# The effect of food on the pharmacokinetics of the potassium-competitive acid blocker vonoprazan

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## OBJECTIVE

To report the effect of food on the pharmacokinetics of a 20 mg oral dose of vonoprazan and its safety/tolerability in healthy subjects.

## RESULTS

**Table 1. Demographic and baseline characteristics**

| | |
|---|---|
| Mean age, y (SD) | 25.5 (6.09) |
| Gender, N (%) | |
| Male | 12 (50) |
| Female | 12 (50) |
| Mean weight, kg (SD) | 72.6 (12.44) |
| Mean height, cm (SD) | 174.6 (10.78) |

**Table 2. Mean (SD) pharmacokinetic parameters for vonoprazan following a 20 mg oral dose in fed vs fasted conditions (N = 24)**

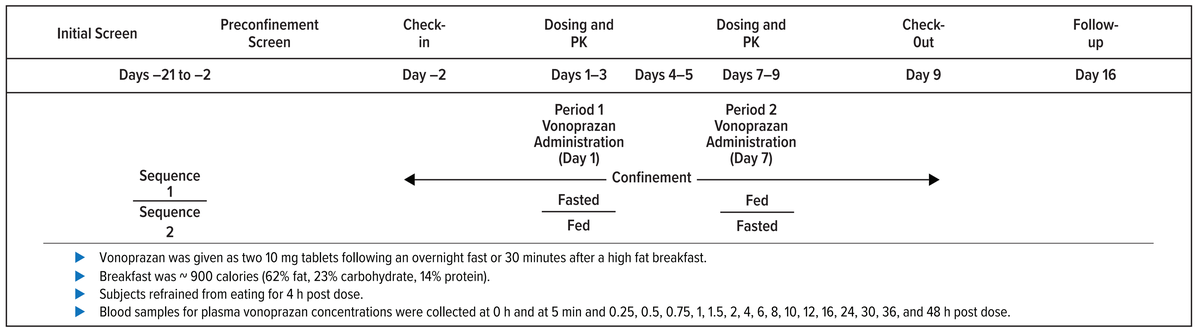
| | Fed | Fasted |
|---|---|---|
| $C_{max}$ (ng/mL) | 18.9 (5.12) | 18.2 (5.76) |
| $AUC_t$ (hr·ng/mL) | 181.5 (52.84) | 160.8 (49.50) |
| $AUC_\infty$ (hr·ng/mL) | 206.1 (66.62) | 179.3 (58.37) |
| $T_{max}$ (hr); median (min, max) | 4.0 (1.98, 6.02) | 2.0 (0.75, 4.00) |
| $T_{½}$ (hr) | 6.9 (1.21) | 6.9 (1.45) |

$AUC_\infty$, area under the plasma concentration-time curve from time zero extrapolated to infinity; $AUC_t$, area under the plasma concentration-time curve from time zero to last quantifiable concentration; $C_{max}$, maximum observed concentration; max, maximum; min, minimum; SD, standard deviation; $T_{max}$, time at which the maximum observed concentration occurred; $T_{½}$, terminal elimination half-life.

**Table 3. Ratios and confidence intervals for vonoprazan $C_{max}$ and AUC following a 20 mg oral dose in fed versus fasted conditions (N = 24)**

