Omadacycline (formerly PTK-0796) In Vitro Spectrum of Activity and Confirmation of Disk Mass Using Fresh Media for MIC Testing

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Abstract

Background: Omadacycline (OMC) is the first aminoacyclohexyclic lincosamide in development as a once-daily oral and IV antibiotic for the treatment of skin and soft tissue and respiratory infections. Testing of OMC using current disk mass methods can be limited by the low MICs of many strains tested. The aim of this study was to develop a fresh medium disk mass method for OMC that includes an inoculum to better simulate the normal oropharyngeal flora.

Materials and Methods

• All strains were tested for minimum inhibitory concentrations (MIC) using the CLSI reference broth microdilution (BMD) test.
• Cation-adjusted Mueller-Hinton broth was used for all MIC tests. This broth was supplemented with 3% lysed horse blood for testing streptococci and made up as haemolysin test media for testing Haemophilus influenzae.
• DD tests followed the CLSI reference disk diffusion method using Mueller-Hinton, Mueller-Hinton with 5% sheep blood or Haemolysin Test agar.
• A single inoculum preparation was used for both disk diffusion (DD) tests and MIC tests.

Results

Table 1: Error Rates Omadacycline Disk Diffusion to MIC

<table>
<thead>
<tr>
<th>Organism Group (%)</th>
<th>Error Rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae (n=105)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>S. aureus (n=104)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>B. cepacia (n=29)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>P. aeruginosa (n=22)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>A baumannii (n=53)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>H. influenzae (n=167)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Non Enterobacteriaceae Gram-positives (n=30)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Enterobacteriaceae (n=310)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Conclusions: For all strains, Gram-positive species, Micrococcus species and Haemophilus influenzae, disk diffusion error rates were essentially zero with a 30 µg disk when compared to CLSI, disk diameters were increased to 30 mm in the Primax, Primax, Moraxella catarrhalis group and new formulations based on species.

Background

Omadacycline is the first aminoacyclohexyclic lincosamide to enter clinical development. OMC is being developed globally as an intravenous and oral, once daily monotherapy therapy for ABSSSI and CABP. OMC was designed to overcome tetracycline resistance mechanisms and has been shown to have potent in vitro activity and in vivo efficacy against the key pathogens of ABSSSI and CABP, including isolates resistant to standards of care. The IV and oral formulations are bioequivalent and neither shows the dose-limiting nausea and vomiting exhibited by other lincosamide derivatives.

Acknowledgement

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References


Summary

• Omadacycline has broad spectrum activity with potent activity against the primary pathogens causing acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia.
• There was no evidence of a resistant subpopulation amongst the highly susceptible species, while some Enterobacteriaceae and P. aeruginosa were not susceptible to OMC.
• Fresh media is important for broth dilution testing.
• Zone diameters correlate well with MICs.
• The 30 µg disk was chosen based on testing 15, 30, and 60 µg disk masses giving the best dynamic range without overly large zones against highly susceptible organisms.