Background. Omadacycline is a novel aminomethylcycline that recently completed Phase 3 clinical trials for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and community-acquired bacterial pneumonia (CABP). This study evaluated the activity of omadacycline against a broad collection of recent (2016) clinical isolates with molecularly characterized tetracycline resistance mechanisms.

Methods. A total of 177 Gram-positive and -negative clinical isolates were identified as carrying acquired tetracycline resistance genes and were included in this study. Isolates were previously subjected to next-generation sequencing followed by screening of known tetracycline resistance mechanisms. Susceptibility testing and interpretation were performed according to CLSI methods.

Results. Omadacycline demonstrated MIC<sub>50</sub> values of 0.06–0.12 µg/mL against Gram-positive isolates carrying tet genes. Similar MIC results (0.06–0.12 µg/mL) were obtained against Gram-positive organisms carrying tet(K), tet(L), tet(M), or tet(T). Omadacycline (MIC<sub>50</sub> 0.12/0.25 µg/mL and tigecycline (MIC<sub>50</sub> 0.06/0.25 µg/mL) showed similar MIC results when tested against Staphylococcus aureus carrying tet(K). While tigecycline was less active (0.0–7.86% susceptible) than Tet(K)-producing S. aureus, doxycycline (MIC<sub>50</sub> 0.5/0.5 µg/mL; 100.0% susceptible) was active in vitro. Omadacycline (MIC<sub>50</sub> 0.25–1.25 µg/mL and tigecycline (MIC<sub>50</sub> 0.12–1 µg/mL) showed potent MIC results against Gram-positive isolates carrying tet(L) and/or tet(M). Tetracycline and doxycycline had MIC<sub>50</sub> values of 26 µg/mL. Omadacycline (MIC<sub>50</sub> 0.32 µg/mL) and tigecycline (MIC<sub>50</sub> 0.5–2 µg/mL) were active against Gram-negative isolates harboring tet(A), tet(B) or tet(D) or a combination of tet. Tetracycline (MIC<sub>50</sub> >16/16 µg/mL and doxycycline (MIC<sub>50</sub> >8/>8 µg/mL) had elevated MIC<sub>50</sub> results against these isolates.

Conclusion. Results presented here indicate that omadacycline is not adversely affected by tet genes present in contemporary Gram-positive and -negative clinical isolates, a characteristic that differs from the legacy tetracycline agents.

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1378. Evaluation of the In vitro Activity of Meropenem-Vaborbactam Against Carbapenem-Resistant Enterobacteriaceae, Including Isolates Resistant to Cefazolin-Avibactam

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Background. Meropenem-vaborbactam (M-V) is a novel antibiotic for treatment of carbapenem-resistant Enterobacteriaceae (CRE) infections. Our objective was to determine the in vitro activity of meropenem-vaborbactam against genetically diverse CRE isolates, including those with the developed resistance to Cefazolin-Avibactam (C-A).

Methods. Minimum inhibitory concentrations (MICs) were determined for meropenem (M), V-C, and C-A by reference broth microdilution (BMD) methods in triplicate. Vaborbactam and avibactam were tested at fixed concentrations of 8 and 16 µg/mL. Minimum MICs were determined against a broad collection of recent (2016) clinical isolates with molecularly characterized carbapenemase production and/or acquired carbapenem resistance in Enterobacteriaceae. Minimum MICs were determined for meropenem (M), M-V, and C-A by reference broth microdilution (BMD) methods in triplicate. Vaborbactam and avibactam were tested at fixed concentrations of 8 and 16 µg/mL. Minimum MICs were determined against a broad collection of recent (2016) clinical isolates with molecularly characterized carbapenemase production and/or acquired carbapenem resistance in Enterobacteriaceae.

Results. A total of 117 CRE isolates were tested, including K. pneumoniae (Kp; n = 83), E. cloacae (n = 17), E. coli (n = 10), and E. aerogenes (n = 2). Seventy-nine percent harbored bl<sub>a<sub>Kp<sub>; KPC subtypes included KPC-2 (n = 32), KPC-3 (n = 41), KPC-3 variants (n = 16), and KPC [not typed] (n = 4), all E. coli). Among 74 K. pneumoniae, 95% had a premature stop codon in ompK35 and ompK36 genes inherited wild type in n = 1 (KPC-3 variant). Minimum MICs for meropenem were (µg/mL): M 8 (0.06 to 2128), K 1 (0.02 to 1216), and C-A 12 (0.0015–16), respectively. Corresponding rates of susceptibility were 90–97% for M and 85–96% for C-A. Among K. pneumoniae, C-A was more active than M-V for KPC-positive isolates, whereas M-V was more active for MDR. In contrast, M-V was more active than C-A for KPC-negative isolates.