Efficacy of Omadacycline against Molecularly Characterized Gram-Positive and Gram-Negative Pathogens Causing Infections in the Phase 3 CABP and ABSSI Clinical Trials

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Introduction

• Omadacycline represents a new class of tetracycline-related compounds, the minocyclinehexanes, that possess antibacterial activity from a ability to bind to the 33S subunit of the bacterial ribosome and inhibit bacterial protein synthesis.
• Structural modifications at the C-17 C17-ethyl group allow omadacycline to overcome the spontaneous mutations that lead to tetracycline efflux pumps and resistance mechanisms.

Materials and Methods

Bacterial organisms

• Comparative (positive) and -negative (clinical isolates recovered from subjects enrolled in the OPTIC CABP and 2 phase III trials for acute bacterial skin and skin infections (ABSSSI) CABP-1 and CABP-2) were included.

Genomic isolates were selected based on the presence of tetracycline and/or macrolide resistance phenotypes.

Antimicrobial susceptibility testing

• Selected isolates were tested for antimicrobial susceptibility using Vitek-2® automated microdilution panels containing cation-adjusted Mueller-Hinton broth and panels were inoculated per protocol. The Clinical and Laboratory Standards Institute (CLSI) specifications described in the CLSI M100 (2017) document.

Antimicrobial agents

• MIC values were validated by concurrently testing the appropriate gram-positive and -negative strains recommended by the CLSI M100 document.

• MIC results against ATCC quality-control strains were interpreted according to published criteria per CLSI M100 guidelines.

• MIC values obtained against clinical isolates were interpreted using published CLSI (2017) breakpoints, when available.

Characterizing tetracycline resistance mechanisms

• Whole genome extraction and sequencing

This study expands on the analysis of omadacycline efficacy data among subjects infected with molecularly characterized Gram-positive and Gram-negative pathogens, highlighting the efficacy of omadacycline against non-susceptible isolates.

Sequence analysis

Clinical trial isolates

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Clinical success was noted in 14/16 (87.5%) omadacycline-treated subjects in OPTIC, consistent with the efficacy of omadacycline against clinical isolates with nonsusceptibility to tetracyclines.

Materials and Methods

• All omadacycline-treated subjects with clinical success at post-therapy evaluation (PTE) were evaluated, and the outcome of the clinical trial isolate was determined.

Results

• Of 24 and -negative clinical isolates recovered from subjects included in the OPTIC CABP and 2 phase III trials for acute bacterial skin and skin infections (ABSSSI) CABP-1 and CABP-2, were compared.

Conclusions

• Omadacycline demonstrated clinical success and resistance mechanisms of MIC of results in clinical trial isolates infected with nonsusceptible pathogens.

Acknowledgements

This study was sponsored by Paratek Pharmaceuticals, Inc., King of Prussia, Pennsylvania.

References


