categories using the following definition: multidrug-resistant (MDR) non-susceptible (NS) to ≥1 agent in ≥3 different antimicrobial classes, extensive drug-resistant (XDR) NS to 4 or 5 different classes, and pan drug-resistant (PDR) NS to all 6 classes except colistin.

Results. Forty-two *P. aeruginosa* respiratory isolates from 32 patients with CF were included. The overall susceptibility to C/T and CZA was 59.5% and 42.9%, respectively. Thirty-eight (90%) isolates were considered MDR with susceptibility of 55.3% to C/T and 44.7% to CZA. Among the 11 XDR isolates, susceptibility to C/T was 81.8% vs. CZA 72.7%. Susceptibility to C/T vs. CZA was also higher (37.5% vs. 25%) among the 24 PDR isolates.

Conclusion. Among *P. aeruginosa* isolated from CF respiratory cultures, C/T appears to have better in vitro activity compared with CZA, and remained true among isolates considered XDR and PDR. These results suggest using C/T while awaiting susceptibilities when standard anti-pseudomonal agents cannot be used. Future studies evaluating clinical outcomes for the treatment of pulmonary CF exacerbations are needed to assess the applicability of *in vitro* susceptibility data.

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1595. Comparative *In Vitro* Activity of Imipenem–Relebactam Against Drug-Resistant Gram-Negative Isolates from Pediatric Patients

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Background. Drug resistance in Gram-negative bacteria is of particular concern in children. Relebactam, a novel diazabicyclooctane inhibitor, coupled with imipenem has broad-spectrum activity against β-lactamase producing organisms. Here, we compare the *in vitro* activity of imipenem-relebactam to 10 standard comparator drugs against resistant Gram-negative isolates from two US pediatric hospitals.

Methods. We tested 100 isolates (50 per site) from pediatric clinical specimens tested during 2015–2017. All isolates were extended-spectrum cephalosporin-resistant (ESC-R); more than half were multidrug resistant (67%). Selected ESC-R isolates included *Escherichia coli* (90), *Klebsiella pneumoniae* (8), *Klebsiella oxytoca* (1), and *Enterobacter cloacae* (1) that were resistant or intermediate to ≥1 cephalosporins and/or aztreonam. A 0.5 McFarland suspension was prepared from colonies grown on blood agar plates (Thermo Scientific) at 35 ± 1°C for 18–24 hours. A final inoculum of 5 × 10^5 CFU/mL was prepared in Mueller–Hinton broth. Sensititre plates (Thermo Fisher Scientific) containing graded concentrations of imipenem/relebactam and 10 comparator drugs were inoculated and incubated at 35 ± 1°C for 18–24 hours. The minimum inhibitory concentration (MIC) was determined using the Sensititre Vizion system (Thermo Fisher Scientific) and endpoints were interpreted using CLSI (2019) breakpoint criteria, with the exception of colistin (EUCAST 2019).

Results. Selected ESC-R isolates had high rates of resistance to cephalosporins (64%–97%), aztreonam (80%), and levofloxacin (61%). All isolates were susceptible to imipenem/relebactam, imipenem and meropenem (MIC, ≤1 μg/mL for all). The imipenem/relebactam MIC_{50} (0.06 μg/mL) and MIC_{90} (0.12 μg/mL) values for ESC-R isolates were within one dilution of MICs of imipenem alone (0.12 μg/mL and 0.25 μg/mL). Among the comparators, colistin, amikacin, and piperacillin/tazobactam demonstrated comparable activities with 100%, 99%, and 94% susceptibilities, respectively.

Conclusion. Meropenem, imipenem alone and in combination with relebactam exhibited 100% susceptibilities against ESC-R *Enterobacteriaceae* isolated from pediatric specimens, demonstrating the high potency of carbapenems.

Drug	% susceptible	MIC50(µg/ml)	MIC90(µg/ml)
Amikacin	99	4	8
Aztreonam	20	32	32
Cefepime	20	16	32
Ceftazidime	36	16	32
Ceftriaxone	3	16	16
Colistin	100	1	1
Imipenem	100	0.12	0.25
Imipenem/Relebactam	100	0.06	0.12
Meropenem	100	0.06	0.12
Levofloxacin	39	16	32
Piperacillin/Tazobactam	94	3	16

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1596. Impact of Vancomycin Area Under Curve on Persistent Methicillin-Resistant *Staphylococcus aureus* (MRSA) Bloodstream Infections (BSI)

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Background. Persistent Methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI) are associated with significant morbidity, mortality, and healthcare expenditures. Vancomycin (VAN) remains the treatment of choice for invasive MRSA BSI. Current guidelines for the treatment of MRSA BSI recommend a VAN AUC_{24h}/MIC ratio ≥400. The Detroit Medical Center (DMC) implemented an AUC guided dosing strategy. However, data on the association between AUC_{24h} and clinical outcomes in MRSA BSI are limited. We aimed to evaluate the association between VAN AUC_{24h} and persistent bacteremia (PB) among patients with BSI.

