HEARTBURN FREQUENCY AND SYMPTOM IMPROVEMENT RATES OF TREATED EPISODES WHEN SWITCHING FROM DAILY TO ON-DEMAND VONOPRAZAN TREATMENT FOR NON-EROSIVE REFLUX DISEASE

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Background

On-demand treatment for non-erosive GERD is suitable if:

- Patients do not have high frequency of heartburn
- Symptom relief is rapid and durable

Current options for on-demand dosing are limited

- Antacids and H2 receptor antagonists are effective, but with limited potency and lack of durable response[1]
- PPIs are not suitable for providing rapid relief of new onset heartburn episodes due to their PK/PD profile[2]

Vonoprazan,* a P-CAB, is a good candidate for on-demand therapy[3-5]

- Rapid onset and potent acid suppression
- Durable 24-hour acid control after single dose
- Food-independent

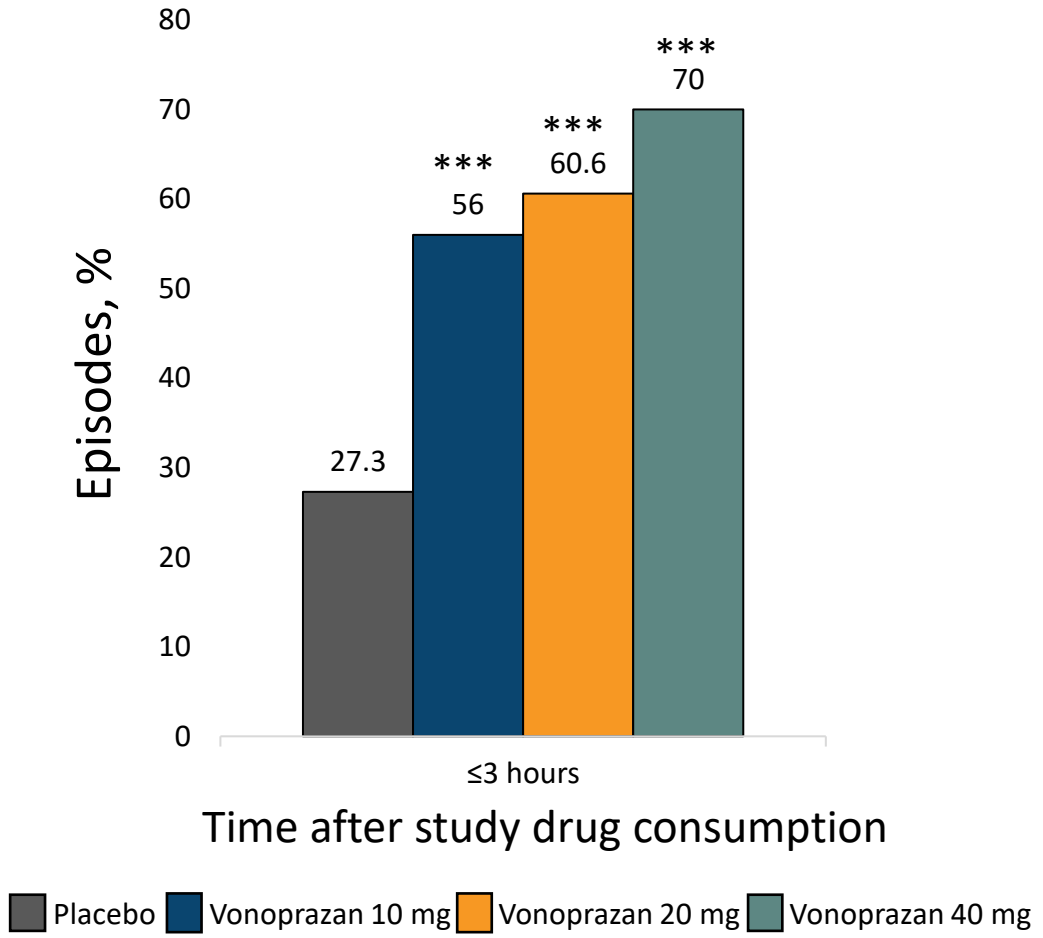
* Vonoprazan is FDA-approved for daily use for heartburn relief associated with non-erosive GERD

1. Fass. *Clin Gastroenterol Hepatol* 2012; 10(4):338-45;quiz e39-40. **2.** Abdel-Aziz, et al. *Aliment Pharmacol Ther* 2021; 53(7):794-809. **3.** Laine L, et al. *Am J Gastroenterol* 2022; 117(7):1158-1161. **4.** Jenkins H, et al. *Aliment Pharmacol Ther* 2015; 41(7):636-48. **5.** Sakurai Y, et al. *Aliment Pharmacol Ther* 2015; 42(6):719-30.

