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

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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

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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.

Disclosures. **A. H. Groll**, Merck Sharp & Dohme: Consultant, Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium. **T. Lehrnbecher**, Merck/MSD: Scientific Advisor and Speaker's Bureau, Speaker honorarium. Astellas: Scientific Advisor and Speaker's Bureau, Speaker honorarium. Basilea: Scientific Advisor, Consulting fee. Gilead: Investigator, Scientific Advisor and Speaker's Bureau, Research grant and Speaker honorarium.Pfizer: Speaker's Bureau, Speaker honorarium. **W. Steinbach**, Merck: Consultant, Consulting fee. Astellas: Consultant, Consulting fee. Gilead: Consultant, Consulting fee. **R. Murray**, Merck: Employee, Salary. **A. Paschke**, Merck: Employee, Salary. **E. Mangin**, Merck: Employee, Salary. **G. A. Winchell**, Merck: Research Contractor, Consulting fee. **C. J. Bruno**, Merck: Employee and Shareholder, Salary and Stock.

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

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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

of Southern Nevada. Treatment was considered empiric when antibiotic was given prior to culture results. Escalation was the additional of an aminoglycoside or colistin after the start of C/T.

Results. There were 30 patients in the study. Average age was 57 (SD = 16) and most 19 (63%) were male, Caucasian 22 (73%) and were admitted from the community or home 18 (60%). The most frequent comorbidities were diabetes 13 (43%), heart disease 12 (40%) and chronic pulmonary disease 10 (33%). Previous medical history within 90 days included 15 (50%) hospitalizations, 13 (43%) infections, 6 (20%) Intensive Care Unit stays and 7 (23%) surgeries. All patients received a GN antimicrobial within 30 days prior to C/T. Ninety-three percent of infections were due to PSA and 17 (57%) were polymicrobial. All but 4 patients had multidrug-resistant PSA. The most frequent source of infection (some multiple sources) was respiratory 20 (67%), cUTI 8(27%) and sepsis 5 (17%). Empiric C/T therapy was given to 7 (23%) patients. One patient required escalation of therapy after C/T. Average duration of C/T was 10 (SD = 5.4) days. 23 (77%) patients were discharged within 30 days of last dose of therapy. Microbiological eradication was documented for 12 patients. There were 5 (17%) readmissions, but none associated with a GN infection. Six patients died (1 bilateral stroke, 1 cancer, 2 septic shock, 1 pneumonia and 1 complications of burn).

Conclusion. In this study, C/T was used in patients with serious infections primarily due to PSA, with most patients discharged within 30 days and no patients readmitted due to GN infection. This study provides important insights on how C/T is used in clinical practice.

Disclosures. **R. Kullar**, Merck & Co., Inc.: Employee, Salary. **B. Jayakumar**, Merck: Grant Investigator, Research grant. **L. Puzniak**, Merck: Employee, Salary.

829. Therapeutic Drug Monitoring (TDM) of Suspension (SUS), Extended-Release (ER), and Intravenous (IV) Posaconazole (POS) at a Large Transplant Center

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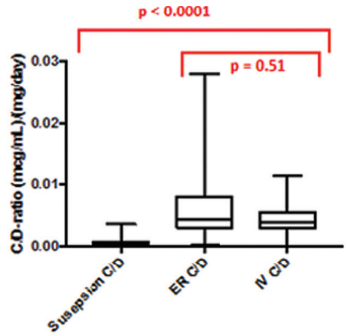
Background. Data on ER and IV POS among organ transplant recipients (OTRs) are limited, and the role of TDM is unclear.

Methods. Retrospective study of patients (pt) receiving any formulation of POS who had serum troughs checked. Therapeutic was defined as ^{3} 1 mcg/mL.

Results. We analyzed 88 pt and 340 levels (SUS: 88, ER: 197, IV: 55). Eighty-five pt were OTRs (97%), 73 were lung transplant recipients (LT) (83%), 17 had cystic fibrosis (CF) (19%). POS was used for treatment (70%) (probable aspergillosis (38%), possible aspergillosis (10%), mucormycosis (16%), other mycoses (6%)), prophylaxis (19%), and pre-emptive therapy (14%). POS was given for intolerance of or contraindication to other azoles (47%), salvage therapy (10%), resistance (19%), and failure to achieve therapeutic levels with other azoles (6%). Serum concentration/dose ratios were lower with SUS *vs.* ER/IV (P < 0.0001) but were similar in ER/IV groups (*P* = 0.51) (Figure). There was no difference in serum levels between pt receiving ER *vs.* IV POS at 300 mg once daily (median 1.2 *vs.* 1.3 mcg/mL, therapeutic 70% *vs.* 73%, P = 0.57 and >0.99, respectively). 3 pt had levels £ 0.2 mcg/mL on 300 mg ER: 2 had CF and had undergone LT (0.2 and 0 mcg/mL) and 1 had short-gut syndrome (0.1 mcg/mL). Sixty-six percent and 67 % of pt receiving ER or IV POS (300 mg once daily) achieved initial therapeutic levels, respectively; of these, 87% and 83% had median therapeutic follow-up levels, respectively. Serial levels were available for 7 pt whose dose was increased from 300 to 400 mg ER once daily for subtherapeutic levels. 4/7 pt achieved therapeutic levels on 400 *vs.* 0/7 on 300 mg ER once daily (P = 0.069). Metoclopramide use and CF were associated with subtherapeutic *vs.* therapeutic levels (25% *vs.* 4% and 37% *vs.* 13%, respectively, P = < 0.05). When pt with CF were excluded, neither age nor body mass index were associated with POS levels. CF pt had lower levels than non-CF pt on a dose of 300 mg ER once daily (median 0.8 vs. 1.3 mcg/mL, P = 0.018).

