Omadacycline In Vitro Activity against a Molecularly Characterized Collection of Clinical Isolates with Known Tetracycline Resistance Mechanisms

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Introduction

• The tetracycline class of antibiotics have been in clinical use for approximately 70 years and have a well-documented safety and tolerability profile.

• Omadacycline is an investigational oxazolidinone antibiotic agent related to tetracycline.

• This investigational agent has a broad spectrum of activity against many gram-negative aerobes, anaerobes, and atypical bacterial pathogens.

• This study evaluated the in vitro activity of omadacycline against a broad collection of clinical isolates, including enterococci and non-fermentative gram-negative pathogens.

Materials and Methods

Bacterial organisms

• A total of 605 gonococcal and non-gram negative isolates from the worldwide SENTRY Antimicrobial Surveillance Program were included in this study, including >70% of isolates from the 2016 sampling year.

• Antimicrobial susceptibility panels were procured from the National Committee for Clinical Laboratory Standards (CLSI, North Liberty, IA) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST, North Liberty, IA) for tetracycline resistance testing.

Characterizing tetracycline resistance mechanisms

• Bacterial genotypes were examined on an MSQ Advantage (JMI Laboratories). FastPLOT sequencing files for each sample set were assembled to identify known tetracycline resistance determinants.

Results

• Activity of omadacycline against the population of gram-positive and -negative isolates (Table 1 and Figure 1).

• Omadacycline (MICc MBC; 0.06-0.12/0.06-0.25 µg/mL) showed similar MIC results when tested against Staphylococcus aureus (n=313) and Enterococcus faecalis (n=71).

• Omadacycline (MICc MBC; 0.06-0.25/0.06-0.5 µg/mL) showed higher MIC results against gram-positive isolates compared to enterococci (n=30).

• Tetracycline and doxycycline had MIC50 values of 1/2 µg/mL against gram-negative isolates undergoing surveillance (n=337).

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• Overall, omadacycline demonstrated MIC50 values between 0.06-0.12/0.06-0.25 µg/mL and 1-4 µg/mL against the population of gram-positive and -negative isolates or subsets thereof.

• These results indicate that omadacycline potency is not adversely affected against molecularly characterized gram-positive and -negative isolates carrying clinically acquired resistance mechanisms.

• This MIC distribution suggests minimal differences in activity against molecularly characterized wild-type and resistance-mutated isolates.

• Omadacycline demonstrated MIC50 values of ≤0.03 µg/mL against >70% of isolates, and 1 µg/mL against the population of gram-positive and -negative clinical isolates or subsets thereof, respectively.

• These results indicate that omadacycline penetration is not adversely affected against molecularly characterized gram-positive and -negative isolates carrying clinically acquired resistance mechanisms.

Conclusions

• Omadacycline demonstrated MBC values of ≤0.03-0.12 µg/mL and 1 µg/mL against the population of gram-positive and -negative clinical isolates or subsets thereof, respectively.

• The MIC distribution suggests minimal differences in activity against molecularly characterized wild-type and resistance-mutated isolates.

• This may be due to the presence of additional resistance mechanisms (e.g. plasmid-mediated) other than tetracycline resistance.