1590. Activity of Meropenem-Vaborbactam and Single-Agent Comparators against *Enterobacterales* Isolates Including KPC-Producing Isolates, from European Patients Hospitalized with Pneumonia Including Ventilator-Associated Pneumonia (2014-2019)

Dee Shorttidge, PhD[1]; Lalitagauri M. Deshpande, PhD[1]; Leonard R. Duncan, PhD[1]; Jennifer M. Streit, BS[1]; Mariana Castanheira, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Meropenem-vaborbactam (MVB) was recently approved in Europe for the treatment of complicated UTIs, including acute pyelonephritis, complicated intra-abdominal infections, hospital-acquired bacterial pneumonia, ventilator-associated pneumonia (VAP), and bacteremia. KPC-producing *Enterobacterales* (ENT) isolates have disseminated worldwide. We analysed the activity of MVB and single-agent comparators against 6,846 ENT isolates from patients hospitalised with pneumonia (PHP) including VAP in European hospitals (2014–2019).

Methods. Among 6,846 ENT clinical isolates from PHP collected in 40 European hospitals located in 20 countries that were susceptibility (S) tested using reference broth microdilution methods. Of the carbapenem-resistant isolates submitted to whole genome sequencing, 75 carried bla_{KPC}. ENT isolates were also characterized for an extended spectrum beta-lactamase (ESBL) phenotype as described (CLSI, 2020). EUCAST (2020) interpretive criteria were used. %S from patients in the intensive care unit (ICU), ICU patients with VAP, and non-ICU isolates were also analysed.

Results. The most common ENT pathogens isolated from PHP were *Klebsiella pneumoniae* (KPN; n=1,877) and *Escherichia coli* (EC; n=1,646). The %S of MVB and comparators to ENT, ICU, ICU/VAP, and non-ICU are shown in the table. Overall, 98.2% of ENT were S to MVB. For 3,218 ENT isolates from ICU patients, MVB %S was 96.6% and for 2,627 non-ICU isolates MVB %S was 98.5%. The %S of comparators for ICU vs non-ICU isolates were similar, except for levofloxacin. 29 KPC-producing isolates were from ICU (11 from VAP), 46 were from non-ICU. Most KPC-producing isolates were KPN (n=71; 54 bla_{KPC-3}, 16 bla_{KPC-2} and 1 bla_{KPC-12}). 4 EC contained bla_{KPC-3}. KPC were from 7 countries, Italy had the highest number of KPC-producing isolates at 42 (56%). MVB inhibited 100% of KPC-producing isolates. Amikacin was the most active comparator against all ENT (94.2%S); colistin was the most active comparator against KPC-producing isolates (79.7%S).

Conclusion. These results demonstrate MVB has potent activity against ENT isolates from PHP including those producing KPC enzymes and suggest MVB is a useful treatment option for ICU and non-ICU PHP including VAP.

Table 1

Organisms and organism groups (n)	% susceptible using EUCAST breakpoints					
	Meropenem-vaborbactam	Meropenem	Amikacin	Gentamicin	Levofloxacin	Colistin
Enterobacterales (6,846)	98.0	95.1	94.2	85.3	75.0	76.8
ESBL-phenotype (1,368)	90.6	77.4	75.1	48.8	22.6	88.3
KPC-producing (75)	100.0	0.0	48.0	60.0	6.7	81.3
ICU isolates (3,218)	96.6	94.2	93.0	84.6	76.0	76.4
ESBL-phenotype (706)	87.5	75.3	71.2	45.7	22.8	86.1
KPC-producing (29)	100.0	0.0	37.9	75.9	6.9	62.1
ICU-VAP isolates (1,890)	96.7	93.2	91.5	82.6	74.3	76.8
ESBL-phenotype (455)	86.8	73.8	67.3	44.6	20.7	86.5
KPC-producing (11)	100.0	0.0	18.2	81.8	0.0	72.7
non-ICU isolates (2,627)	98.5	94.5	94.0	83.7	70.3	78.2
ESBL phenotype (530)	92.8	75.1	76.6	48.9	19.2	89.4
KPC-producing (46)	100.0	0.0	54.3	50.0	6.5	93.5

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1591. Antibiotic Utilization Trends in Veterans Affairs (VA) Patients with Carbapenem Resistant Enterobacteriaceae (CRE) Infections

Alfredo Traversa, PharmD[1]; Linda Poggensee, MS[2]; Geneva M. Wilson, PhD[1]; Katie J. Suda, PhamD, MS[3]; Charlesnika T. Evans, PhD, MPH[4]; Ursula Patel, PharmD[1]; Margaret A. Fitzpatrick, MD, MS[5]; [1]Hines VA, Chicago, Illinois; [2]Hines VA Hospital, Hines, IL; [3]Center of Innovation for Complex Chronic Healthcare (CINCCH), Hines VA Hospital and University of Illinois at Chicago College of Pharmacy, Hines, IL; [4]Northwestern University and VA, Hines, Illinois; [5]Center of Innovation for Complex Chronic Healthcare, Edward Hines Jr. VA Hospital, Hines, IL

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. Carbapenem-resistant Enterobacteriaceae (CRE) are classified as an "urgent threat" to public health. Historically, colistin and tigecycline had been considered the drugs of choice for CRE infections, while other agents such as aminoglycosides and carbapenems had been used as adjunctive therapy. However, the FDA approval of ceftazidime-avibactam in 2015, meropenem-vaborbactam in 2017, and plazomicin in 2018 has expanded treatment options. Our purpose was to assess trends in CRE treatment for "new" antibiotics (ceftazidime-avibactam, meropenem-vaborbactam, plazomicin) as compared with other antibiotics with CRE activity.