Methods. Multi-center, retrospective cohort study from January 2015 to November 2018. We included adult patients with MRSA bacteremia treated with VAN for which AUC_{24h} monitoring was performed. AUC was measured using 2-level guided dosing. The primary outcome was PB defined as continued positive cultures >72 hours after VAN initiation. Classification and Regression Tree (CART) analysis was performed to determine the AUC_{24h} breakpoint (BP) most predictive of PB in the cohort. Mann–Whitney and Fischer exact tests were used for univariate analysis. The independent association between AUC_{24h}, dichotomized at the CART-derived cut-point, was then examined through multivariable logistic regression analysis.

Results. Overall, 137 patients were included. The median age was 59 (18–85) years, 69.3% male, and 75.2% African American predominance. Most common sources of BSI were skin/soft tissue (39.4%), pneumonia (25.5%), and osteoarticular (16.8%). The median APACHE II score was 13 (8–20). Median time to microbiological clearance was 2.5 days (0.5–12). Patients with AUC_{24h} ≤ 406.25 were more likely to have PB compared with those with AUC_{24h} > 406.25 (59.4% and 35.2%, respectively; *P* = 0.002). After controlling for age, intensive care stay, and concomitant β-lactam therapy; AUC of ≤ 406.25 (aOR 2.767, 95% CI 1.212–6.318) and endocarditis (aOR 2.87, 95% CI 1.079–7.638) were independently associated with PB.

Conclusion. VAN AUC_{24h} BP of <406.25 was independently associated with PB in patients with MRSA BSI. Our findings underscore the importance of VAN dose optimization to achieve timely bacterial clearance in MRSA bacteremia.

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1597. Evaluation of Ceftaroline Resistance (CPT-R) in Chile Across Time and a Comparison of CLSI vs. EUCAST Breakpoints in Methicillin-Resistant *Staphylococcus aureus* (MRSA)

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Background. CPT-R in MRSA is associated with clonal complex (CC) 5 lineages. Chile, with wide dissemination of the CC5 Chilean-Cordobes clone, has high MRSA rates. In 2019, CLSI revised the breakpoints (BPs) keeping susceptible (S, minimum inhibitory concentration [MIC mg/L] ≤1), added susceptible dose-dependent (SDD, MIC 2–4), removed intermediate (MIC 2); resistant (R) is now MIC ≥8. EUCAST S is MIC ≤ 1, but R differentiates among pneumonia (MIC > 1) and nonpneumonia (NP) isolates (MIC > 2). We evaluated CPT-R across time and agreement between agencies for broth microdilution (BMD), E-test and Disk Diffusion (DD)

Methods. Hospital- (HA; *n* = 320, 10 centers) and community-associated (CA, *n* = 37) clinical MRSA isolates collected between 1999 and 2018 were confirmed with MALDI-TOF, cefoxitin DD, and *mecA* PCR. CPT susceptibilities were evaluated by BMD, E-test and DD (5 and 30 mg) across revised and old CLSI or EUCAST BPs. We determined essential and categorical agreement (EA, CA), very major, major, and minor errors (VME, ME, MiE)

Results. The MIC_{50}/MIC_{90} of HA-MRSA with BMD was 2/2 mg/L (64% of isolates considered CPT non-susceptible) and 0.5/0.5 mg/L for CA-MRSA. MIC_{50}/MIC_{90} was 1/1.5 with E-test. Strains collected in 1999–2008 (*n* = 161) and 2009–2018 (*n* = 159) both had a MIC_{50}/MIC_{90} of 2/2. The EA of E-test with BMD was 82%; results of

CA-VME-ME-MiE were 51-0-0-48% using the new CLSI BPs or 51-81-0-45% using EUCAST or old CLSI BPs. For BMD, CA-VME-ME-MiE between new CLSI and EUCAST was 95-0-0-5 with 100% CA for E-test. Under NP EUCAST BPs, R isolates increase from 5 to 21% by BMD and 0 to 8% by E-test. CA-VME-ME-MiE between new CLSI and NP EUCAST BPs for BMD is 79-0-0-21 and for E-test is 91-0-0-8. For DD vs. BMD, CA-VME-ME-MiE is 55-0-1-44 with new CLSI BPs, 53-63-1-43 with old CLSI and 36-6-35-51 with EUCAST. With EUCAST DD (5 µg CPT) as reference vs. CLSI DD (30ug CPT), CA-VME-ME-MiE is 25-70-0-38.

