Methods. Nine subjects with CF were enrolled in the 2 to <18 y old cohort of an ongoing Phase 1 PK study of a single dose of intravenous TOL/TAZ in pediatric subjects with suspected or proven Gram-negative infection (NCT02266706). Population PK models for TOL and TAZ were developed using PK data from 12 adult studies and preliminary PK data from pediatric subjects. An exploratory analysis comparing model-derived plasma TOL and TAZ PK parameters between CF ($N = 9$) and non-CF ($N = 9$) pediatric subjects was conducted.

Results. Mean (range) age and weight of the 9 CF subjects were 11.4 y (5.5–17.5 y) and 37.4 kg (17.4–60 kg), respectively. For TOL, the mean (SD) systemic clearance (CL) normalized by weight was 0.16 (0.03) and 0.15 (0.03) L/hours/kg in CF and non-CF subjects, respectively, suggesting no difference in CL; similar observations were made for volume of the central compartment normalized by weight. All subjects achieved the plasma PK/pharmacodynamic (PD) target of %*f*T>MIC of at least 30% for an MIC of 4 µg/mL.

Differences in weight-normalized CL were more pronounced for TAZ in CF and non-CF subjects (mean [SD]: 0.73 [0.25], 0.42 [0.13] L/hours/kg, respectively). However, the half-life was similar in CF and non-CF subjects (mean [SD]: 0.99 [0.15] hours, 1.08 [0.15] hours, respectively), suggesting that differences are unlikely to be clinically meaningful. At the recommended dose being advanced into Phase 2, subjects are projected to achieve the TAZ plasma PK/PD target of %*f*T>threshold concentration (Ct) of >20% for a Ct of 1 µg/mL.

Conclusion. Preliminary exploratory analysis of TOL/TAZ PK in a small group of pediatric patients supports evaluation of the same TOL/TAZ dose in children with and without CF in future clinical studies.

Disclosures. **K. Larson**, Merck: Employee, Salary. **S. Yang**, Merck: Employee, Salary.; **B. Yu**, Merck: Employee, Salary. **M. G. Johnson**, Merck: Employee, Salary. **M. Rizk**, Merck: Employee, Salary. **E. Rhee**, Merck: Employee, Salary.

826. Incidence of Nephrotoxicity Among Patients Initiated on Vancomycin and B-lactam Combination Therapies

Megha Shah, PharmD[1]; Suraj Rajasimhan, PharmD, BCPS[1] and Tiffany Bias, PharmD, BCPS, AAHIVP[2]; [1]Pharmacy, Hahnemann University Hospital, Philadelphia, PA, [2]Hahnemann University Hosp., Philadelphia, Pennsylvania

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Background. Vancomycin and β-lactam combinations are used to provide empiric coverage in hospitalized patients. Recent literature has illustrated an increased incidence of nephrotoxicity with such combinations, predominantly with piperacillin-tazobactam and vancomycin. The objective of this study is to evaluate the incidence of nephrotoxicity among patients receiving vancomycin and piperacillin-tazobactam vs., cefepime, or aztreonam.

Methods. A retrospective, observational, cohort study was conducted at Hahnemann University Hospital in adult patients who received vancomycin plus piperacillin-tazobactam, cefepime, or aztreonam for at least 48 hours between June 2013 and August 2016. Patients were excluded if they had chronic kidney disease Stage III or higher or on continuous renal replacement therapy. The following data were collected: demographics, renal function, number of concomitant nephrotoxic agents, total duration of combination therapy, and vancomycin levels. The primary outcome was the incidence of nephrotoxicity according to the Risk Injury Failure End Stage Renal Disease (RIFLE) criteria. Secondary outcomes were the total length of hospital (LOS) and intensive care unit (ICU) LOS. Statistical analyses were conducted using the Analysis of Variance and the Chi-square test.

Results. A total of 757 charts were reviewed of which 203 were included in the analysis; 69 in the piperacillin-tazobactam arm, 74 in the cefepime arm, and 60 in the aztreonam arm. The incidence of nephrotoxicity as assessed by the RIFLE criteria was higher in the piperacillin-tazobactam arm (41%) compared with cefepime (15%) and aztreonam arms (17%); $P = 0.052$. Majority of patients with nephrotoxicity experienced injury according to the RIFLE criteria. No differences were found in the total LOS, ICU LOS, or duration of nephrotoxicity. Patients who experienced nephrotoxicity in the piperacillin-tazobactam arm occurred earlier upon antibiotic initiation at 48 hours compared with the other arms extending past 72 hours; $P = 0.004$.

Conclusion. There was a trend towards more patients experiencing nephrotoxicity in the piperacillin-tazobactam arm compared with the other groups. Clinicians should remain vigilant when utilizing combination therapy.

Disclosures. **T. Bias**, Merck: Grant Investigator, Research grant. The Medicines Company: Speaker's Bureau, Speaker honorarium.

