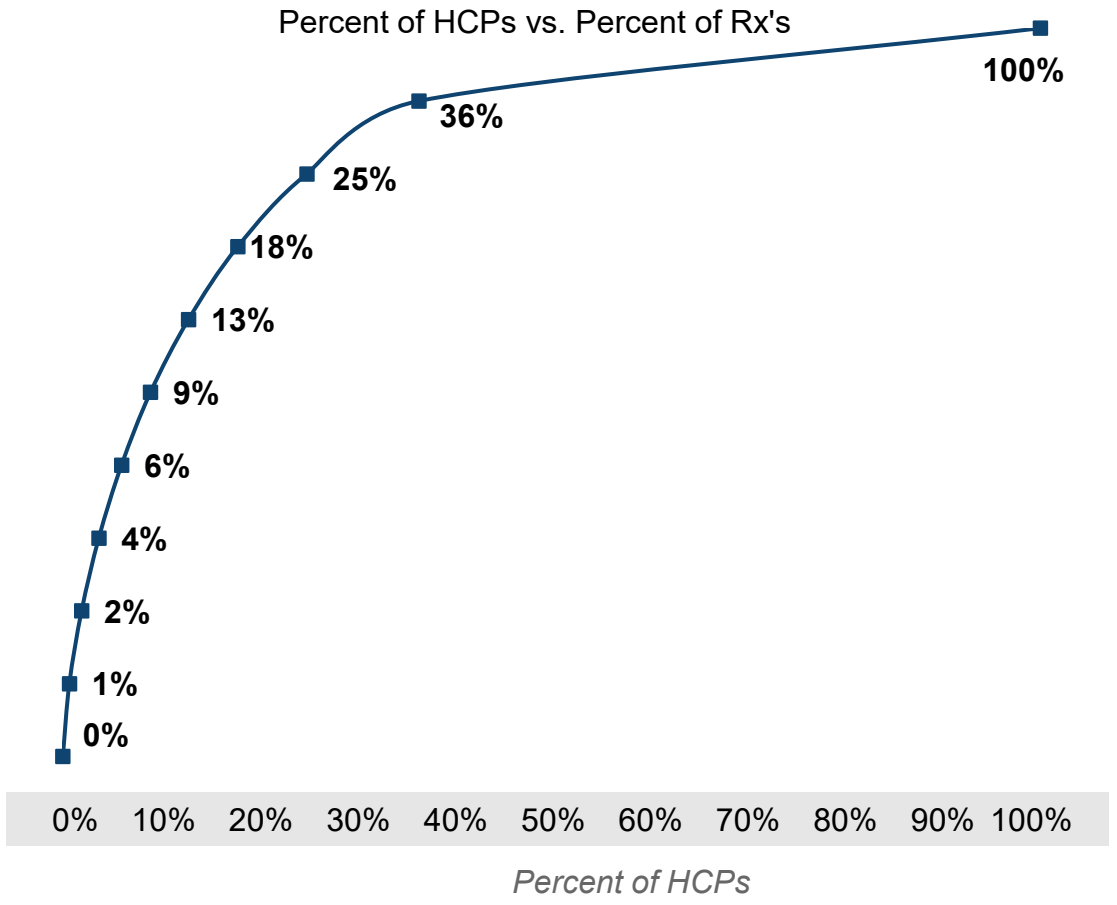
Life Science Strategy Group, August 2019 | N= 200 US HCPs (100 GI & 100 PCP)

Highly concentrated prescriber base allows for focused targeting of impactful HCPs

~20% of Physicians Write 70% of *H. pylori* Scripts



~20% of HCPs Write 70% of GERD Scripts



Symphony Health claims analysis (Jan 2019 – Dec 2019)

Success begins with building a leading and experienced organization

Sales

Joe Jones

Ironwood

- US Commercial Brand Lead, LINZESS
- Area VP, Sales, LINZESS
- Regional Sales Manager

AstraZeneca

- HCP Brand Leader, CRESTOR

Market Insights

Christine Fischer

Regeneron

- Exec. Dir, Customer Insights

Sanofi

- Sr. Dir, CV Market & Customer Insights

Merck & Co.

