Poster C-1473

Activity of Solithromycin and Comparators against *Streptococcus pneumoniae* isolated from Respiratory Samples Collected from Pediatric, Adult and Elderly Patients in 2012-2013

Ian Morrissey[1], Prabhavathi Fernandes[2], Kara Keedy[2], Barbara Lemos[1], Stephen P. Hawser[1],
[1]IHMA Europe, Sárl, Epalinges, Switzerland.
[2] Cempra Inc., Chapel Hill, North Carolina, USA

IHMA Europe, Sárl
9A Route de la Corniche,
Epalinges 1066,
Switzerland
Email:
imorrissey@ihmainc.com
Tel: +44 (0)1279 724929

Revised Abstract

Background: Solithromycin is a fourth-generation macrolide, the first fluoroketolide, undergoing Phase III clinical trials for the treatment of moderate to moderately-severe community-acquired bacterial pneumonia (CABP). This study evaluated the *in vitro* activity of solithromycin against *Streptococcus pneumoniae* (*SP*) collected in 2012-2013 from patients of varying age groups.
Methods: A total of 996 *SP* isolated from respiratory samples were collected from Europe, Asia-Pacific, North America and other locations world-wide. 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 (S), 2 (I) & ≥4 (R) were used for solithromycin and FDA breakpoints for tigecycline. Differences in % susceptibility (%S) by age group were evaluated for statistical significance with the Fisher Exact Test.
Results: **%S by age group (pediatric <12 years old; adult 12 to 64 years old & elderly >64 years old) are shown in the Table (>90 %S in bold) in the poster body.** Ceftriaxone activity was significantly lower in pediatrics than compared with adults or elderly (p-value 0.036 & 0.017, respectively). Other agents showed no or only slight differences in activity between age groups.
Conclusions: Solithromycin showed very good activity against isolates from all age groups. These data positively support the continued development of solithromycin for the treatment of respiratory infections caused by *SP*.

Introduction

Solithromycin is a fluoroketolide available in both oral and intravenous formulations. It is being developed for the treatment of community-acquired bacterial pneumonia (CABP) and gonorrheae. 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 more than 1000 respiratory streptococcal isolates collected in Europe, Asia-Pacific and North America during 2012-2013.

Materials & Methods

- A total of 996 pneumococcal isolates from Europe, Asia-Pacific, North America and other locations world-wide were identified to the species level and MICs determined at a central testing laboratory (IHMA Europe, located in Epalinges, Switzerland). Isolates were from three different age groups: pediatric <12 years old, adult 12 to 64 years old & elderly >64 years old.
- 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. Differences in % susceptibility (%S) by age group were evaluated for statistical significance with the Fisher Exact Test.
- 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 of the susceptibility of different age groups to solithromycin and comparators is shown in Table 1 and Summary MIC data for solithromycin and comparators against pneumococci from these patient age groups are shown in Table 2.
Summary Susceptibility data for antimicrobial agents against *S. pneumonaie* from pediatric, adult and elderly patients are shown in Figure 1, 2 and 3, respectively.

Table 1: Summary of the Susceptibility of *S. pneumonaie* from Different Age Groups to Solithromycin and Comparators.

Drug (%Susceptible)	Pediatric (n=161)	Adult (n=509)	Elderly (n=326)
Solithromycin	100	100	100
Azithromycin	63.4	58.4	59.2
Amoxicillin/Clavulanic Acid	85.1	89.8	89.9
Clindamycin	73.9	74.7	70.6
Penicillin (oral bp)	59.6	58.0	62.0
Ceftriaxone*	83.2	89.6	**90.8**
Levofloxacin	**98.1**	**98.6**	**98.8**

*significant difference between age groups (ceftriaxone susceptibility significantly lower in pediatrics compared to adults (p=0.036) and elderly (p=0.017).

All values in bold, >90 percent susceptible.

Table 2: Summary MIC Data (µg/ml) for Solithromycin and Comparators Against Pneumococci Isolated from Pediatric, Adult and Elderly Patients

	Pediatric (n = 161)		Adult (n = 509)		Elderly (n = 326)	
	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}	MIC_{50}	MIC_{90}
Solithromycin	0.008	0.25	0.008	0.25	0.008	0.25
Azithromycin	0.12	> 1	0.12	> 1	0.12	> 1
Amoxicillin/Clavulanic Acid	0.03	4	0.03	4	0.03	4
Clindamycin	0.06	> 0.5	0.06	> 0.5	0.06	> 0.5
Penicillin	≤ 0.06	4	≤ 0.06	2	≤ 0.06	2
Ceftriaxone	0.03	2	0.03	2	0.03	1
Levofloxacin	1	2	1	2	1	2

Figure 1: Summary of the Susceptibility of Pneumococci isolated from Pediatric patients to Solithromycin and Comparators

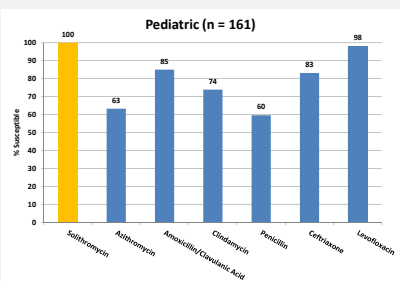


Figure 2: Summary of the Susceptibility of Pneumococci isolated from Adult patients to Solithromycin and Comparators

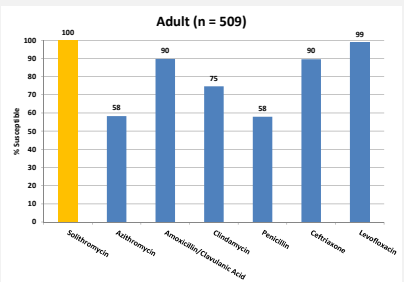
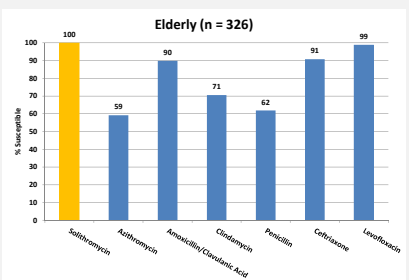


Figure 3: Summary of the Susceptibility of Pneumococci isolated from Elderly patients to Solithromycin and Comparators



Conclusions

- Safe orally-available antibiotics are important for the treatment of CABP.
- Solithromycin showed very good activity against all pneumococci irrespective of patient age group from which the strains were isolated.
- Using provisional solithromycin breakpoints of ≤1 (susceptible), 2 (intermediate) & ≥4 (resistant), 100% of pneumococci were susceptible to solithromycin irrespective of their resistance phenotypes.
- Ceftriaxone susceptibility was significantly lower in *S. pneumoniae* from pediatric patients than compared with adults or elderly but age group had no effect on the susceptibility to solithromycin.
- The oral agents showed no difference or only slight differences in activity between age groups (none being statistically significant).
- However, resistance to azithromycin, penicillin and most other oral agents was high in all age groups.
- Levofloxacin susceptibility was almost as high as solithromycin, but levofloxacin is associated with several adverse events and is also not approved for use in pediatrics.
- 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

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