respectively, 2.1 (IQ 1.4-2.8) mL/kg/min, 0.6 (IQ 0.5-0.7) L/kg and 3.2 (IQ 2.3-4.0) hours. After the initial dose regimen, 5 (42%) patients reached the therapeutic target.

Conclusion. Using the one-compartment model, we evaluate the pharmacokinetic parameters of vancomycin in pediatric patients after liver transplantation. Most of patients did not reach the therapeutic target with empirical regimen, so it is prudent to monitor the exposure to vancomycin directly by AUC/MIC ratio to maximize antimicrobial efficacy.

Disclosures. **All Authors**: No reported disclosures

1120. Absorption, Metabolism, and Excretion of [^{14}C]-Tebipenem Pivoxil Hydrobromide (TBP-PI-HBr) Following a Single Oral Dose in Healthy Male Subjects

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Session: P-62. PK/PD Studies

Background. Tebipenem pivoxil hydrobromide (TBP-PI-HBr) is an oral prodrug that is converted to tebipenem (TBP), the active moiety, with activity against multidrug-resistant gram-negative pathogens, including extended-spectrum-β-lactamase (ESBL)-producing Enterobacterales. TBP-PI-HBr is the first oral carbapenem intended for treating complicated urinary tract infections and acute pyelonephritis. This study evaluated the absorption, metabolism, and excretion (AME) of TBP-PI-HBr following a single oral dose of [^{14}C]-TBP-PI-HBr to healthy males and characterized metabolites in plasma, urine, and feces.

Methods. This was a Phase 1, open-label, single-dose study in healthy subjects. Study drug was provided as radiolabeled and non-radiolabeled active pharmaceutical ingredient containing approximately 150 µCi of [14C]-TBP-PI-HBr. On Day 1, each subject received a 600 mg dose of TBP-PI-HBr. administered with 240 mL of water and fasted overnight for at least 10 hours. Blood samples were collected to determine TBP concentrations (whole blood), total radioactivity (whole blood and plasma), and metabolite profiling and identification were determined from plasma, urine, and feces. For mass balance, total radioactivity derived from urine and feces collections were determined. PK parameters were calculated using noncompartmental methods.

Results. Total radioactivity in plasma and whole blood decreased rapidly with geometric mean $t_{½}$ values of 6.0 hours and 3.5 hours, respectively and T_{max} of 1 hour. The cumulative mean recovery of radioactivity was 38.7% in urine and 44.6% in feces. Most of the administered radioactivity was recovered in the first 144 hours post dose in urine and feces (80.0%). Six of 8 subjects achieved a mass balance recovery ranging from 80.1% to 85.0%. The TBP plasma to total radioactivity ratio of 0.536 indicated that other metabolites contribute to the total radioactivity AUC in plasma. Metabolite profiling and identification results indicated that TBP was the major component in plasma and urine. The inactive ring open metabolite of TBP (LJC 11,562) was also found in plasma

(>10%), urine (5.27%), and feces (>10%) as a secondary metabolite.

Conclusion. This study adequately characterized the AME of TBP-PI-HBr in humans.

Disclosures. **Vipul K. Gupta, Ph.D.**, **Spero Therapeutics** (Employee, Shareholder) **Gary Maier, PhD**, **Spero Therapeutics, Inc.** (Consultant) **Leanne Gasink, MD**, **Spero Therapeutics, Inc.** (Consultant) **Amanda Ek, MS**, **Spero Therapeutics, Inc.** (Employee) **Mary Fudeman, BA, MBA**, **Spero Therapeutics, Inc.** (Employee) **Praveen Srivastava, MS, BS**, **Spero Therapeutics, Inc.** (Employee) **Angela Talley, MD**, **Spero Therapeutics, Inc.** (Employee)

1121. Bioequivalence of Two Formulations of Oral Tebipenem-Pivoxil Hydrobromide in Healthy Subjects

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Session: P-62. PK/PD Studies

Background. Tebipenem-pivoxil-hydrobromide (TBP-PI-HBr) is a novel oral carbapenem being developed to treat serious bacterial infections including complicated urinary tract infection. The objectives of this study were to assess the bioequivalence (BE) of two tablet formulations of TBP-PI-HBr in healthy adult subjects under fasted conditions and to evaluate the food-drug interactions of the registration drug product.

Methods. This was an open-label, randomized, single-dose, semi-replicate, 3-sequence, 4-period crossover, BE, and food effect study. Subjects were randomized to one of three sequences where they received a single 600 mg oral dose of TBP-PI-HBr, as either the reference clinical study drug product (Treatment A) or the registration drug product (Treatment B) under fasted conditions. Subsequently, all subjects received a single 600 mg oral dose of TBP-PI-HBr as the registration drug product under fed conditions. There was by a 7-day washout between each period. Whole blood sampling to determine TBP pharmacokinetics (PK) was conducted predose and up to 24 hours post dose in each period. Safety and tolerability were monitored throughout the study.

