In Vitro Activity of Omadacycline Against Legionella pneumophila

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Materials and Methods

Omadacycline is the first aminomethylcycline in late stage clinical development for CABP and AESS as oral and IV once-daily formulations. The in vitro activity against a variety of L. pneumophila isolated from 1995 to 2005 and from 2006 to 2014 was investigated to determine whether any change in susceptibility has occurred. The in vitro activity of omadacycline (OMC), telithromycin (TE), levofloxacin (LE), and doxycycline (DO) against a total of 50 Legionella pneumophila strains tested from 1995 to 2005 (serogroup 1 [n=45] and serogroup 2, 3, 4, 5 and 6 [n=1 each serogroup]) and a total of 50 L. pneumophila isolates from 2006 to 2014 were collected from mostly nosocomial or acquired respiratory tract sources and were identified by standard methods such as described by Versalovic et al. [1].

Determination of MICs

MICs were determined using the CLSI broth microdilution method using microdilution plating of the organisms onto a series of broth medium microplates of increasing concentrations from 0.004 mg/L (2, 1, 0.5, 0.25, 0.12, 0.06, 0.03 and 0.016 mg/L). Results: BYE without iron and cation adjusted M (0.5 mg/L Mg2+). Only data for OM, TE, DO obtained in BYE for Legionella pneumophila ATCC29213, Legionella pneumophila ATCC33152, Legionella pneumophila ATCC27853, Legionella pneumophila ATCC35218, Legionella pneumophila ATCC35240, and Legionella pneumophila ATCC35242 were included as controls. Growth conditions S. aureus ATCC29213, E. coli ATCC25922, P. aeruginosa ATCC27853 and L. pneumophila ATCC33152 were tested in a media testing study during the activities of antibiotics in cation adjusted Mueller Hinton Broth (MH), standard BYE, and modified BYE. ("Mod BYE"; lacking ferric pyrophosphate). Only data for E. coli and L. pneumophila is shown in Table 1.

Conclusions: The activity of OMC has not changed between the 1995-2005 isolates and the 2005-2014 isolates. This data suggest that OMC may have use in infections caused by L. pneumophila and highlights the potential utility of this oral and IV agent for the treatment of CABP.

Table 1. Media Susceptibility of OD, E. coli and ATCC29213, P. aeruginosa ATCC27853 and L. pneumophila ATCC33152

<table>
<thead>
<tr>
<th>Organism (no. tested)</th>
<th>Collection Date</th>
<th>Antibiogram</th>
<th>Minimum Inhibitory Concentration (MIC) (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Legionella pneumophila</td>
<td>1995-2015</td>
<td>S. aureus</td>
<td>ATCC29213, E. coli ATCC25922, P. aeruginosa</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ATCC27853, L. pneumophila ATCC33152</td>
</tr>
</tbody>
</table>

Discussion

• Omadacycline and doxycycline MICs were 5–7 dilution higher in BYE broth with iron, compared to broth without the iron supplement, indicating that the MIC’s for OM may be artificially elevated in vitro due to media effects.

Against Legionella pneumophila all serogroups (n=100), the MICs for omadacycline ranged from ≤0.08 – 1 mg/L, and were either comparable or up to 2 dilutions lower than the most commonly used drugs for the treatment of Legionella, such as azithromycin and erythromycin.

Macrolide and levofloxacin are the most active compounds tested followed by telithromycin, omadacycline, azithromycin, erythromycin and doxycycline against L. pneumophila all serogroup.

Against Legionella pneumophila serogroup 2, 3, 4, 5 and 6 (n=10), omadacycline may be important in the treatment of Legionella, such as azithromycin and erythromycin.

Activity of omadacycline has not changed between the 1995-2005 isolates and the 2006-2014 isolates.

References


Conclusion

Based on the in vitro results of this study, omadacycline exhibits potent extracellular activity against L. pneumophila and warrants further study as an oral and IV antibacterial agent for the treatment of pneumonia caused by L. pneumophila.