Support)**Mutabilis** (Grant/Research Support)**Nabriva Therapeutics AG** (Grant/Research Support)**Naeja-RGM Pharmaceuticals** (Grant/Research Support)**Nosopharm SAS** (Grant/Research Support)**Novartis Pharmaceuticals Corp.** (Grant/Research Support)**NuCana Biomed** (Grant/Research Support)**Paratek Pharmaceuticals, Inc.** (Grant/Research Support)**Polyphor, Ltd.** (Grant/Research Support)**Prothena Corporation** (Grant/Research Support)**PTC Therapeutics** (Grant/Research Support)**Rempex Pharmaceuticals** (Grant/Research Support)**Roche TCRC** (Grant/Research Support)**Sagimet** (Grant/Research Support)**scPharmaceuticals Inc.** (Grant/Research Support)**Scynexis** (Grant/Research Support)**Spero Therapeutics** (Grant/Research Support)**TauRx Therapeutics** (Grant/Research Support)**Tetraphase Pharmaceuticals** (Grant/Research Support)**Theravance Biopharma Pharmaceutica** (Grant/Research Support)**USCAST** (Grant/Research Support)**VenatoRx** (Grant/Research Support)**Vical Incorporated** (Grant/Research Support)**Wockhardt Bio AG** (Grant/Research Support)**Zavante Therapeutics** (Grant/Research Support)**Zogenix International** (Grant/Research Support)

1114. Effectiveness and Safety of Beta-lactam Antibiotics with and without Therapeutic Drug Monitoring in Patients with *Pseudomonas aeruginosa* Pneumonia or Bloodstream Infection

Ashlan J. Kunz Coyne, Pharm.D.[1]; Mohammad H. Al-Shaer, PharmD[2]; Anthony M. Casapao, PharmD, MPH[3]; Jason Ferreira, PharmD, BCPS, BCCCP, FCCM[1]; Carmen Isache, M.D.[1]; Christopher Jankowski, Pharm.D., BCPS[1]; [1]UF Health Jacksonville, Jacksonville, Florida; [2]University of Florida, Gainesville, FL; [3]University of Florida College of Pharmacy, Jacksonville, Florida

Session: P-62. PK/PD Studies

Background. *Pseudomonas aeruginosa* (PSAR) is challenging to treat due to its multiple resistance mechanisms, limited anti-PSAR agents, and population pharmacokinetic (PK) variances. Beta-lactam antibiotics (BLA) are commonly used to treat PSAR infections and although they have a wide therapeutic index, suboptimal exposures may lead to treatment failure and antimicrobial resistance while high exposure may result in adverse effects. Certain patient populations may benefit from BLA therapeutic drug monitoring (TDM) due to their significant PK variability. The purpose of this study was to compare clinical outcomes in patients with PSAR pneumonia (PNA) or bloodstream infection (BSI) receiving BLA with and without the guidance of TDM.

Methods. Retrospective, parallel cohort study conducted at UF Shands Gainesville and UF Health Jacksonville evaluating five years of patients with PSAR PNA or BSI. TDM group was defined for routine BLA TDM compared to nonroutine BLA TDM service (non-TDM). Patients were excluded if they died before a culture result, transferred in with a positive PSAR culture, were transplant recipients, cystic fibrosis or burn injury patients. The primary outcome was a composite of presumed clinical cure defined as the absence of the following: all-cause in-hospital mortality, escalation, and/or additional antimicrobial therapy for PSAR infection after 48 hours of treatment with primary susceptible regimen due to worsening clinical status or transfer to a higher level of care.

Results. Two-hundred patients were included (TDM n=95; non-TDM n=105). The overall primary composite outcome of presumed clinical cure occurred in 73% of patients (82% and 75% of the TDM and non-TDM cohorts, respectively; p=0.301). A post-hoc multivariate analysis was conducted to assess predictors of not attaining clinical cure.

Table 1. Patients' demographics and baseline characteristics

Characteristics[b]	Cohort[a] TDM (n=95)	Non-TDM (n=105)	p value
Age (years)	61±11	61±11	0.683
Male	56 (59)	73 (70)	0.005
BMI (kg/m^2)	26 (22-33)	25 (20-31)	0.175
CL_{CR} (mL/min)	69 (36-111)	69 (43-105)	0.589
NH/LTC Resident	7 (7)	15 (14)	0.118
Immunosuppressed	9 (9)	4 (4)	0.105
IVDU	13 (14)	20 (19)	0.308
Charlson Comorbidity Index	4 (2-5)	5 (3-7)	0.081
SOFA score	5 (2-8)	5 (2-8)	0.808
APACHE II score	19 (14-26)	22 (17-28)	0.059
Positive culture source			
Blood	49 (52)	36 (34)	0.013
skin and soft tissue	11 (12)	15 (14)	0.057
urine	17 (18)	11 (10)	0.688
catheter-associated	5 (5)	5 (5)	0.534
intra-abdominal	7 (7)	5 (5)	0.959
other	4 (4)	7 (7)	0.191
Respiratory	46 (48)	69 (66)	0.019
Respiratory and blood	8 (8)	2 (2)	0.035
Hospital acquired infection	41 (43)	49 (47)	0.618
Antibiotic used for PSAR infection			
Cefepime	69 (73)	51 (49)	<0.001
Ceftazidime	0 (0)	1 (1)	0.999
Piperacillin-tazobactam	7 (7)	39 (38)	<0.001
Meropenem	18 (19)	10 (10)	0.055
Aztreonam	1 (1)	0 (0)	0.475
Ceftazidime-avibactam	0 (0)	1 (1)	0.999
Prolonged infusion BLA*	26 (27)	103 (96)	<0.001
Polymicrobial infections	32 (34)	47 (45)	0.109
Gram-positive	7 (7)	13 (12)	0.561
Gram-negative	23 (24)	31 (30)	0.579
both	2 (2)	3 (3)	0.999
Infectious Diseases Consult	66 (69)	29 (28)	<0.001