- Sr. Dir, Global Market Research & Analytics

Marketing

Susan Kim, PharmD

Amgen/Celgene

- Exec. Dir, US Marketing, OTEZLA
- Exec. Dir, Global Marketing, GI

Bausch + Lomb

- Director, Global Marketing

Merck & Co.

- Brand Lead, Global Marketing, REMICADE, GI

Medical Affairs

Philippe Brudi, MD

Liquidia Technologies

- Head, Medical Affairs

Merck & Co.

- Exec. Dir, Global Brand Strategy Medical Affairs Diabetes & Cardiovascular
- Sr. Dir, Global Medical Affairs Cardiovascular
- Regional Sr. Dir, Medical Affairs Atherosclerosis

Market Access

Mark Devlin

Allergan PLC

- SVP, Managed Markets

Forest Laboratories

- SVP, Managed Markets, Gov't & Policy
- VP, Sales/Operations
- VP, Sales

Pursuing access to large patient segments with minimal restrictions

Large patient population in need

- ~65M people with GERD; ~50% of treated patients progress lines of therapy annually
- Declining *H. pylori* eradication rates with current regimens

Health system utilization

- Erosive esophagitis recurrence and *H. pylori* eradication failures utilize additional healthcare resources

Lack of alternatives

- 25+ years of lack of alternatives in GERD

Access drivers[1]

- Health plan objectives to meet unmet needs
- Clinical superiority vs. PPIs
  - Lower Erosive Esophagitis recurrence rates
  - Faster Erosive Esophagitis healing
  - Greater *H. pylori* eradication
- Advanced pharmacology
  - Rapid, potent, and durable acid control
- Novel MOA – different from all other approaches

Potential branded price commensurate with value

- Value proposition to address unmet need
- Market analogues have achieved broad access
  - e.g., Dexilant (PPI with a non-differentiated MOA): WAC of $9.69/dose[2]

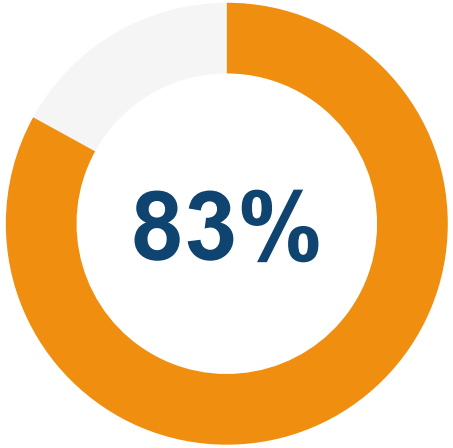
[1] Subject to data from ongoing phase 3 studies
[2] First Databank database as of Dec 2020

Key drivers of eradication failure: complexity and antibiotic resistance

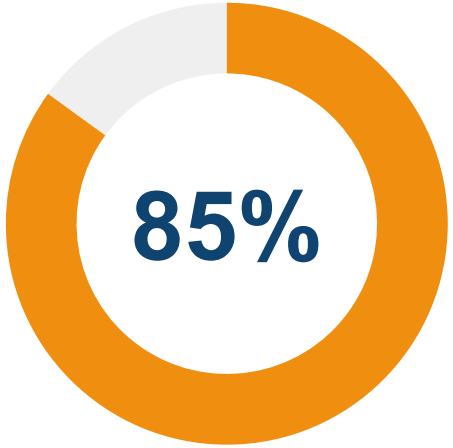
Percentage of HCPs that agree with statement[1]

Patients fail *H. pylori* Eradication due to….

