Antimicrobial activity of solithromycin tested against serotyped macrolide-resistant *Streptococcus pneumoniae* collected from medical centers across the USA (2012)

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Objective: To evaluate the activity of solithromycin, a fourth generation macrolide and a novel fluoroketolide, tested against a contemporary (2012) collection of serotyped United States (USA) macrolide-resistant *S. pneumoniae* isolates associated with community-acquired bacterial pneumonia. Solithromycin was designed to overcome macrolide-resistant *S. pneumoniae.* With the introduction of new pneumococcal conjugate vaccines, the serotype distribution of *S. pneumoniae* has been dynamic in recent years, and hence monitoring the activity of new agents against circulating serotypes is prudent.

Methods: A total of 272 macrolide-resistant (erythromycin MIC, >=1 mg/L) *S. pneumoniae* collected during 2012 from 49 medical centers (35 states) across the USA were included (SENTRY Antimicrobial Surveillance Program). Isolates were recovered from lower respiratory tract specimens (82.7%) and blood cultures (17.3%) in patients across all age groups with a diagnosis of community-acquired bacterial pneumonia. Species identification was performed using biochemical test algorithms and/or PCR assays. Serotyping was performed by *cps*B sequencing and multiplex PCR methodology. Susceptibility testing applied CLSI methods (M07-A9) and interpretations were performed using CLSI M100-S23 (2013) breakpoint criteria.

Results: Against all 272 isolates, solithromycin demonstrated high potency ($MIC_{50/90}$, 0.06/0.25 mg/L) and inhibited all strains at MIC values <=0.5 mg/L. Although potency remained high, solithromycin activity was slightly lower against the two most prevalent serotypes - 19A ($MIC_{50/90}$, 0.25/0.25 mg/L) and 35B ($MIC_{50/90}$, 0.12/0.25 mg/L) - compared to other serotypes and the overall population (Table). In total, 29 serotypes/serogroups were represented in this population. Penicillin resistance by CLSI oral penicillin V criteria (>=2 mg/L) was high overall (39.0%) and extremely high in serotype 19A (91.2%) and serotype 35B (82.4%) isolates. Ceftriaxone-nonsusceptibility (>=2 mg/L, CLSI non-meningitis criteria) was 19.9% overall and very high in serotype 19A (67.6%), but not serotype 35B (2.9%) isolates.

Conclusions: Solithromycin demonstrated sustained activity against a geographically diverse set of macrolide-resistant *S. pneumoniae* isolated from patients with CABP across the USA in 2012. Solithromycin was shown to be very active against the two most prevalent macrolide-resistant serotypes (19A and 35B) in addition to the other prevalent serotypes/serogroups present in the overall population. These data support and encourage the continued clinical development of solithromycin for the treatment of multidrug resistant community-acquired bacterial pneumonia.