Conclusion. CPT nonsusceptibility is frequent in the CC5 HA-MRSA clone circulating in Chile across time. All methods had poor performance against BMD, but revision of CLSI BPs decreased error rates. E-test under called the MIC. CLSI DD (under called nonsusceptibility) and EUCAST DD (overcalled resistance) are drastically discordant. Respiratory isolates evaluated under NP BPs increased rates of resistance.

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1598. Antimicrobial Activity of the Novel β-Lactam Enhancer Combination Cefepime–Zidebactam (WCK-5222) Tested Against Gram-Negative Bacteria Isolated in United States Medical Centers from Patients with Bloodstream Infections

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Background. Zidebactam (ZID) is a β-lactam enhancer antibiotic with a dual mechanism of action: high binding affinity to gram-negative PBP2 and β-lactamase (BL) inhibition. We evaluated the activity of cefepime (FEP) combined with ZID against contemporary clinical isolates of gram-negative bacilli (GNB) causing bloodstream infections (BSIs) in the US hospitals.

Methods. 1,239 GNB were consecutively collected (1/patient) from 34 US medical centers in 2018. Susceptibility (S) testing against FEP-ZID (1:1 ratio) and comparators were performed by reference broth microdilution method in a central laboratory. The FEP S breakpoint of ≤ 8 mg/L (CLSI, high dose) was applied to FEP-ZID for comparison purposes. An FEP-ZID S breakpoint of ≤ 64 mg/L has been proposed for non-fermentative GNB based on pharmacokinetic/pharmacodynamic target attainment and was also applied. Selected *Enterobacterales* (ENT) isolates were evaluated by whole-genome sequencing.

Results. FEP-ZID was highly active against ENT (MIC_{50}/MIC_{90}, 0.03/0.12 mg/L; highest MIC, 4 mg/L; Table), including multidrug-resistant (MDR, MIC_{50}/MIC_{90}, 0.12/0.25 mg/L) and carbapenem-resistant isolates (n = 7; MIC_{50}, 0.5 mg/L). The highest FEP-ZID MIC values among *E. coli*, *K. pneumoniae*, and *E. cloacae* were 1, 2, and 0.25 mg/L, respectively. The most active comparators tested against MDR ENT were ceftazidime–avibactam (CAZ-AVI; MIC_{50}/MIC_{90}, 0.25/1 mg/L; 98.0%S), meropenem (MEM; MIC_{50}/MIC_{90}, 0.03/0.12 mg/L; 93.1%S) and amikacin (AMK; MIC_{50}/MIC_{90}, 4/16 mg/L; 92.1%S). The most active agents tested against *P. aeruginosa* were FEP-ZID (MIC_{50}/MIC_{90}, 1/4 mg/L; highest MIC, 8 mg/L), colistin (MIC_{50}/MIC_{90}, 0.5/1 mg/L; 100.0%S), and AMK (MIC_{50}/MIC_{90}, 4/8 mg/L; 99.2%S); whereas CAZ-AVI and ceftolozane–tazobactam were active against 96.5–96.7% of isolates. FEP-ZID exhibited good activity against *Acinetobacter* spp. (MIC_{50}/MIC_{90}, 2/8 mg/L) and *S. maltophilia* (MIC_{50}/MIC_{90}, 4/32 mg/L). *S. maltophilia* displayed low S rates to most comparators.

Conclusion. FEP-ZID demonstrated potent activity against a large collection GNB from BSI, including isolates resistant to other BL inhibitor combinations and/or carbapenems. These results support further clinical development of FEP-ZID.

Organism (no.)	No. of isolates (cumulative %) inhibited at cefepime-zidebactam MIC (mg/L) of:											
	≤0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32
Enterobacterales	113	584	286	160	33	6	1	1	1			
(1,185)	(9.5)	(58.8)	(83.0)	(96.5)	(99.2)	(99.7)	(99.8)	(99.9)	100.0)			
P. aeruginosa					2	19	49	26	18	7		
(121)					(1.7)	(17.4)	(57.9)	(79.3)	(94.2)	(100.0)		
Acinetobacter				3	1	1	3	6	4	3	1	
spp. (22)				(13.6)	(18.2)	(22.7)	(36.4)	(63.6)	(81.8)	(95.5)	(100.0)	
S. maltophilia							3	1	8	4	1	3
(20)							(15.0)	(20.0)	(60.0)	(80.0)	(85.0)	(100.0)

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1599. AUC24 Vancomycin Bayesian-Based Dosing: Increasing Therapeutic Target Attainment with Decreased TDM Cost

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Background. Vancomycin efficacy is optimally predicted by the area under the concentration–time profile (AUC24), however, traditional AUC24-based dosing methods involve analytic PK calculations that require both peak and trough drug levels, increasing cost and time compared with trough-based dosing. Recent literature (e.g., Rybak et al 2019) suggest that Bayesian dosing tools alleviate the cost and difficulty of implementing AUC24-based dosing in order to improve patient outcomes. In this study, we compare therapeutic range attainment across 5 hospitals using trough-based dosing vs. 5 hospitals using Bayesian-supported AUC24 dosing.

