

Vonoprazan Efficacy Across BMI Subgroups in Non-Erosive Reflux Disease

Catiele Antunes, MD¹, Gaurav Ghosh, MD², Loren Laine, MD, FACP^{1,3}, Rena Yadlapati MD, FACP⁴, Yu-Ming Chang, MD⁵, Hillary Graham, MS⁵, Eckhard Leifke, MD⁵, Philip Katz, MD, MACG²

¹ Yale School of Medicine, New Haven, CT, USA. ² Weill Cornell Medicine, New York, NY, USA. ³ VA Connecticut Healthcare System, West Haven, CT, USA. ⁴ University of California San Diego, La Jolla, CA, USA. ⁵ Phathom Pharmaceuticals, Buffalo Grove, IL, USA.

Background

- Obesity is associated with greater reflux symptom burden and severity. Current guidelines recommend weight loss as part of gastroesophageal reflux disease (GERD) management for patients with obesity.¹
- Obesity affects more than 40% of adults in the United States, underscoring the clinical relevance of evaluating treatment efficacy across body mass index (BMI) categories.²

Objective

- To assess whether the potassium-competitive acid blocker (PCAB) vonoprazan maintained efficacy in individuals with obesity and symptomatic NERD.

Methods

- In this post hoc analysis of a Phase 3 randomized trial, adults with heartburn ≥ 4 days/week and no erosive esophagitis were randomized to placebo or vonoprazan 10 mg or 20 mg once daily for 4 weeks.
- Electronic diaries captured daytime and nighttime symptoms twice daily.
- The mean percentage of 24-hour heartburn-free days was summarized, as were the percentages of heartburn-free days and heartburn-free nights, separately.
 - Generalized linear models were conducted separately within BMI subgroups to evaluate 24-hour, daytime, and nighttime heartburn-free days, with each model adjusted for treatment group and baseline heartburn frequency and severity corresponding to the specific heartburn-free endpoint; models were also adjusted for glucagon-like peptide-1 (GLP-1) agonist use in high-BMI subgroups, and treatment-by-BMI interactions were assessed.
- Patient Assessment of Upper Gastrointestinal Disorders Symptoms Questionnaire (PAGI-SYM) heartburn/regurgitation scores and regurgitation-specific scores were assessed at baseline and Week 4.
 - The regurgitation score was defined as the mean of Q18 (regurgitation during the day), Q19 (regurgitation when lying down), and Q20 (bitter, acid, or sour taste in the mouth).
- Outcomes were analyzed separately in patients with a BMI ≥ 30 kg/m² versus BMI < 30 kg/m², with a sensitivity analysis in those with BMI ≥ 35 kg/m².

Results

- Among 772 individuals included in the study, 341 met criteria for obesity.
- Baseline demographic and clinical characteristics were similar across BMI subgroups; concomitant GLP-1 agonist use was more common among individuals with higher BMI (Table 1).

Table 1. Baseline Demographic and Clinical Characteristics by BMI Subgroup

	BMI <30 N=428	BMI ≥30 N=341	BMI ≥35 N=170	ITT Population N=772
Age, mean (SD) years	50.3 (15.6)	51.6 (12.7)	50.5 (12.7)	50.9 (14.4)
Sex, n (%)				
Female	276 (64.5)	249 (73.0)	128 (75.3)	527 (68.3)
Male	152 (35.5)	92 (27.0)	42 (24.7)	245 (31.7)
Concomitant GLP-1 use, n (%)	5 (1.2)	26 (7.6)	14 (8.2)	31 (4.0)
Hiatus Hernia, n (%)	45 (10.5)	36 (10.6)	14 (8.2)	81 (10.5)
Type II Diabetes, n (%)	34 (7.9)	53 (15.5)	28 (16.5)	87 (11.3)

BMI, body mass index; GLP-1, glucagon-like peptide-1; ITT, intent-to-treat; SD, standard deviation.