FDA, Food and Drug Administration; **GERD,** gastroesophageal reflux disease; **P-CAB**, potassium-competitive acid blocker; **PD,** pharmacodynamics; **PK,** pharmacokinetics; **PPI**, proton pump inhibitor

Background

The NERD-201 phase 2 study[1] reported that vonoprazan on-demand was significantly better than placebo in providing rapid and sustained relief from evaluable heartburn episodes in patients with NERD who had responded to 4 weeks of vonoprazan therapy.



1. Fass et al. *Aliment Pharmacol Ther* 2023; 58(10):1016-1027.
NERD, non-erosive gastroesophageal reflux disease. *** P<0.0001 for difference from placebo.

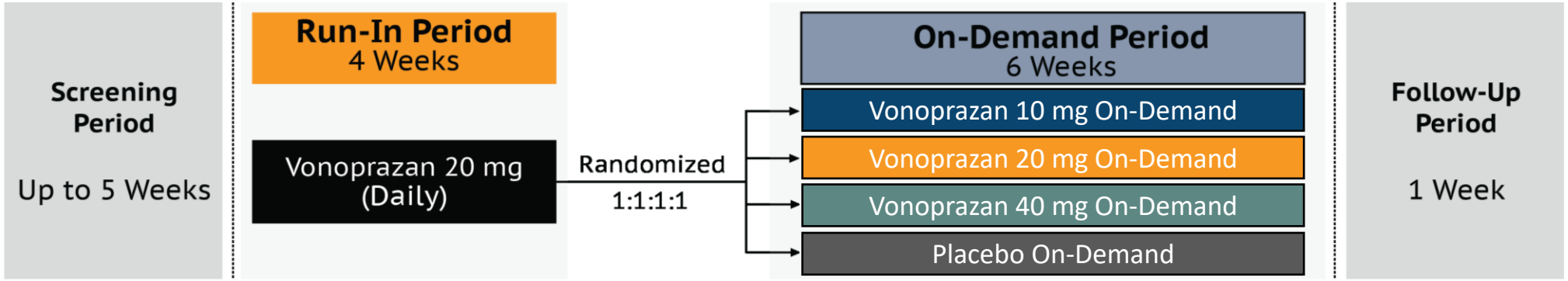
Aim

This is a post hoc analysis that evaluates:

- Frequency of heartburn episodes when switching to on-demand treatment after achieving symptom control with daily treatment
- Rate of symptom improvement of treated episodes