Methods. De-identified data were available from 5 hospitals across the United States, EU, and Australia that used a trough-based dosing method (375 adult patients, 13,024 doses, 4,654 drug levels), and from 5 hospitals that implemented Bayesian-based AUC24 dosing (370 patients, 13,080 doses, 3,520 drug levels) using commercially available software (DoseMeRx). The proportion of doses in the therapeutic target range was determined for each hospital, and the number and cost of therapeutic drug monitoring (TDM) levels required were compared.

Results. In the 5 trough-based dosing hospitals, only 49.1% of doses achieved the therapeutic target of 10–20mg/L with significant variance per-hospital in the proportion of sub- and supra-therapeutic doses (range 11–35% and 14–41% respectively). Hospitals that implemented Bayesian-based AUC24 dosing successfully attained the target AUC24 (400–700mg.h/L) for 73.5% of doses, similar to a previous AUC24-based dosing intervention using increased sampling intensity (Meng et al. 2019). The number of TDM levels used for trough-based dosing was 1 per 1.34 days compared with 1 per 2.14 days in the AUC24 group (37.4% fewer levels). Bayesian-based AUC24 dosing hospitals not only avoided increased TDM costs, but counter-intuitively had decreased cost relative to the trough-based group. At a cost of $35USD per level (Meng et al. 2019), for a 500-bed hospital, this equates to savings of $60,305 per annum.

Conclusion. This study demonstrates that implementing Bayesian-based AUC24 dosing results in improved therapeutic target attainment. TDM levels were less frequent in the Bayesian-based AUC24 dosing group, leading to decreased cost.

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1600. Susceptibility of β-Lactam-Resistant *Pseudomonas aeruginosa* to Other β-Lactams: Is There Truly a Lack of Cross-Resistance?

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Background. Resistance to β-lactams in *P. aeruginosa* is complex with multiple mechanisms contributing. Since different mechanisms impact different β-lactams to differing degrees, a common dogma is that resistance to one β-lactam does not lead to resistance to others. The purpose of this analysis was to assess the frequency of β-lactam cross-resistance in *P. aeruginosa*.

Methods. Unique *P. aeruginosa* isolated in 2017 at Michigan Medicine were included. Overall, susceptibility (using CLSI breakpoints) and MIC distributions of β-lactams were assessed in all isolates and those with β-lactam resistance.

Results. 3,836 unique *P. aeruginosa* isolates were included. Resistance to traditional anti-pseudomonal β-lactams ranged from 15–23%, whereas ceftolozane/tazobactam resistance was 6%. Overall, cross-resistance between β-lactams was common. The table displays select β-lactam MIC distributions for all isolates and in those resistant to ≥1 β-lactam. When resistance of one agent was present susceptibility to other β-lactams was generally <40% with the majority of susceptible isolates having MICs at or near the breakpoint. Ceftolozane/tazobactam provided the best activity in this setting with 65–77% susceptibility.

Conclusion. Cross-resistance between β-lactams in *P. aeruginosa* is common. In patients at risk for resistant *P. aeruginosa*, ceftolozane/tazobactam should be considered for empiric coverage.

Table 1. Beta-lactam MIC distributions for *P. aeruginosa*

Target agent	*P. aeruginosa* population	≤1	2	4	8	16	≥32	
Cefepime	ALL (n=3836)	29	50	67	82	91	100	
	CAZ-R (n=559)	0	0	1	16	48	100	
	MEM-R (n=81)	4	9	20	41	66	100	
	TZP-R (n=882)	3	6	14	36	66	100	
Target agent	*P. aeruginosa* population	≤1	2	4	8	16	32	≥64
Meropenem	ALL (n=3836)	72	80	85	90	94	97	100
	CAZ-R (n=559)	26	32	43	60	75	87	100
	FEP-R (n=677)	26	32	41	58	75	87	100
	TZP-R (n=882)	26	35	45	60	76	87	100
Target agent	*P. aeruginosa* population	≤1	2	4	8	16	32	≥64
Ceftolozane/ tazobactam	ALL (n=3836)	82	90	94	96	97	98	100
	CAZ-R (n=559)	15	42	65	76	82	88	100
	MEM-R (n=781)	43	61	75	84	88	92	100
	FEP-R (n=677)	16	49	69	80	85	90	100
	TZP-R (n=882)	38	62	77	85	89	93	100

* Data presented as cumulative percentage of isolates inhibited at increasing MICs; Shaded area represents breakpoints; CAZ-ceftazidime, FEP-cefepime, TZP-piperacillin/tazobactam, MEM-meropenem

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