Results

Figure 1. Least Squares (LS) Mean Percentage of 24-Hour Heartburn-Free Days at Week 4 by BMI Subgroup

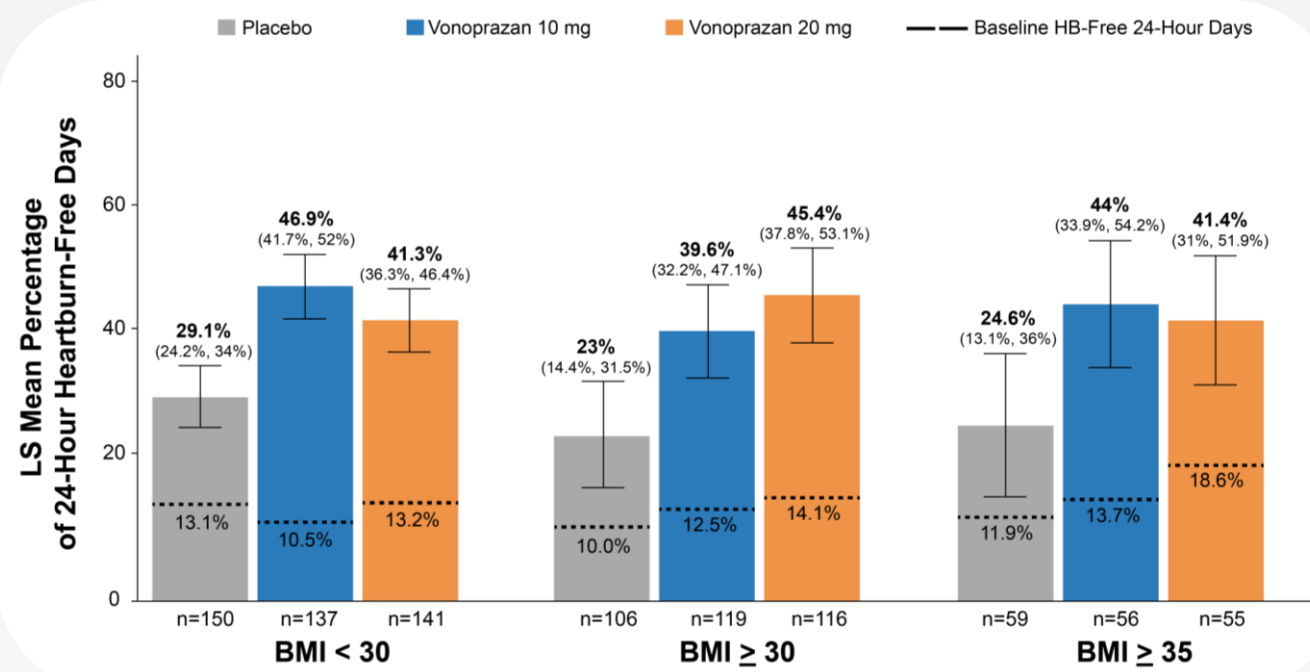


Figure 2. Least Squares (LS) Mean Percentage of Nights Without Heartburn at Week 4 by BMI Subgroup