H. pylori resistance to antibiotics



Lack of drug therapy compliance due to complexity



“Long-lasting and superior eradication, those are huge for us. Right now, effective treatment rates are maybe 75%.” – GI[2]

[1] Life Science Strategy Group, August 2019 | N= 200 US HCPs (100 GI & 100 PCP) | Top Three Box on 1-7 Scale
[2] New Leaf Research, October 2020 | Qualitative HCP interviews

H. pylori patient experience demonstrates the reality of the unmet need

H. pylori patient experience demonstrates the reality of the unmet need

- Most patients contact an HCP within a few months of symptoms
- Half found the regimen easy and the other half found it confusing
- When starting treatment, patients expected the infection would be eradicated and they would have no more symptoms at the conclusion of treatment
- One-quarter of patients continue to use PPIs

The anticipated vonoprazan *H. pylori* launch

Aspiring to solve challenges and building the future

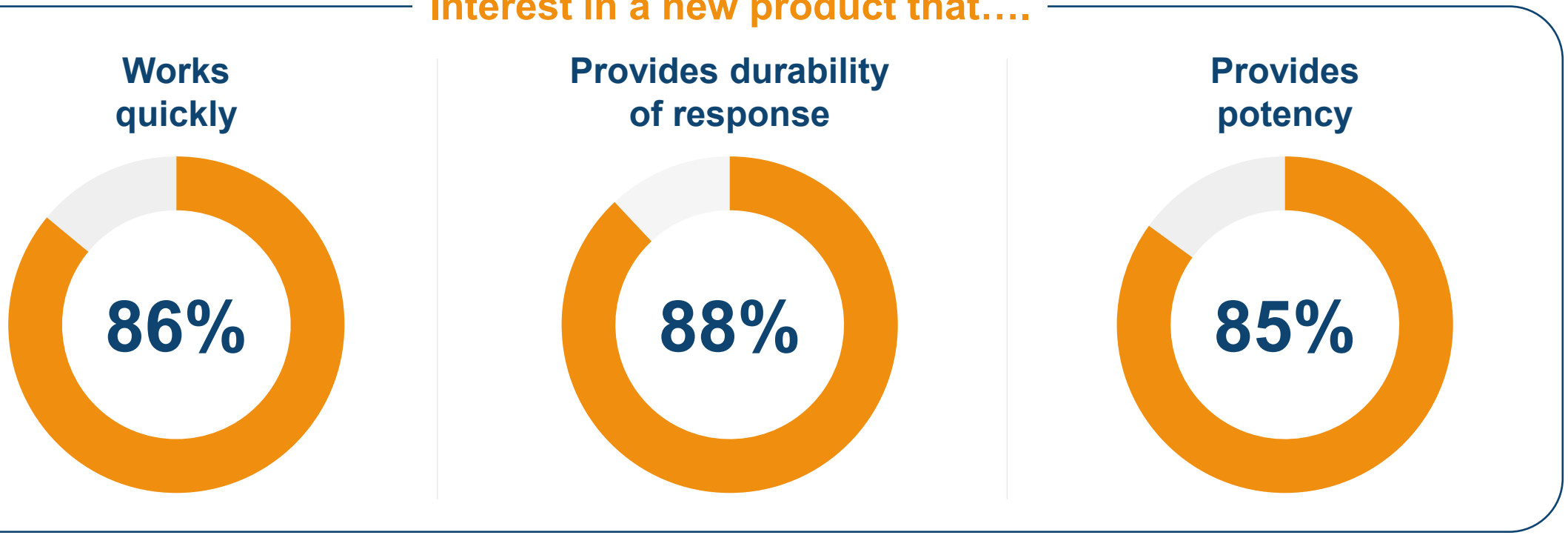
Reverse the curve of declining eradication rates

Set a strong launch foundation and ramp for Erosive Esophagitis

Physicians interested in new therapies that are rapid, durable and potent

Percentage of HCPs that agree with statement[1]

Interest in a new product that….