Results. Thirty-six healthy, adult male and female subjects were enrolled and completed the study. The TBP-PI-HBr registration product was bioequivalent to the clinical study product (**Figure 1**). For TBP, 90% confidence intervals (CIs) for AUC_{0-t}, AUC_{0-inf}, and C_{max} were within the 80% to 125% BE limits when administered under fasted conditions. A standard high-fat/high-calorie meal had no meaningful effect on the total plasma exposure of TBP after administration of the registration product, thus, overall exposure based on AUC_{0-t} and AUC_{0-inf} was comparable under fed and fasted conditions (**Figure 2**). Five (14%) subjects reported adverse events of mild severity. No deaths, serious AEs or discontinuations due to AEs were reported, and no clinically relevant ECGs, vital signs or safety laboratory findings were observed.

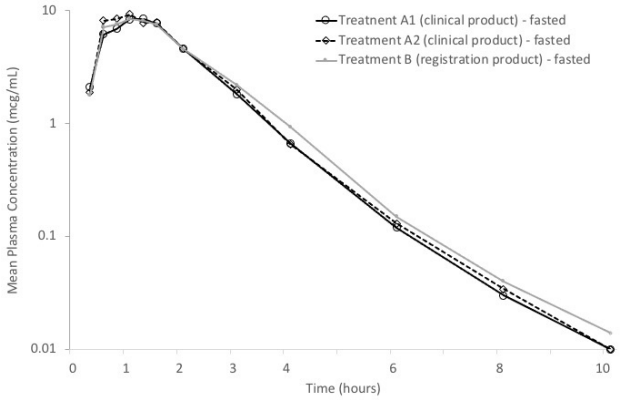

Figure 1. Arithmetic mean plasma TBP concentrations following a 600 mg dose of clinical study drug product (A1 and A2) and registrational drug product (B) – PK population.

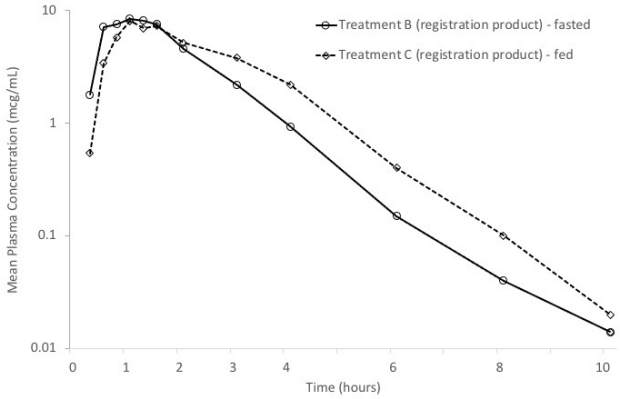

Figure 2. Arithmetic mean plasma TBP concentrations following a 600 mg dose of registrational drug product (B) under fasted and fed conditions – PK population.

Conclusion. The TBP-PI-HBr registration product was bioequivalent to the clinical study product under fasted conditions, and no meaningful effect of a high fat meal on TBP PK was observed.

Disclosures. **Vipul K. Gupta, Ph.D.**, **Spero Therapeutics** (Employee, Shareholder) **Gina Patel, PhD**, **Spero Therapeutics, Inc.** (Consultant) **Leanne Gasink, MD**, **Spero Therapeutics, Inc.** (Consultant) **Floni Bajraktari, MSc**, **Spero Therapeutics, Inc.** (Employee) **Yang Lei, PhD**, **Spero Therapeutics, Inc.** (Employee) **Akash Jain, PhD**, **Spero Therapeutics, Inc.** (Employee) **Praveen Srivastava, MS, BS**, **Spero Therapeutics, Inc.** (Employee) **Angela Talley, MD**, **Spero Therapeutics, Inc.** (Employee)

1122. Effect of Aluminum Hydroxide/Magnesium Hydroxide/Simethicone and Omeprazole on the Pharmacokinetics of Tebipenem Pivoxil Hydrobromide (TBP-PI-HBr) in Healthy Adult Subjects

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Session: P-62. PK/PD Studies

Background. Tebipenem pivoxil hydrobromide (TBP-PI-HBr) is an oral prodrug that is converted to tebipenem (TBP), the active moiety being developed for treating complication urinary tract infections. Antacids and proton pump inhibitors are known to change gastric pH after administration, which could affect the absorption of oral medications. This study evaluated the effect of a single dose of aluminum hydroxide/magnesium hydroxide/simethicone and the effect of multiple doses of omeprazole on the PK of TBP, following a single dose of TBP-PI-HBr.

Methods. This was an open-label, 3-period, fixed sequence drug-drug interaction study. On Day 1, Period 1, subjects received a single oral dose of TBP-PI-HBr