Activity of Solithromycin and Comparators Against Antimicrobial-resistant Streptococcus pneumoniae Isolated from Respiratory Samples Collected in 2012-2013.

Poster C-1472

IAHMA Europe, Sàrl
9A Route de la Corniche,
Epalinges, Switzerland

Email: info@ihma.ch
Tel: +44 (0)1279 724929

Revised Abstract

Background: Solithromycin is a fourth-generation macrolide, the first fluoroquinolone, undergoing Phase III clinical trials for the treatment of moderate to moderately-severe community-acquired bacterial pneumonia. This study evaluated the in vitro activity of solithromycin against Streptococcus pneumoniae (SP) collected in 2012-2013.

Methods: A total of 996 SP isolated from respiratory samples were collected from Europe, Asia-Pacific, North America and other locations worldwide. Isolates were tested in a central laboratory with MIC and susceptibility for solithromycin and comparators determined according to CLSI broth microdilution methodology and breakpoints. Provisional breakpoints of ≤1/4 (S), 1/2 (I) & ≥2 (R) were used for solithromycin and FDA breakpoints for tigecycline. Susceptibility was analyzed for sub-sets of SP resistant to azithromycin (AZI-R), clindamycin (CLI-R), penicillin (PEN-R), amoxicillin/clavulanic acid (AMC-R), 3 drugs (MDR-3) or 4 drugs (MDR-4).

Results: %S is shown in the Table in the poster text (>90 %S in bold). Solithromycin was fully active against all isolates. Penicillin and azithromycin, in particular, were inactive against all resistant strains. AMC, CLI and ceftriaxone were also inactive against the MDR strains.

Conclusions: Solithromycin showed very good activity against antimicrobial-resistant isolates, including MDR strains. These data positively support the continued development of solithromycin for the treatment of respiratory infections caused by SP.

Introduction

Solithromycin is a fluoroquinolone available in both oral and intravenous formulations. It is being developed for the treatment of community-acquired bacterial pneumonia (CABP) and gonorrhea. Solithromycin is currently undergoing phase 3 clinical trials for the treatment of moderate to moderately-severe CABP. Phase 2 clinical trial data showed solithromycin to be equivalent to levofloxacin in efficacy and to have a more favorable safety profile [1]. This study evaluated the in vitro activity of solithromycin against drug-resistant pneumococci isolated worldwide during 2012-2013.

Materials & Methods

• A total of 996 pneumococcal isolates from Europe, Asia-Pacific, North America and other locations worldwide were identified to species level and MICs determined at a central testing laboratory (IHMA Europe, located in Epalinges, Switzerland).

• Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method using panels prepared at IHMA [2].

• MIC interpretive criteria followed the guidelines of CLSI published in 2014 [3]. Provisional solithromycin breakpoints of ≤1 (susceptible), 1/2 (intermediate) & ≥2 (resistant) were used in the analysis.

• Quality controls were performed on each day of testing using appropriate ATCC control strains, following CLSI and manufacturer guidelines. Results were included in the analysis only when corresponding QC results were within the acceptable ranges [3].

• A summary of the susceptibility of different resistance groups of \( S. \) pneumoniae to solithromycin and comparators is shown in Table 1.

• Summary susceptibility data for solithromycin and comparators against azithromycin-resistant pneumococci, clindamycin-resistant pneumococci, penicillin-resistant pneumococci, amoxicillin/clavulanic acid-resistant pneumococci, multi-drug resistant pneumococci (3 antibiotic classes) and multi-drug resistant pneumococci (4 antibiotic classes) are shown in Figures 1 to 6.

Table 1: Summary of the Susceptibility of Pneumococci in Different Resistance Groups to Solithromycin and Comparators

<table>
<thead>
<tr>
<th>Drug</th>
<th>AMC-R (n = 57)</th>
<th>CLI-R (n = 148)</th>
<th>PEN-R (n = 167)</th>
<th>MDR-3 (n = 68)</th>
<th>MDR-4 (n = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Susceptible (%)</td>
<td>100</td>
<td>98</td>
<td>100</td>
<td>97</td>
<td>96</td>
</tr>
<tr>
<td>Intermediate (%)</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Resistant (%)</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>3</td>
<td>10</td>
</tr>
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</table>

References


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