Conclusion. Therapeutic levels are more reliably achieved with ER & IV POS compared with SUS POS. Serial TDM is unnecessary for most, but is recommended for pt with CF or those on metoclopramide. Dose increases may effectively increase levels. Novel dosing strategies are needed for CF.



Box-plot of concentration/dose (C/D) ratios of the three different formulations (whiskers are min/max). There was no statistically significant difference in ratios between the ER and IV formulations. However, the IQR was wider for the ER formulation, suggesting variability in absorption among different patients compared to the IV formulation.

Disclosures. **R. K. Shields**, Astellas: Received research funding, Research support. Merck: Received research funding, Research support. **C. J. Clancy**, Merck: Received research funding, Research support. Astellas: Received research funding, Research support. Cidara: Received research funding, Research support. Astellas: Scientific Advisor, Advisory board. Merck: Scientific Advisor, Advisory board. Cidara: Scientific Advisor, Advisory board. Medicines Company: Scientific Advisor, Advisory board.

830. Clinical Manifestations and Outcome of Fluoroquinolone Associated Acute Interstitial Nephritis

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Background. Fluoroquinolones (FQ) are among the most commonly prescribed antibiotics. Nephrotoxicity related to FQ use is infrequently reported and the mechanism of renal injury is incompletely elucidated. We describe clinical manifestations and outcome of patients with biopsy proven acute interstitial nephritis (AIN) associated with FQ use at our institution.

Methods. We conducted a retrospective review of biopsy-proven AIN attributed to FQ use at Mayo Clinic Rochester from 1993 to 2016. Cases were reviewed by a renal pathologist and attributed to FQ use by an expert nephrologist. We also reviewed and summarized all published case reports of biopsy proven AIN that were attributed to FQ use.

Results. We identified 24 patients with FQ-related biopsy-proven AIN. The most commonly used FQ was ciprofloxacin (71%) with median antibiotic treatment duration of 7 days (Figure 1). The median duration between starting FQ and the diagnosis of AIN was 8.5 (IQR: 17). Common clinical manifestations included fever (50%), flank pain (8%), and skin rash (21%). However, 17% of the patients were asymptomatic at the time of diagnosis (Figure 2). Majority (58%) of the patients recovered following discontinuation of antibiotics and returned to baseline renal function at a median of 20.5 (IQR: 15.5). Six patients required temporary hemodialysis and 9 patients received steroids.

Conclusion. Onset of FQ-related AIN can be delayed and a high index of suspicion is needed by physicians prescribing these agents. Overall outcomes are favorable with recovery to baseline renal function within 3 weeks of discontinuing the offending drug.

Figure 1: Types of Fluoroquinolone used

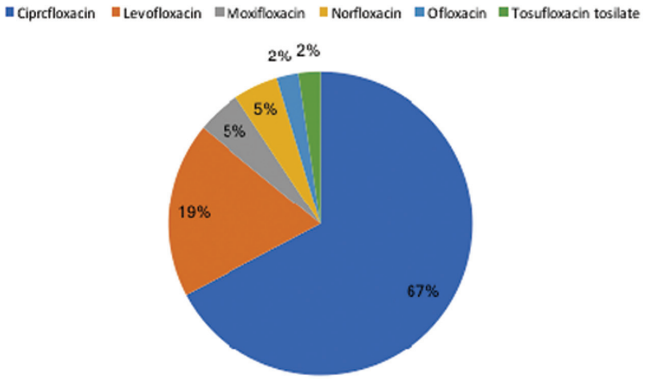
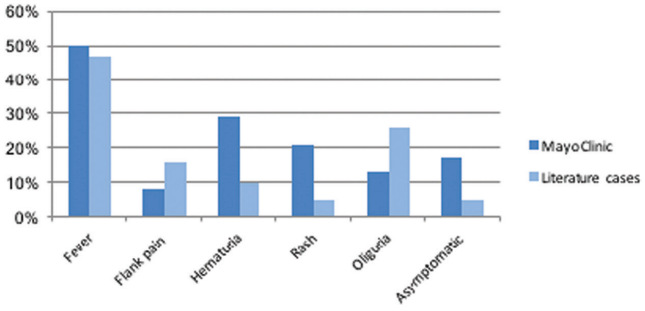


Figure 2: Presenting clinical features



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