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

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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 from patients located in various European countries.

Methods: A total of 418 SP isolates from respiratory samples were collected from Europe. 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 ≤4 (S), 2 (I) & >4 (R) were used for solithromycin. Susceptibility was analyzed for sub-sets of SP from European countries where n ≥30.

Results: %S is shown in the Table (see Table 1, poster text). Solithromycin was fully active against all isolates. Pencillin susceptibility was only above 80% in Denmark and azithromycin susceptibility was only at this high level in Denmark and Russia. Overall antibiotic susceptibility was particularly low in Turkey.

Conclusions: Solithromycin showed very good activity against antimicrobial-resistant isolates, despite low susceptibility to azithromycin and pencillin in most countries and multidrug resistance in Turkey. 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 pneumococci isolated from different European countries during 2012-2013.

Materials & Methods

• A total of 418 pneumococcal isolates from Europe were identified to the 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), 2 (intermediate) & >4 (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].

Results

• Summary percent susceptibility data for solithromycin and comparators by country is shown in Table 1. Summary MIC data for solithromycin against SP is shown in Table 2.
• Cumulative MIC distribution for solithromycin, azithromycin/clavulanic acid, ceftriaxone, azithromycin and levofloxacin against pneumococci from combined European isolates is shown in Figure 1.
• Susceptibility data for antimicrobial agents with lower susceptibility is shown in Figure 2.

Conclusions

• Effective and safe oral antibiotics are essential to the successful treatment of CABP.
• However, low susceptibility was observed to oral antibiotics such as azithromycin, clindamycin and penicillin in most countries and amoxicillin clavulanic acid in Spain and Turkey – with multi-drug resistance in this country.
• On the other hand, all pneumococci were susceptible to solithromycin (MIC ≤ 0.5 µg/ml), irrespective of resistance to other agents.
• Levofloxacin was also very active against the pneumococci (lower susceptibility in Turkey) but this oral agent is associated with several adverse events [1].
• Taken together, the MIC90 for solithromycin was <0.06 µg/ml with a maximum MIC of 0.5 µg/ml.
• Using provisional solithromycin breakpoints of ≤1 (susceptible), 2 (intermediate) & >4 (resistant), 100% of pneumococci from all countries were susceptible to solithromycin.
• These data positively support the continued development of solithromycin as a safe oral agent for the treatment of respiratory infections caused by *S. pneumoniae*.

References


Acknowledgments: This study was sponsored by a grant from Cempra Pharmaceuticals.