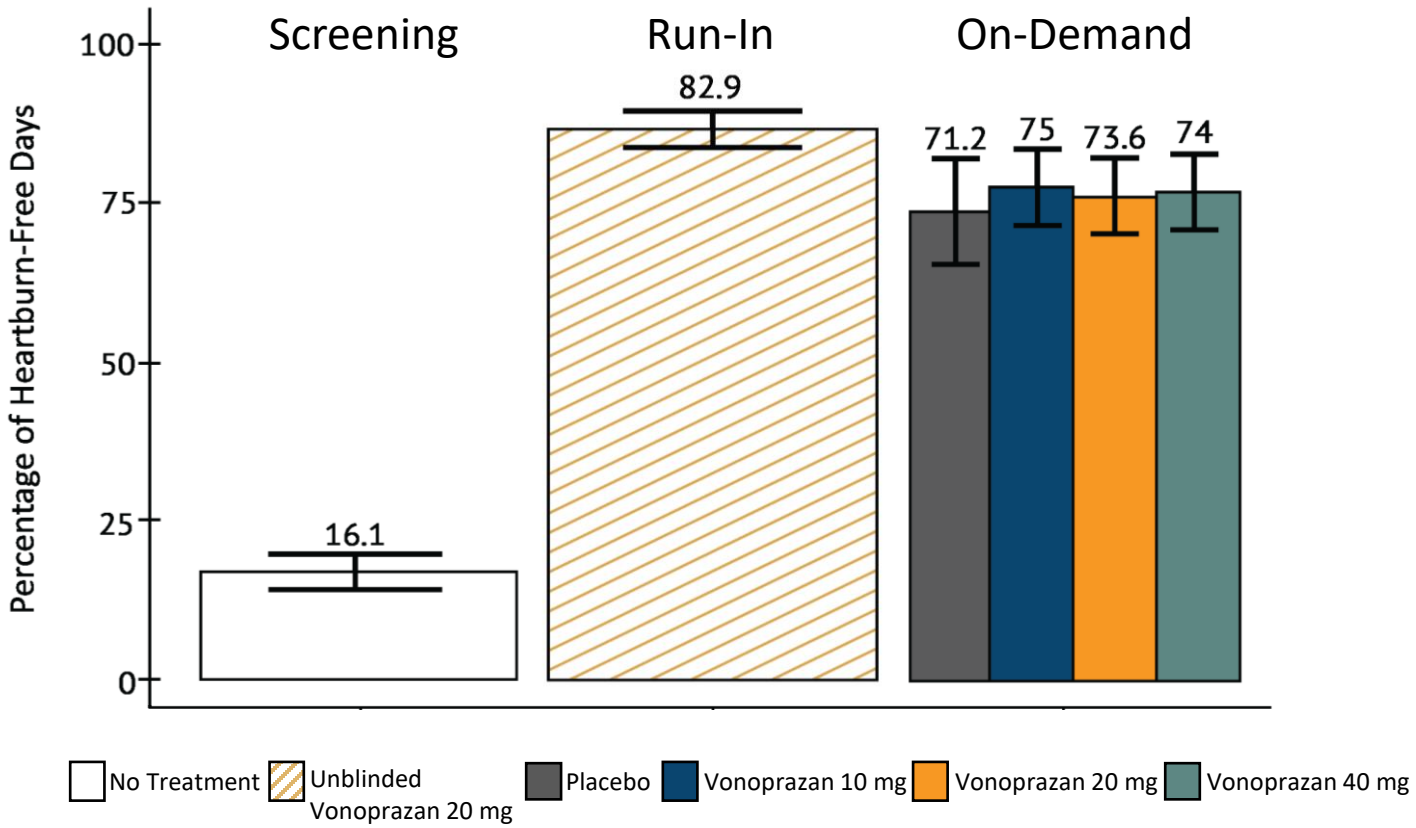
Methods

- Patients eligible to enter the on-demand period:
  - Completed run-in period of daily vonoprazan 20 mg for 4 weeks
  - Were 80% compliant with run-in period study drug and electronic diary entries
  - Reported no heartburn during the last seven days of run-in period



- Patients recorded heartburn episodes as they occurred
  - Symptoms assessed at time of treatment and 0.5, 1, 1.5, 2, and 3 hours after taking study drug
  - Heartburn severity reported as none, mild, moderate, severe, or very severe
  - Patients also documented if they did not have a heartburn episode within 24 hrs of drug consumption
  - Improvement in severity was defined as minimum of one grade reduction from initial severity
- On-demand dosing permitted only one dose of study drug every 24 hrs

