

# A Phase 1, Open-Label Study to Evaluate Vonoprazan Concentrations in Breast Milk of Healthy Lactating Women Receiving Vonoprazan 20 mg Once Daily or Vonoprazan 20 mg Twice Daily

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## Background

- Pregnancy-related heartburn can persist postpartum, presenting a therapeutic challenge for breastfeeding women.<sup>1</sup>
- Vonoprazan is a potent and long-lasting potassium-competitive acid blocker (P-CAB) and may be an effective treatment option.<sup>2,3</sup>
- Steady-state vonoprazan plasma concentrations are typically achieved after 3-4 days of once- or twice-daily dosing.<sup>4</sup>
- There is currently no clinical data describing the transfer of vonoprazan into human breast milk.
- In animal studies, vonoprazan has been shown to be excreted in milk, highlighting the need for human lactation data.<sup>5</sup>
- Characterizing drug concentrations in breast milk and estimating infant exposure may help inform treatment decisions in lactating women.

## Objective

- To determine the steady state pharmacokinetics of vonoprazan in the breast milk of healthy lactating women following vonoprazan 20 mg once daily (QD) or 20 mg twice daily (BID) dosing.

## Methods

- Phase 1, nonrandomized, open-label study in healthy lactating women
  - Subjects received vonoprazan 20 mg QD (N=5) or 20 mg BID (N=10) for four consecutive days
  - Breast milk samples were collected over a 24-hour period following the morning dose on Day 4 at prespecified intervals (0-4, 4-8, 8-12, 12-18, 18-24 hours)
  - Concentrations were measured using liquid chromatography with tandem mass spectrometry
- Inclusion criteria**
- Healthy lactating women ≥18 years who delivered a full-term infant (≥37 weeks gestation)
  - Actively breastfeeding or pumping for at least four weeks postpartum
  - Subjects agreed to discontinue breastfeeding from first dose through at least five days after last dose

## Results

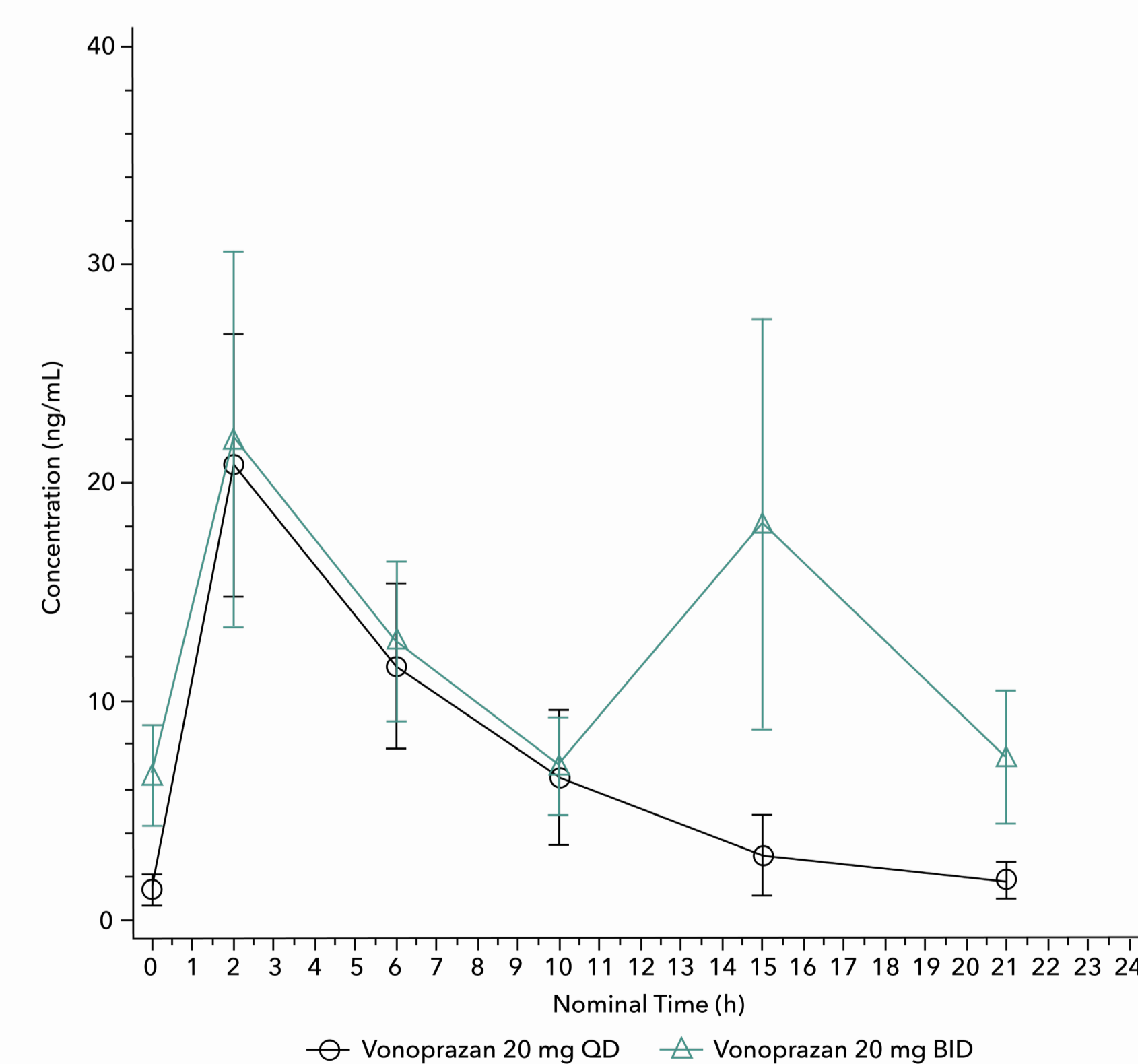
- Fifteen female subjects (5 QD; 10 BID) completed the study (Table 1).