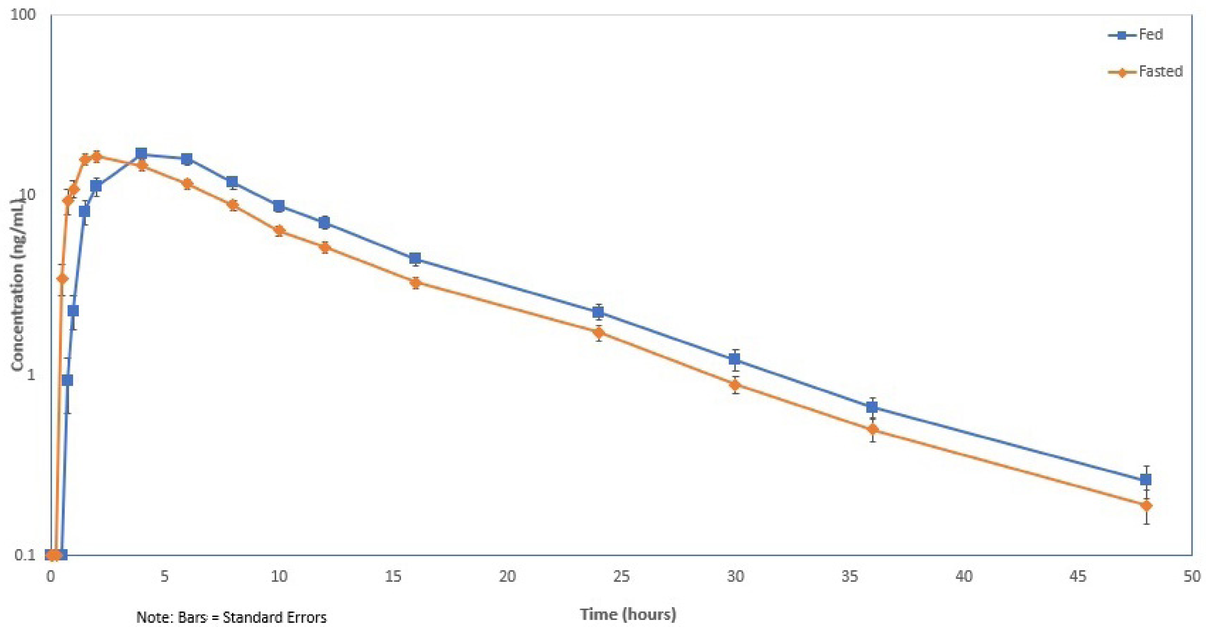
| | Least-Squares Means | | | |
|---|---|---|---|---|
| | Fed | Fasted | Fed/Fasted Ratio | 90% CI |
| $C_{max}$ (ng/mL) | 18.2 | 17.3 | 1.05 | 0.98, 1.12 |
| $AUC_t$ (hr·ng/mL) | 193.2 | 168.2 | 1.15 | 1.11, 1.19 |
| $AUC_\infty$ (hr·ng/mL) | 196.2 | 170.6 | 1.15 | 1.11, 1.19 |

**Figure 1. Study schema**




- Vonoprazan was given as two 10 mg tablets following an overnight fast or 30 minutes after a high fat breakfast.
- Breakfast was ~ 900 calories (62% fat, 23% carbohydrate, 14% protein).
- Subjects refrained from eating for 4 h post dose.
- Blood samples for plasma vonoprazan concentrations were collected at 0 h and at 5 min and 0.25, 0.5, 0.75, 1, 1.5, 2, 4, 6, 8, 10, 12, 16, 24, 30, 36, and 48 h post dose.

**Figure 2. Mean vonoprazan plasma concentration versus time profiles (semi-logarithmic scale)**




- 24 Caucasian subjects completed the study **(Table 1).**
- Pharmacokinetic parameters of vonoprazan following administration in fed or fasted states are summarized in **Table 2.**
- Plasma concentrations **(Figure 2)** and exposure to vonoprazan **(Table 3)** were not meaningfully affected by food.
  - Confidence intervals for all pharmacokinetic parameters were within the pre-defined equivalence limits of 0.80 to 1.25 **(Table 3)**.
- Four subjects experienced 6 treatment-emergent adverse events: dizziness (3), paresthesia (1), nasal discomfort (1), and rash (1).
  - All were mild and considered unrelated to study drug.

## CONCLUSIONS

- Given the very limited effect of food on pharmacokinetic parameters, vonoprazan can be administered without regard to food intake.
- In this study, vonoprazan was well tolerated by healthy subjects.
- The ability to administer vonoprazan irrespective of food intake differentiates it from most PPIs.

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## BACKGROUND

- Most proton pump inhibitors (PPIs) are recommended to be taken in a fasting state, 30–60 minutes before a meal,[1,2] given their reduced bioavailability when given with or after food.[3,4]
- Vonoprazan fumarate is a novel, orally active, potassium-competitive acid blocker (P-CAB) under development in the USA and Europe for the treatment of erosive esophagitis and, in combination with antibiotics, *H pylori* infection.
  - Vonoprazan is already approved in several Asian and South American countries.
  - In contrast to PPIs, P-CABs are acid-stable and do not require an enteric coating to protect them from acid degradation in the stomach.[5,6]

## METHODS

- Phase I, randomized, open-label, cross-over study.
- Healthy male and female Caucasian subjects aged 18–45 years.
- Randomized (stratified by gender) to fed/fasted or fasted/fed state sequence: 20 mg dose of vonoprazan either following an overnight fast or 30 minutes after a high-fat breakfast **(Figure 1).**

### References

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### Disclosures

**Dr. Helen Jenkins** was a consultant with Certara Strategic Consulting.

**Dr. Howden** is a consultant for Alfasigma, Allakos, Clexio, Ironwood, Phathom and RedHill Biopharma.

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### Meeting details

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