Results: % of Heartburn-Free Days by Study Period

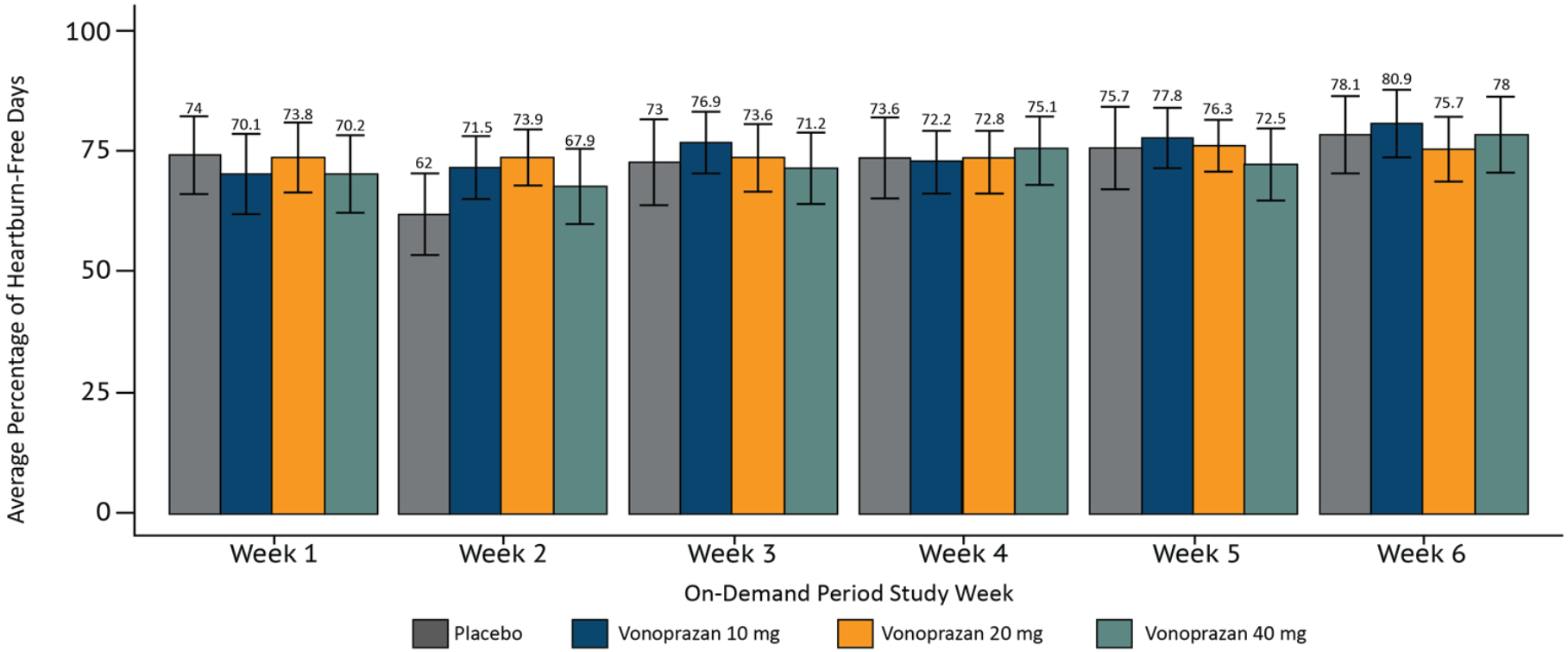


- Patients randomized to on-demand treatment phase were highly symptomatic during screening, with only 16.1% of days heartburn-free.
- With daily vonoprazan treatment during the run-in period, symptom control was achieved, increasing the % of heartburn-free days to 82.9%.
- After transition to on-demand, % of heartburn-free days decreased slightly but remained well above pretreatment levels.

Mean (top of bar) and 95% CI (brackets at the top of each bar)