[a] Data are presented as "mean (standard deviation)", "number (%)" or "median (interquartile range)" as appropriate.
[b] SD, standard deviation; BMI, body mass index; CL_{CR}, creatinine clearance; NH/LTC, nursing home/long-term care; IVDU, intravenous drug use; SOFA, Sequential Organ Failure Assessment; APACHE, Acute Physiologic Assessment and Chronic Health Evaluation; PSAR, *Pseudomonas aeruginosa*.
* BLA administration via infusions of ≥ 3 hours

Table 2. Primary and secondary outcomes

Outcomes[b]	Cohort[a] BLA TDM (n=95)	No BLA TDM (n=105)	p value
Composite presumed clinical cure	78 (82)	75 (79)	0.301
All-cause mortality	12 (13)	21 (20)	0.185
Antibiotic escalation/addition	4 (4)	6 (6)	0.724
Escalation in level of care	3 (3)	0 (0)	0.497
All-cause in-hospital mortality	14 (15)	23 (22)	0.198
Hospital length of stay	21 (15-33)	21 (11-29)	0.337
Intensive care unit length of stay	19 (11-28)	14 (8-23)	0.019
Adverse event during BLA therapy			
Acute kidney injury	31 (30)	29 (28)	0.440
Clostridioides difficile	3 (3)	6 (6)	0.497
Neurotoxicity/encephalopathy	5 (5)	3 (3)	0.481
Readmission rates			
30-day	25 (26)	21 (20)	0.289
60-day	12 (13)	14 (13)	0.883
90-day	17 (17)	9 (9)	0.050

[a] Data are presented as "number (%)" or "median (interquartile range)" as appropriate.

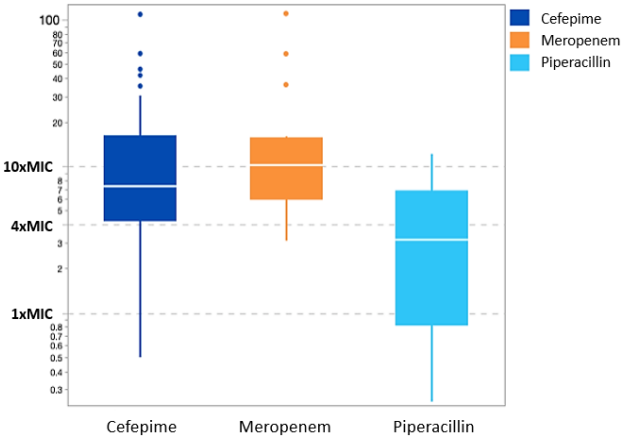
Table 3. Predictors of not attaining presumed clinical cure

Candidate Variables[a,b]	p value	OR	Lower 95%	Upper 95%
Age ≥ 61 years	0.018	1.027	1.001	1.054
SOFA Score ≥ 7	0.008	2.962	1.357	6.469
ICU admission	0.040	3.006	1.008	8.968
RRT during BLA therapy	0.005	3.359	1.313	8.596
MIC ± 1 dilution from CLSI breakpoint	0.042	3.109	1.040	9.294

[a] Candidate variables with univariate p < 0.2.
[b] RRT, renal replacement therapy; MIC, minimum inhibitory concentration; CLSI, Clinical and Laboratory Standards Institute

Conclusion. While there was no difference in the primary composite outcome of presumed clinical cure, future studies can use these data to assess TDM patient selection and whether a bundled care approach of BLA regimens with known clinical benefit, early TDM-guided dose optimization, and continued clinical assessment improves outcomes in patients with PSAR PNA or BSI compared to use of each modality individually.

Figure 1. Boxplot of fC_{min}:MIC ratios for BLA administered



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

1115. Evaluation of Gepotidacin (GSK2140944) Pharmacokinetics and Food Effect in Japanese Subjects

Mohammad Hossain, PhD[1]; Courtney Tiffany, BSc[1]; Aline Barth, MSC;PHD[2]; Aparna Raychaudhuri, Ph.D.[2]; Etienne F. Dumont, MD[1]; [1]GlaxoSmithKline plc., Collegeville, PA, USA, Collegeville, Pennsylvania; [2]GSK

Session: P-62. PK/PD Studies

Background. Gepotidacin, a novel, first-in-class triazaacenaphthylene antibiotic, inhibits bacterial replication and has *in vitro* and *in vivo* activity against key pathogens, including drug-resistant strains, associated with a range of infections. Gepotidacin is currently in Phase 3 clinical studies for the treatment of uncomplicated urinary tract infections and gonorrhea. This study (NCT02853435) was designed to assess gepotidacin pharmacokinetics (PK) in Japanese subjects (fasted and fed).

Methods. A tablet formulation of 750 mg gepotidacin free base was used in the study, which was conducted in two parts: Part 1, gepotidacin PK was assessed following 1500 and 3000 mg single oral doses in the fasted state; and Part 2, gepotidacin PK was assessed following 1500, 2250, and 3000 mg single oral doses in the fed state. Serial blood and urine samples were collected in both study parts.

Results. Part 1: The area under the plasma drug concentration-time curve from time 0 to infinity ($AUC_{[0-\infty]}$) and maximum observed concentration (C_{max}) were slightly higher in Japanese subjects than in Caucasian subjects at the same dose levels and with the same formulation. Following gepotidacin dosing in the fasted state, the 1500 mg dose was tolerated, while the 3000 mg dose was poorly tolerated with mild or moderate gastro-intestinal adverse effects (GI AEs) reported by most subjects shortly