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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Session: 162. PK/PD and Susceptibility Testing
Friday, October 4, 2019: 12:15 PM

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 (1,185)	113 (9.5)	584 (58.8)	286 (83.0)	160 (96.5)	33 (99.2)	6 (99.7)	1 (99.8)	1 (99.9)	1 100.0)			
P. aeruginosa (121)					2 (1.7)	19 (17.4)	49 (57.9)	26 (79.3)	18 (94.2)	7 (100.0)		
Acinetobacter spp. (22)				3 (13.6)	1 (18.2)	1 (22.7)	3 (36.4)	6 (63.6)	4 (81.8)	3 (95.5)	1 (100.0)	
S. maltophilia (20)							3 (15.0)	1 (20.0)	8 (60.0)	4 (80.0)	1 (85.0)	3 (100.0)

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

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Session: 162. PK/PD and Susceptibility Testing
Friday, October 4, 2019: 12:15 PM

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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Session: 162. PK/PD and Susceptibility Testing
Friday, October 4, 2019: 12:15 PM

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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