827. Safety, Tolerability, and Pharmacokinetics (PK) of Posaconazole (POS) Intravenous (IV) Solution and Oral Powder for Suspension in Children With Neutropenia

Andreas H. Groll, MD[1]; Hisham Abdel-Azim, MD, MS[2]; Thomas Lehrnbecher, MD[3]; William Steinbach, MD[4]; RoseAnn Murray, PhD[5]; Amanda Paschke, MD, MSCE[5]; Eric Mangin, MS[5]; Gregory A. Winchell, MD[5] and Christopher J. Bruno, MD[5]; [1]Infectious Disease Research Program, Department of Pediatric Hematology and Oncology, University Children's Hospital Münster, Münster, Germany, [2]Division of Hematology, Oncology and Blood & Marrow Transplantation, Children's Hospital Los Angeles, University of Southern California Keck School of Medicine, Los Angeles, California, [3]Pediatric Hematology and Oncology, Hospital for Children and Adolescents, University of Frankfurt, Frankfurt, Germany, [4]Pediatric Infectious Diseases, Duke University Hospital, Durham, North Carolina, [5]Merck & Co., Inc., Kenilworth, New Jersey

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Background. POS, a triazole antifungal approved for prophylaxis and treatment of adults with invasive fungal infections, is available as an IV solution and 2 oral formulations: an oral suspension and a tablet with improved bioavailability. A novel powder for oral suspension (PFS) has been developed to offer the bioavailability of the tablet in a formulation optimized for weight-based dosing in children. The objective of this study is to evaluate the safety, tolerability, and PK of POS IV and POS PFS in pediatric patients (patients) aged 2 to 17 y with documented or expected neutropenia.

Methods. This is an ongoing, nonrandomized, multicenter, open-label, sequential dose-escalation study evaluating POS IV and POS PFS. Pts are divided into 2 age groups: 2 to <7 and 7 to 17 y. Each age group includes 2 dose cohorts: 3.5 mg/kg/d and 4.5 mg/kg/d. Patients received 10–28 d of POS initially as IV solution with the option to switch to PFS after 10 d for the remainder of the treatment period. PK sampling was conducted after 7–10 days on each formulation. Target PK exposure was ~90% of patients with C_{avg} 500–2,500 ng/mL. C_{avg} is defined as AUC over a dosing interval.

Results. 57 of 66 patients (86%) who received POS IV were PK evaluable; 35 patients (53%) received POS PFS, of whom 30 (86%) were PK evaluable. Table 1 shows C_{avg} and proportion in target range of PK-evaluable patients by dose cohort and age group. The safety profiles of POS IV and PFS were similar to those previously reported for adults treated with oral/IV POS.

Table 1. C_{avg} and proportion in target range of PK-evaluable pts

Dose, mg/kg	Age, y	Formulation	n	Mean C_{avg}, ng/mL	n (%) within C_{avg} range, ng/mL			
					200-<500	500-<2500	2500-<3650	>3650
3.5	2-<7	IV	11	743	2 (18)	**9 (82)**	0	0
		PFS	5	511	3 (60)	**2 (40)**	0	0
	7-17	IV	19	1140	0	**18 (95)**	1 (5)	0
		PFS	10	861	1 (10)	**9 (90)**	0	0
4.5	2-<7	IV	13	1080	0	**13 (100)**	0	0
		PFS	7	976	1 (14)	**6 (86)**	0	0
	7-17	IV	14	1310	0	**13 (93)**	1 (7)	0
		PFS	8	1190	0	**8 (100)**	0	0

Conclusion. POS PFS resulted in lower POS exposure than IV across age groups at both dose levels. POS exposure was substantially lower in the younger age group for both IV and PFS. At 4.5 mg/kg, the patients in this study achieved the predefined target but did not achieve systemic exposures (mean C_{avg}) comparable to those seen in adults with POS IV or tablet. These results suggest that study of POS IV and PFS dosing >4.5 mg/kg/d is warranted.

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828. Real-world Evaluation of Ceftolozane/Tazobactam (C/T) Use and Clinical Outcomes at an Academic Medical Center in Las Vegas

Kimberly D. Leuthner, PharmD, FIDSA[1]; Ravina Kullar, Pharm.D., M.P.H.[2]; Becky Jayakumar, PharmD[3]; David A. Hewlett, PharmD[4]; Truong Nguyen, PharmD Candidate[4] and Laura Puzniak, PhD, MPH[5]; [1]University Medical Center of Southern Nevada, Las Vegas, NV, [2]Merck & Co. Inc., Kenilworth, New Jersey, [3]Roseman University of Health Sciences, Las Vegas, Nevada, [4]Pharmacy, University Medical Center of Southern Nevada, Las Vegas, Nevada, [5]Merck & Co., Inc., Kenilworth, New Jersey

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Background. There is a global increase in Gram-negative (GN) pathogens, with Enterobacteriaceae and *Pseudomonas aeruginosa*(PSA) being the major threats in clinical practice. C/T is a novel antipseudomonal cephalosporin combined with an established β-lactamase inhibitor, approved for the treatment of complicated intra-abdominal and urinary tract infections. The objective was to describe the real-world clinical use and outcomes associated with C/T.

Methods. This retrospective descriptive study included adult patients treated with C/T > 48 hours from July 1, 2015–February 28, 2017 at University Medical Center