Effect of Aluminum Hydroxide/Magnesium Hydroxide/Simethicone and Omeprazole on the Pharmacokinetics of Tebipenem Pivoxil Hydrobromide (TBP PI-HBr) in Healthy Adult Subjects

Tebipenem pivoxil hydrobromide (TBP-PI-HBr) is a novel orally bioavailable carbapenem produg in development for treatment of serious bacterial infections including complicated urinary tract infections.

TBP-PI-HBr is active in vitro against gram-positive and gram-negative pathogens, including extended-spectrum β-lactamase (ESBL)-producing and non-ESBL-resistant Enterobacteriaceae (Jain et al., 2018).

In a single- and multiple-ascending dose study of TBP-PI-HBr, plasma concentrations of TBP increased in a linear and dose proportional manner (Exkborg et al., 2019).

A completed Phase 3 study of patients with complicated urinary tract infection or acute pyelonephritis found that oral TBP-PI-HBr was non-inferior to intravenous ertapenem for clinical and microbiological response (Exkborg et al., 2021).

Because gastric acid reducing agents are commonly used in older adults, and hospitalized patients, the assessment of a potential DDIs for TBP-PI-HBr with gastric acid reducing agents was explored.

### Methods

**Pharmacokinetic Analysis**

- Mean ± standard deviation

**Pharmacokinetic Analysis**

- Table 1. Baseline characteristics are shown in Table 1.
- **Table 2.** Pharmacokinetic parameters for each treatment group
- **Table 3.** Comparisons were performed on the natural log (ln) transformed plasma TBP PK parameters (AUC0-t, AUC0-inf, and Cmax) to assess the effect of aluminum hydroxide/magnesium hydroxide/simethicone and omeprazole on the PK of TBP.
- **Table 4.** Incidence (%) of Adverse Events (AE) by Treatment (safety population)

**Results**

- **Objective**
  - To evaluate the effect on the TBP pharmacokinetic profile upon co-administration of TBP-PI-HBr with gastric acid reducing agents, including an antacid (aluminum hydroxide/magnesium hydroxide/simethicone) or a proton pump inhibitor (omeprazole) in healthy adult subjects.

**Summary**

- Results from this study confirm no clinically meaningful drug-drug interaction for TBP-PI-HBr with gastric acid reducing agents following coadministration with omeprazole or aluminum hydroxide/magnesium hydroxide/simethicone.
- As the PKPD driver for TBP efficacy depends on AUC which was minimally affected, coadministration with omeprazole or aluminum hydroxide/magnesium hydroxide/simethicone is not expected to impact the efficacy of TBP-PI-HBr.
- Co-administration of TBP-PI-HBr either antacid or proton pump inhibitor appeared to be generally safe and well tolerated.

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**References**


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- Spero Therapeutics, Inc., Cambridge, MA. Clinicaltrials.gov: NCT04368585