OXA-935 is very similar to OXA-14; however, comparison revealed that the F153S variant has unique structural features and is functionally distinct. Despite these differences, both enzymes confer high-level CTZ resistance. As we increase Natryla (individual amoxicillin therapy (e.g. cefazidine, cefepime) and combination (e.g. cefazidine-avibactam) therapy to treat MDR PA infections, it is critical that we continue to explore the mechanistic basis of β-lactam AMR in an effort to preserve existing treatments and design novel ones.

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1238. Comparative Activity of Meropenem-Vaborbactam and Ceftazidime-Avibactam Against Multidrug-Resistant Enterobacter cloacae from Hospitals in Europe and United States

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Session: P-72. Resistance Mechanisms

**Background.** Enterobacter spp. are part of the ESKEAPE pathogens that have been recognized as a threat to human health. Among this genus, *E. cloacae* species complex (ECL) is the most common species that causes human infections. ECL can develop resistance to β-lactams and other antimicrobial classes due to alterations in gene regulatory pathways. We evaluated the activity of meropenem-vaborbactam, ceftazidime-avibactam, and comparator agents against 235 multidrug resistant (MDR) ECL isolates collected in Europe and the US during 2017-2019.

**Methods.** A total of 2,459 ECL clinical isolates were collected in 40 European and 33 US hospitals. Isolates were susceptibility tested by reference broth microdilution methods and results were interpreted using CLSI, EUCAST, and US FDA breakpoints. Meropenem was defined as resistant to 3 or more drug classes when applying the CLSI breakpoints.

**Results.** MDR ECL were observed among 9.6% of the overall isolates. The MDR rate in Europe (12.0% / 155/1,295) was considerably higher than in the US (6.9% / 40/5,804). Meropenem-vaborbactam inhibited 94.5% and 97.4% of the MDR ECL isolates applying CLSI and EUCAST breakpoints, respectively (Table). Meropenem inhibited 77.9%/85.5% of the isolates (CLSI/EUCAST breakpoints). Cefepime inhibited only 26.0%/16.2% of the MDR ECL isolates while piperacillin-tazobactam inhibited only 13.2%/6.4%. Ceftazidime-avibactam inhibited 93.6% of the MDR ECL isolates.

In a global surveillance, ECL is the second most common Enterobacteriaceae species/species complex displaying MDR and carbapenem-resistance phenotypes, behind only *Klebsiella pneumoniae*. Meropenem-vaborbactam and ceftazidime-avibactam can be important options to treat infections caused by MDR ECL.

Table. Susceptibility rates for MDR *E. cloacae* species complex isolates

| Antimicrobial agent | MDR E. cloacae (235 isolates) | Meropenem-monosusceptible (225 isolates) | Carbapenem-resistant (228 isolates) |
|---------------------|-----------------------------|------------------------------------------|----------------------------------|
| Aztreonam | 52.9/54.9 | 72.1/63.5 | 87.8/87.8 |
| Ceftazidime | 74.3/74.3 | 91.5/91.5 | 91.5/91.5 |
| Vaborbactam | 56.0/56.0 | 91.7/91.7 | 91.7/91.7 |
| Meropenem | 44.4/44.4 | 97.1/97.1 | 97.1/97.1 |
| Cefepime | 70.4/70.4 | 91.5/91.5 | 91.5/91.5 |

*Oxacillin resistance (91.8% of isolates) are susceptible by CLSI and EUCAST criteria. Oxyiminocephalosporin resistance was not available. Reverse susceptibility (susceptible to resistance) was obtained in the ECL isolates.*
Background. Beta-lactams have demonstrated superior outcomes over vancomycin for this A. baumannii bacteremia. Although the anti-MRSA beta-lactam cefotaxime in MRSA bacteremia (MRSA-AB) are largely limited in size or focus on combination or salvage regimens. This study sought to further examine cefotaxime as first-line therapy for MRSA-AB.

Methods. This was a retrospective matched cohort study at the San Diego VA Medical Center between November 2010 and June 2020. Patients had to have received at least 72 hours of cefotaxime or vancomycin for MRSA-AB and less than 72 hours of prior MRSA therapy. Adjunct MRSA therapy was allowed only if routinely indicated (e.g., rifampin for prophylaxis). Patients in the vancomycin group were matched 1:1 to patients in the cefotaxime group by age (>10 years) and Pitt bacteremia score (+/−1 point). The primary outcome was duration of bacteremia after initiation of MRSA therapy, including time on prior MRSA therapy.

Results. Fifteen patients were included in each group, with a median age of 65 years and Pitt bacteremia score of 0. Patients in the cefotaxime group were more likely to have CKD; to have been on a different MRSA agent prior to initiation of the study drug, with a median of 1 day of prior treatment; and to have been on adjunctive rifampin or clindamycin. Though not significant, more patients in the cefotaxime group also had endovascular sources, uncontrolled sources, and longer durations of therapy. The median duration of bacteremia after initiation of MRSA therapy did not significantly differ between cefotaxime and vancomycin (4 vs. 3 days, p = 0.806). In addition, 30-day all-cause mortality, in hospital morbidity, and 30-day readmissions were not significantly different between groups. Rates of adverse events did not significantly differ between groups.

Conclusion. This study suggests cefotaxime may be an appropriate first-line agent for the treatment of MRSA bacteremia with similar outcomes between groups despite the cefotaxime group likely experiencing more difficult-to-treat infections. However, it was not powered to detect differences between groups, and further research is needed to provide the potential to introduce bias. Prospective comparative studies are needed to corroborate these findings.

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1240. Cefotaxime Activity against Drug-Resistant Staphylococcus aureus Clinical Isolates Collected in the United States from 2016 through 2020

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Session: P-72. Resistance Mechanisms

Background. The activity of cefotaxime against Staphylococcus aureus (S. aureus) isolates collected at two multinational studies has been evaluated. This study was conducted to further elucidate the activity of cefotaxime against drug-resistant S. aureus isolates in the United States.

Methods. A total of 13,868 S. aureus isolates were collected from patients with various infection types at 34 US medical centers from 2016-2020. Susceptibility to cefotaxime and comparator agents was tested by CLSI methods. Current CLSI and EUCAST interpretive criteria were applied (Table). Isolates were categorized as MDR if they were resistant to ≥3 classes of antimicrobial agents.

Results. Cefotaxime was more active than ceftobiprole (CPT) against MRSA (99.2% susceptible [S] versus 94.0% S, respectively) (Table). Cefotaxime maintained activity against 88.0% of the CPT-NS isolates, but CPT was only active against 6.5% of the cefotaxime-NS isolates. Cefotaxime was also highly active (97.7–100.0% S) against isolates NS to CM, DAP, ERY, gentamicin (GM), levofloxacin (LEV), linezolid (LZD), tetracycline (TET), tigecycline (TGC), trimethoprim-sulfamethoxazole (TMP-SMX), or vancomycin (VAN). Isolates displaying oxacillin MIC values ≥4 mg/L were categorized as MRSA.

Conclusions. Cefotaxime was more active than ceftobiprole (CPT) against MRSA (99.2% susceptible [S] versus 94.0% S, respectively) (Table). Cefotaxime maintained activity against 88.0% of the CPT-NS isolates, but CPT was only active against 6.5% of the cefotaxime-NS isolates. Cefotaxime was also highly active (97.7–100.0% S) against isolates NS to CM, DAP, ERY, GM, LEV, LZD, TET, TGC, or TMP-SMX. No VAN-NS isolates were detected. Importantly, cefotaxime was more active (97.7% S) than CPT (93.0%) S against the subset of MDR-MRSA isolates.

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