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 (CARB). 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$_{50}$ 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-negative organisms carrying tet(k), tet(t), tet(M) or tet(T). Omadacycline (MIC$_{50}$/MIC$_{90}$ = 0.12/0.25 µg/mL) showed similar MIC results when tested against Staphylococcus aureus carrying tet(K). While tetracycline was less active (0.0–7.86% susceptible) against Tet(K)-producing S. aureus, doxycycline (MIC$_{50}$/MIC$_{90}$ = 0.5/0.5 µg/mL; 100.0% susceptible) was active in vitro. Omadacycline (MIC$_{50}$/MIC$_{90}$ = 0.25–2 µg/mL and tigecycline (MIC$_{50}$/MIC$_{90}$ = 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$_{50}$ values of 26 µg/mL. Omadacycline (MIC$_{50}$/MIC$_{90}$ = 0.02–0.12 µg/mL) were active against Gram-negative isolates harboring tet(A), tet(B), tet(D) or a combination of tet. Tetracycline (MIC$_{50}$/MIC$_{90}$ = 0.06–0.12 µg/mL) and doxycycline (MIC$_{50}$/MIC$_{90}$ = 0.03–0.06 µg/mL) had elevated MIC$_{50}$/MIC$_{90}$ against these isolates.

Conclusions. 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.

Disclosures. R. E. Mendes, Paratek Pharmaceuticals: Research Consultant, Researcher. M. Castanheira, Paratek Pharmaceuticals: Research Consultant, Researcher. E. S. Armstrong, Paratek Pharmaceuticals: Employee, Salary. C. W. Wilson, PharmD: 1, 2, 3, 4, 5, 6, 7, 8; Chelsea Jones, BA; Kristin Morder, BA; Cavaliers, 1-3; Ellen Shields, MD; and Ryan K. Shields, PharmD: 1, 2, 3, 4, 5, 6, 7, 8; Paratek Pharmaceuticals: University of Pittsburgh School of Pharmacy, Pittsburgh, Pennsylvania, 1, 2, 3, 4, 5, 6, 7, 8; University of Pittsburgh, Pittsburgh, Pennsylvania, 1, 2, 3, 4, 5, 6, 7, 8; Infectious Diseases, University of Pittsburgh, Pittsburgh, Pennsylvania, 1, 2, 3, 4, 5, 6, 7, 8; Infectious Disease, University of Pittsburgh, Pittsburgh, Pennsylvania, 1, 2, 3, 4, 5, 6, 7, 8; University of Pittsburgh, School of Medicine, Pittsburgh, Pennsylvania, 1, 2, 3, 4, 5, 6, 7, 8; Paratek Pharmaceuticals: Employee and Shareholder, Salary. R. K. Flamm, Paratek Pharmaceuticals: Research Consultant, Researcher.