**Table 1.** Patient demographics

	Vonoprazan 20 mg QD (N=5)	Vonoprazan 20 mg BID (N=10)	Total (N=15)
Age (years)			
Mean (SD)	34.4 (4.45)	29.7 (3.71)	31.3 (4.45)
Median (Min, Max)	35.0 (27, 39)	30.5 (22, 34)	32.0 (22, 39)
Sex, n (%)			
Female	5 (100.0)	10 (100.0)	15 (100.0)
Race, n (%)			
White	4 (80.0)	8 (80.0)	12 (80.0)
Asian	1 (20.0)	1 (10.0)	2 (13.3)
Multi-Racial	0	1 (10.0)	1 (6.7)
Ethnicity, n (%)			
Not Hispanic or Latino	4 (80.0)	10 (100.0)	14 (93.3)
Hispanic or Latino	1 (20.0)	0	1 (6.7)
Height (cm)			
Mean (SD)	163.54 (4.49)	161.70 (4.29)	162.31 (4.29)
Median (Min, Max)	163.8 (158.2, 169.2)	162.0 (154.3, 168.5)	162.8 (154.3, 169.2)
Weight (kg)			
Mean (SD)	66.03 (11.80)	69.01 (13.00)	68.02 (12.27)
Median (Min, Max)	63.8 (52.35, 82.70)	67.5 (52.60, 85.40)	63.8 (52.35, 85.40)
BMI (kg/m <sup>2</sup> )			
Mean (SD)	24.78 (5.19)	26.48 (5.44)	25.91 (5.24)
Median (Min, Max)	24.9 (19.50, 33.00)	24.9 (20.70, 34.30)	24.9 (19.50, 34.30)

- At steady state, median maximum breast milk concentrations (T<sub>max</sub>) were observed within 4 hours of the morning dose for both regimens. Concentrations declined with QD dosing, while BID showed an expected second peak at 12-18 hours (Figure 1).

**Figure 1.** Mean breast milk concentrations of vonoprazan versus time at steady state (Day 4). Nominal time represented the nominal midpoint of each breast milk collection interval and 0 for pre-dose



**Table 2.** Mean (CV%) breast milk pharmacokinetic parameters of vonoprazan at steady state (Day 4)

Parameter (unit)	Vonoprazan 20 mg QD (N=5)	Vonoprazan 20 mg BID (N=10)
AUC <sub>0-24</sub> (ng·h/mL)	179 (34.2)	317 (33.9)
C <sub>max</sub> (ng/mL)	20.9 (28.8)	24.7 (39.5)
C <sub>min</sub> (ng/mL)	1.82 (45.8)	6.78 (32.3)
C <sub>avg</sub> (ng/mL)	7.55 (34.2)	13.3 (33.9)
Median T <sub>max</sub> <sup>a</sup> (h)	1.88 (1.83, 1.93)	1.91 (1.88, 14.8)

AUC<sub>0-24</sub>, area under the drug concentration-time curve from time 0 to 24 hours following the last dose; C<sub>avg</sub>, average drug concentration in milk; C<sub>max</sub>, maximum drug concentration in milk after dosing; C<sub>min</sub>, minimum drug concentration in milk after dosing; T<sub>max</sub>, time to maximum observed milk concentration.

<sup>a</sup> For T<sub>max</sub>, the median (minimum, maximum) values are presented; actual midpoint of interval in which T<sub>max</sub> occurred.

**Table 3.** Mean (CV%) breast milk infant exposure measures at steady state (Day 4)

Parameter (unit)	Vonoprazan 20 mg QD (N=5)	Vonoprazan 20 mg BID (N=10)
Total Amount Excreted (mg)	0.00241 (49.2)	0.00904 (58.6)
Relative Amount Excreted (%)	0.0120 (49.2)	0.0226 (58.6)
Estimated Infant Dose <sup>a</sup> (mg/kg/day)	0.000401 (49.2)	0.00151 (58.6)
Estimated Relative Infant Dose (%)	0.128 (43.5)	0.269 (69.3)

<sup>a</sup> Calculated based on infant body weight of 6 kg.

**Table 4.** Treatment Emergent Adverse Events

System Organ Class Preferred Term	Vonoprazan 20 mg QD (N=5) n (%)	Vonoprazan 20 mg BID (N=10) n (%)	Total (N=15) n (%)
Any TEAE	1 (20.0)	4 (40.0)	5 (33.3)
Gastrointestinal Disorders	1 (20.0)	3 (30.0)	4 (26.7)
Nausea	1 (20.0)	2 (20.0)	3 (20.0)
Abdominal Discomfort	0	1 (10.0)	1 (6.7)
Dyspepsia	0	1 (10.0)	1 (6.7)
Nervous System Disorders	0	2 (20.0)	2 (13.3)
Headache	0	2 (20.0)	2 (13.3)

Adverse events were coded using MedDRA Version 27.0.

## Conclusions

- Vonoprazan excretion into breast milk was negligible at steady state following 20 mg QD or BID dosing in healthy adult lactating women.
- Total drug excretion into breast milk was <0.03% of the administered dose, with an estimated infant dose <0.3% of the maternal dose, indicating very low infant dose consumed in breast milk.
- Both QD and BID regimens were well tolerated in healthy adult lactating women.
- These findings provide the first clinical data characterizing vonoprazan transfer into human breast milk, which may help support clinical decision-making in lactating patients.

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