> **“Most PPIs can take three to five days, but could take up to six to eight weeks, to work in some patients. There's a clinical urgency for rapidity.” – GI[2]**

[1] SRI, August 2020 | N= 83 US HCPs (41 GI & 42 PCP) | Top Three Box on 1-7 Scale
[2] New Leaf Research, October 2020 | Qualitative HCP interviews

Erosive Esophagitis patients' unmet needs lead to clear opportunities for vonoprazan

ONSET

At start of treatment, patients expect quick symptom relief (heartburn) and no further need for OTCs

Vonoprazan's potential speed of symptom relief and Erosive Esophagitis healing

PHYSICIAN VISIT

Patients do not request a specific product

Opportunity to activate patients through DTC

DOSING

Patients generally take their PPI without food (which is required for activation)

Vonoprazan is not dependent on food to achieve acid suppression

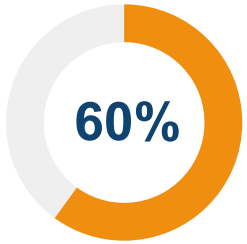
EXPERIENCE

It takes patients up to 3 weeks to experience partial or full symptom relief, and many require BID dosing for continued symptoms

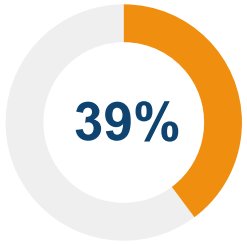
Vonoprazan's potential for rapid and improved symptom relief

HCPs express high enthusiasm for potential vonoprazan NERD indications

Current State

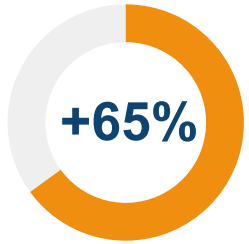


of NERD patients are treated long-term with a PPI



of HCPs have patients supplement PPIs with OTCs due to lack of immediate relief

HCP Top Interest for New Therapy



of HCPs interested in a new class of NERD therapy that

- Works fast to relieve symptoms
- Provides durability of response
- Is indicated for on-demand use

High intention to prescribe vonoprazan in three key patient types

- **New Patients**
- **Non or Partial PPI Responders**
- **Long-term PPI patients appropriate for vonoprazan on-demand**

Note: Questions regarding product characteristics referred to “Product X” and did not reference “vonoprazan”
SRI, August 2020 | N= 83 US HCPs (41 GI & 42 PCP)

HCPs see vonoprazan differently from PPIs… potent acid suppression that has the potential to deliver

- Fast action
- Superior efficacy
- Durability

Significant commercial opportunity

Opportunity

HP + EE + NERD

Large Populations + Unmet Need

Strong Physician Preference + Concentrated High Prescribers

Minimal Branded Competition + High Share of Voice

Novel Profile + Potential for Premium Price


FINANCIAL UPDATE
Todd Branning
Phathom
PHARMACEUTICALS

Financial highlights

Cash and cash equivalents (as of 9/30/2020)[1]	$226.4M
Debt (as of 9/30/2020)[1]	$50.0M
Common shares issued (as of 9/30/2020)[1]	28,964,506

[1] September 30, 2020 Form 10-Q


Q&A
Phathom
PHARMACEUTICALS


CLOSING REMARKS
Terrie Curran
Phathom
PHARMACEUTICALS

Expected key milestones 2021: a catalyst rich year

Jan 2021
- Complete enrollment in Ph 3 PHALCON HP-301

2Q21
- Top-line Ph 3 results for PHALCON HP-301

mid-21
- Initiate Ph 2 NERD on-demand trial

2H21
- *H. pylori* NDA submission
- Top-line Ph 3 results for PHALCON EE-301

2022
- Topline Ph 2 results for NERD on-demand trial
- *H. pylori* NDA approval and US launch
- Erosive Esophagitis NDA submission

2023
- Erosive Esophagitis NDA approval and US launch

Phathom PHARMACEUTICALS

Going Beyond

to advance treatments for patients with acid related disorders

Vonoprazan

- Significant unmet medical need
- Large innovation starved markets
- Differentiated MOA and product profile
- De-risked asset with established success in Japan
- Topline results from two pivotal trials in 2021
- HCP and patient enthusiasm