Results: % of Heartburn-Free Days by Study Week

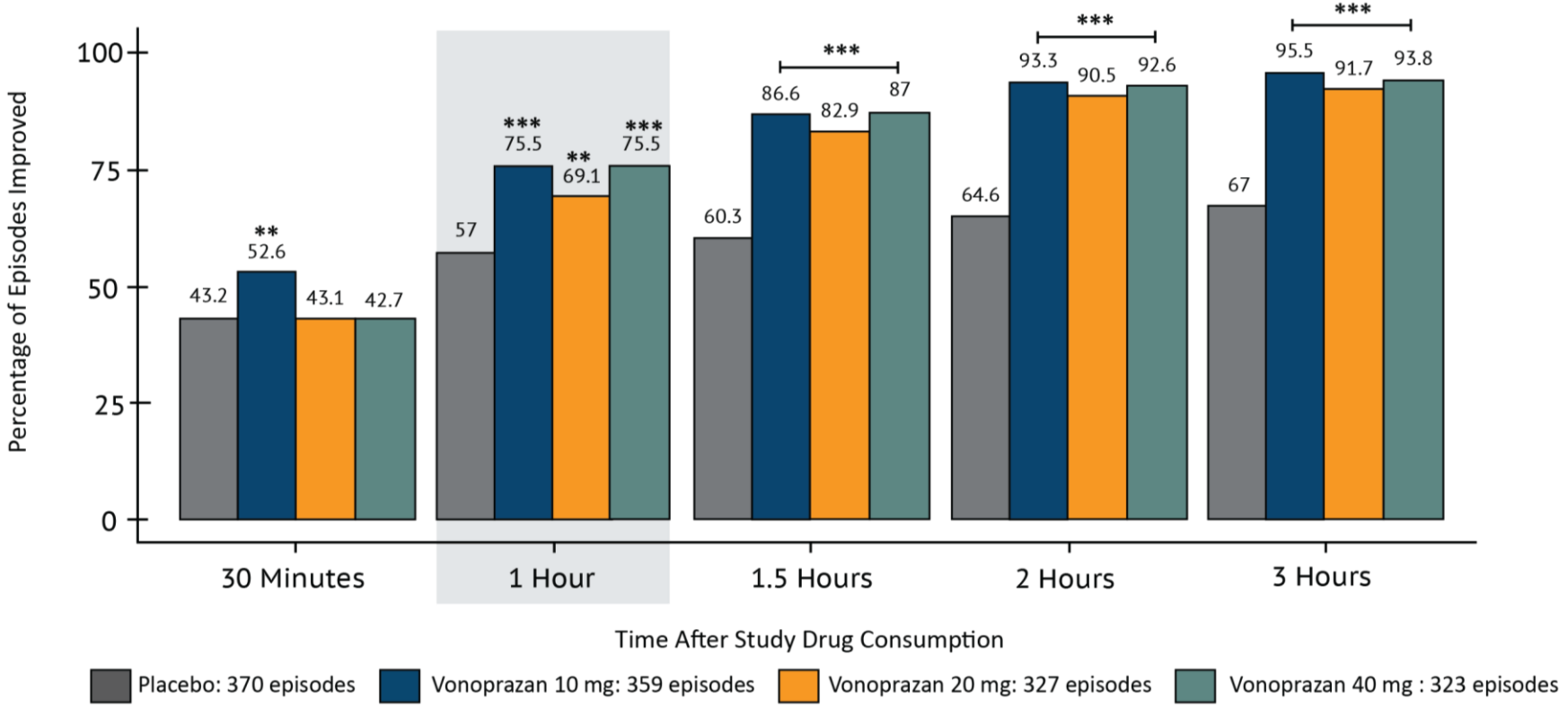
Heartburn-free days were consistent over the entire 6-week on-demand treatment period.



On-demand ITT (intention to treat) population. All patients received vonoprazan 20 mg during the run-in phase

Results: % of Heartburn Episodes Improved After Treatment

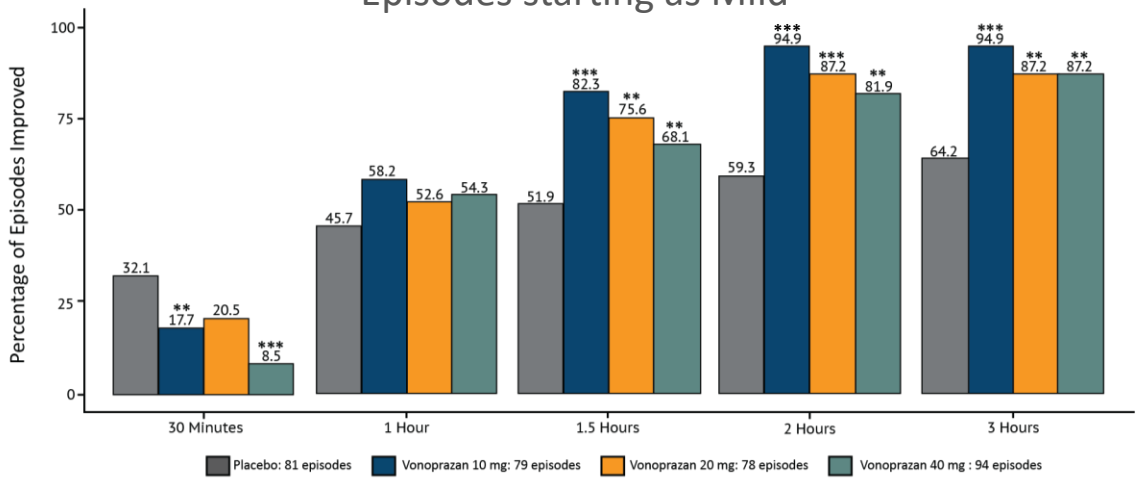
Differences between each vonoprazan dose compared to placebo were evident within the first hour. Over 90% of episodes treated with vonoprazan improved by 2 hours.