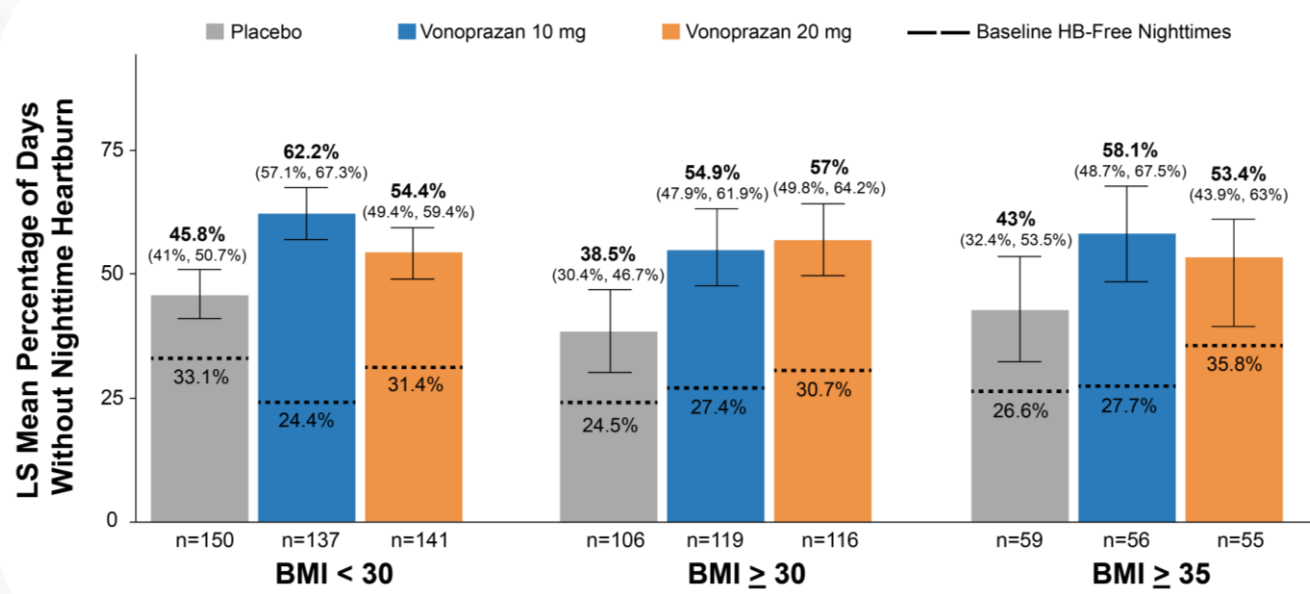
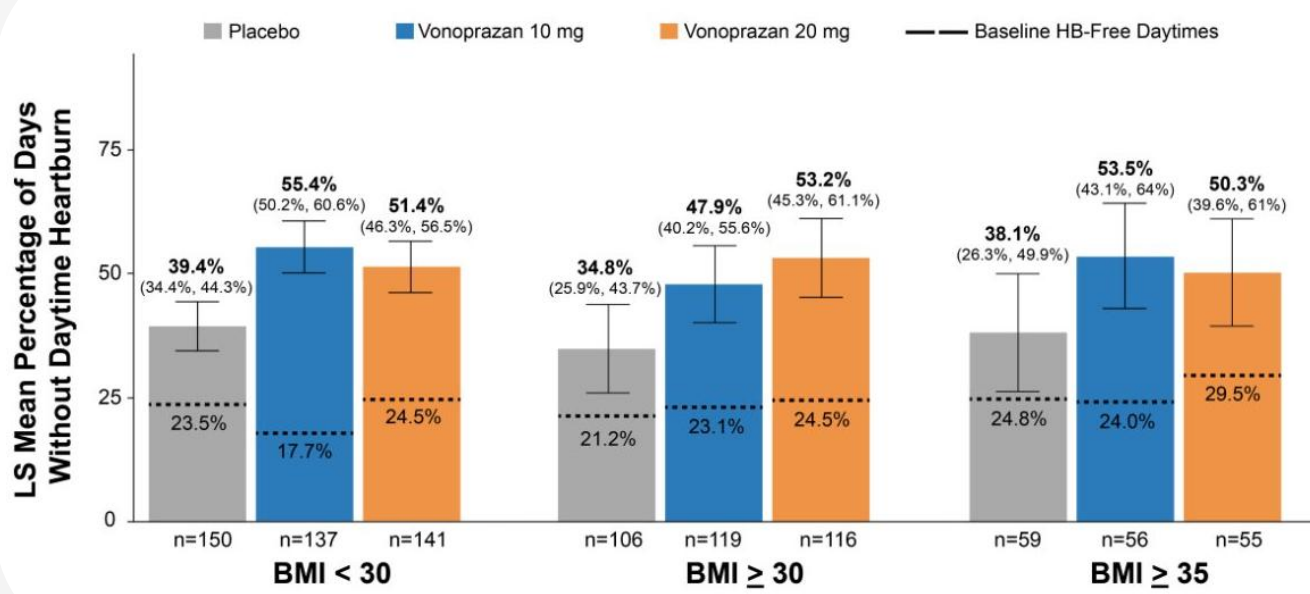


