Antimicrobial Activity of PTK 0796 (Omadacycline) and Comparator Agents Against Contemporaneous Pathogens Commonly Associated with Community-Acquired Respiratory Tract Infections Collected During 2011 from the European Union

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Abstract

Validation of the minimum inhibitory concentration (MIC) values was performed by concurrent testing of CLSIrecommended standard quality control (QC) strains: S. pneumoniae ATCC 49199, and S. aureus ATCC 29213, against MIC ranges for PTK 0796 and comparator agents against ATCC QC strains that were previously published in the CLSI M100-S22. (2012). Susceptibility testing as described above was performed by JMI Laboratories (North Liberty, IA, USA) using current CLSI (M07-A12; 2012) and Good Laboratory Practice (GLP) quality assurance practices.

Results

1. 1024 respiratory isolates (600. S. pneumoniae, 359. H. influenzae, and 56. M. catarrhalis) were collected from 22 medical centers as part of an international surveillance testing program.

2. PTK 0796 demonstrated potent activity against S. pneumoniae (MIC50/90, 0.06/0.06 mg/L) including penicillin-intermediate and penicillin-negative-subgroups (Table 1).

3. Total of 94/3.9% of 600. S. pneumoniae had PTK 0796 MIC of ≤0.25 mg/L, which was the highest PTK 0796 MIC value observed at 0.25 mg/L (Table 1).

4. PTK 0796 was 16-fold more active than levofloxacin (MIC50/90, 1/1 mg/L) in vitro against H. influenzae, and the β-lactamase-positive and negative-subgroups (Table 1 and 3).

5. There was little tetracycline resistance, (1.1/1.4% resistant by CLSI/EUCAST interpretive criteria; Table 3).

6. All agents were very active against M. catarrhalis (Table 3). The PTK 0796 MIC90 values were 0.12/0.12 mg/L, respectively, only one β-lactamase-negative M. catarrhalis isolate (PTK 0796 MIC, 0.06 mg/L) was detected.

Conclusions

PTK 0796 (omadacycline) demonstrated potent activity against the key bacterial respiratory pathogens (S. pneumoniae, H. influenzae, and M. catarrhalis).

PTK 0796 activity was unaffected by pениcillin or tetracyclines. S. pneumoniae and H. influenzae (MIC50 ≤0.06 mg/L).

PTK 0796, which is currently undergoing clinical development for acute bacterial skin and skin structure infections, exhibited activity against key bacterial respiratory pathogens and merits further studies in this clinical indication.

Materials and Methods

Bacterial isolates. A total of 1024 clinical isolates were collected during 2011 from 22 medical centers located in 9 European Union countries: Greece, Italy, Germany, Switzerland, United Kingdom, Norway, Turkey, and the United States.

Susceptibility testing. Susceptibility testing was performed by reference broth microdilution methods by JMI Laboratories and Clinical and Laboratory Standards Institute (CLSI; M07-A9; 2012) using validated dry-panel systems produced by ThermoFisher Inc, form. Cleveland, Ohio, USA. JMI Laboratories validated dry-form panels produced by ThermoFisher Inc, the tetracycline family, which is currently under clinical testing in two medical centers, Israel (9; 0.9%; one medical center), and in France (13%).

Methods: Susceptibility (S) testing for omadacycline and comparator antimicrobials was performed by Clinical and Laboratory Standards Institute (CLSI) broth microdilution methodology on a total of 1,024 isolates in 2011 from medical centers in the SENTRY Antimicrobial Surveillance Program.

Table 1. MIC frequency and percent inhibited distributions of PTK 0796 (omadacycline) for EU respiratory pathogens.

Organism/Susceptibility testing. Number of isolates (cumulative % inhibited) of PTK 0796 (MIC90 ≤0.06 mg/L) by country.

References

1. The efficacy of PTK 0796 in murine models of S. pneumoniae and M. catarrhalis lung infections was studied in this clinical indication.


3. Clinical and Laboratory Standards Institute (2012). M100-S22 Methods for dilution antimicrobial susceptibility testing of bacteria that grow aerobically; 22nd informational supplement. Wayne, PA, CLSI.