Methods. This was a retrospective cohort study describing treatment of CRE blood stream infections (BSI) across 134 VA facilities from 2012-2018. Patients were censored at their first positive blood culture with CRE. Categorical data was assessed with a Fisher's exact test or chi-square test. Trends test and logistic regression were used to describe changes in CRE treatment over time.

Results. 724 patients with positive blood cultures for CRE were identified during the study period. Most patients were male (94%), white (32%) or Hispanic (38%), and the mean age was 71.5+11.9. Of those patients that received antibiotics (N=697), 53.4% carbapenems, 40.3% received aminoglycosides, 39.3% received polymyxins, 32.9% penicillins, 32.6% extended spectrum cephalosporins, 26.1% fluoroquinolones, 11.6% ceftazidime/avibactam, and 0.4% ceftolazone/tazobactam. Over the study period, there was decreased utilization of aminoglycosides ($P < 0.0026$) and colistin ($P< 0.002$) and increases in extended spectrum cephalosporins ($P < 0.001$) and ceftazidime/avibactam ($P < 0.001$).

Conclusion. Utilization of "older" agents such as aminoglycosides and polymyxins for the treatment of CRE blood stream infections is decreasing in the VA. Treating CRE with ceftazidime/avibactam, a newly approved antibiotic, and extended spectrum cephalosporins are increasing.

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1592. Antimicrobial Activity of Ceftazidime-Avibactam and Comparator Agents Against *Enterobacterales* and *Pseudomonas aeruginosa* With Overexpression of AmpC β-Lactamase From Phase 3 Clinical Trials

Lynn-Yao Lin, MS[1]; Dmitri Debabov, PhD[2]; William Chang, BS[2]; Urania Rappo, MD, MS, PharmD[3]; [1]Abbvie, Irvine, California; [2]AbbVie, Irvine, California; [3]Allergan (at time of study conduct and analysis; before its acquisition by AbbVie), Madison, New Jersey

Session: P-71. Treatment of Antimicrobial Resistant Infections

Background. AmpC overproduction is a main mechanism of carbapenem resistance, in the absence of acquired carbapenemases. Ceftazidime-avibactam (CAZ-AVI) has potent in vitro activity against AmpC-producing *P. aeruginosa and Enterobacterales* that are resistant to carbapenems and other β-lactams.

Methods. Activity of CAZ-AVI and comparators was evaluated against AmpC-overproducing *Enterobacterales* (n=77) and *P. aeruginosa* (n=53) collected from 4 CAZ-AVI clinical trials: RECLAIM (complicated intra-abdominal infection [cIAI]), REPRISE (cIAI/complicated urinary tract infection [cUTI]), RECAPTURE (cUTI) and REPROVE (hospital-acquired pneumonia/ventilator associated pneumonia). In vitro susceptibility of CAZ-AVI and comparators was performed by broth microdilution using ThermoFisher custom panels. CLSI breakpoints were used to determine susceptibility. Quantitative PCR and microarray data were used to characterize presence and expression of AmpC. Clinical response at test of cure was assessed.

Results. Against 77 AmpC-overproducing *Enterobacterales* isolates, meropenem-vaborbactam (MVB) (98.7% susceptible [S]), CAZ-AVI (96.1% S), and meropenem (MEM) (96.1% S) had similar in vitro activity **(Table)**, with greater in vitro activity than amikacin (AMK) (84.4% S), gentamicin (61.0% S), and ceftolozane-tazobactam (TZC) (35.1% S). Clinical cures in patients with baseline AmpC-overproducing *Enterobacterales* were 21/26 (81%) in CAZ-AVI group vs 17/20 (85%) in control groups. Against 53 AmpC-overproducing *P. aeruginosa* isolates, CAZ-AVI (73.6% S) showed greater in vitro activity than AMK (69.8% S), TZC (58.5% S), and MEM (37.7% S). Clinical cures in patients with baseline AmpC-overproducing *P. aeruginosa* were 12/14 (86%) in CAZ-AVI group vs 9/12 (75%) in control groups. MIC distributions against the same *P aeruginosa* isolates were CAZ-AVI ($MIC_{50/90}$, 4/ >64 µg/mL), MVB ($MIC_{50/90}$, 8/32 µg/mL), and MEM ($MIC_{50/90}$, 8/32 µg/mL).