Figure 3. Least Squares (LS) Mean Percentage of Days Without Heartburn at Week 4 by BMI Subgroup



- Vonoprazan improved 24-hour heartburn-free days versus placebo across the BMI < 30 , BMI ≥ 30 , and BMI ≥ 35 kg/m² subgroups (Figure 1).
- Improvements with vonoprazan versus placebo were similar across BMI subgroups for both daytime and nighttime heartburn control (Figures 2 and 3).
- No treatment-by-BMI interaction was observed, suggesting that BMI did not modify the treatment effect of vonoprazan.
- Baseline PAGI-SYM heartburn/regurgitation scores were similar across BMI subgroups, with greater improvements following vonoprazan versus placebo in each subgroup (Table 2).

Table 2. PAGI-SYM Heartburn/Regurgitation Composite and Regurgitation-Specific Scores by BMI Subgroup

	Placebo		Vonoprazan 10 mg		Vonoprazan 20 mg	
	Baseline	Change From Baseline	Baseline	Change From Baseline	Baseline	Change From Baseline
BMI <30 Population, n	150	136	136	129	141	125
Average Heartburn/Regurgitation Score, Mean (SD)	2.02 (1.14)	-0.58 (1.06)	2.25 (1.20)	-1.36 (1.24)	2.10 (1.15)	-1.10 (1.14)
Average Regurgitation Score ^a , Mean (SD)	1.82 (1.32)	-0.53 (1.23)	2.14 (1.34)	-1.25 (1.37)	1.89 (1.34)	-1.01 (1.32)
BMI ≥30 Population, n	106	104	118	108	115	105
Average Heartburn/Regurgitation Score, Mean (SD)	2.34 (1.13)	-0.70 (1.03)	2.16 (1.20)	-1.25 (1.24)	2.42 (1.22)	-1.35 (1.26)
Average Regurgitation Score ^a , Mean (SD)	2.09 (1.28)	-0.65 (1.10)	2.05 (1.38)	-1.21 (1.38)	2.30 (1.40)	-1.28 (1.38)
BMI ≥35 Population, n	59	57	56	49	55	51
Average Heartburn/Regurgitation Score, Mean (SD)	2.41 (1.15)	-0.77 (1.15)	2.17 (1.33)	-1.28 (1.32)	2.06 (1.23)	-1.09 (1.35)
Average Regurgitation Score ^a , Mean (SD)	2.25 (1.2)	-0.66 (1.23)	2.08 (1.51)	-1.21 (1.5)	1.87 (1.32)	-0.98 (1.39)

PAGI-SYM, Patient Assessment of Upper Gastrointestinal Symptom Severity Index; BMI, body mass index; SD, standard deviation.

Higher scores indicate greater symptom severity; decreases from baseline indicate improvement.

^a Regurgitation subscore was derived by taking the mean of PAGI-SYM questions 18 (regurgitation during the day), 19 (regurgitation when lying down), and 20 (bitter, acid, or sour taste in the mouth) and can range from 0-5

Conclusions

- In this post hoc analysis, vonoprazan improved 24-hour heartburn-free days, nocturnal heartburn control, and heartburn/regurgitation symptoms across BMI subgroups in individuals with non-erosive reflux disease symptoms.

Acknowledgements & Disclosures

- The authors acknowledge editorial and poster development support provided by Medical Leverage, Emily C. Dunford, PhD, and Cindy Jebara, PharmD, funded by Phathom Pharmaceuticals in accordance with Good Publication Practice (GPP) Guidelines.
- CA: consultant for Phathom Pharmaceuticals; GG: consultant for Phathom Pharmaceuticals; RY: consultant for Braintree Pharmaceuticals, Phathom Pharmaceuticals, Medtronic, and StatLinkMD; YC, HG, and EL are employees of Phathom Pharmaceuticals; PK: consultant for Phathom Pharmaceuticals and Sebella.