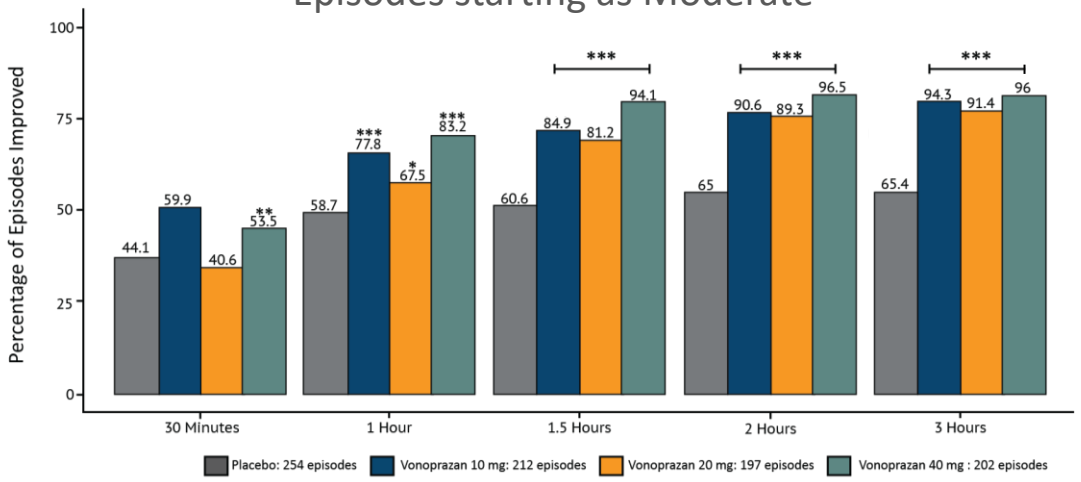
**p< 0.05; ***p< 0.0001 for difference from placebo

Results: Consistency of Improvement Across All Levels of Initial Episode Severity

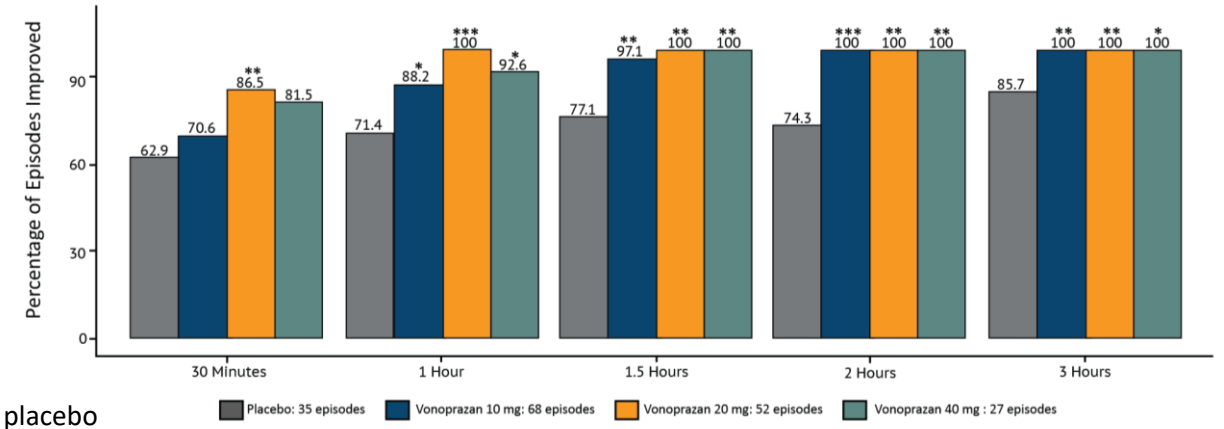
Episodes starting as Mild



Episodes starting as Moderate



Episodes starting as Severe or Very Severe



*p< 0.1 **p< 0.05; ***p< 0.0001 for difference from placebo

Conclusions

- Upon achieving symptom control with daily vonoprazan treatment, a high rate of heartburn-free days was sustained when switching to on-demand therapy over the 6-week placebo-controlled period
  - Initial 4-week run-in period produced a durable reduction in heartburn symptoms that allows consideration to switch to on-demand treatment
- Improvement of new onset heartburn episodes occurred rapidly, with differences observed within one hour compared to placebo

Our findings support the potential use of vonoprazan as an on-demand option for patients with NERD. A confirmatory study in a larger patient population with a longer on-demand period is warranted.