Microbial Characterization Using Multiple Diagnostic Methods in the First Oral Phase 3 Community-Acquired Bacterial Pneumonia (CABP) Trial with Solithromycin

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Background: A Phase 3 oral CABP study of solithromycin (SOLI) versus moxifloxacin (moxi) was successfully completed. This was the first oral CABP trial conducted under the new FDA Guidance and also the first to use molecular methods coupled with traditional culture and serology to identify pathogens.

Methods: Patients with confirmed CABP (PORT II to IV) were enrolled. Baseline microbiological evaluation included cultures of blood and sputum, detection of *Streptococcus pneumoniae* and *Legionella pneumophila* antigen in urine, *L. pneumophila* and *Mycoplasma pneumoniae* serologies (4-fold diagnostic rise in titer between baseline and 4 week sera), quantitative PCR of nasopharyngeal swabs for *S. pneumoniae*, culture and PCR of oropharyngeal swabs for *M. pneumoniae*, and sputum multiplex PCR for respiratory pathogens (Curetis).

Results: The most frequently identified pathogens in order of prevalence were *S. pneumoniae* (23%), *H. influenzae* (16%), *L. pneumophila* (15%), *M. pneumoniae* (9%), *M. catarrhalis* (6%), and *S. aureus* (4%). Macrolide resistance was 19% in *S. pneumoniae* while SOLI MICs were ≤0.5 mg/L (MIC90 = 0.015 mg/L).

	Solithromycin		Azithromycin	
Pathogen (#)	MIC90	Range	MIC90	Range
S. pneumoniae (109)	0.015	0.002 - 0.50	>32	0.06 - >32
H. influenzae (64)	4	0.25 - 4	4	0.25 - 8
M. pneumoniae (26)	≤0.000032	≤0.000032 - 0.25	0.0005	0.00006 - 32
S. aureus (24)	0.12	0.06 - 0.12	8	1 - >32
M. catarrhalis (17)	0.25	0.06 - 0.25	0.12	≤0.015 - 0.12
Legionella spp. (6)	NA	≤ 0.00024 - 0.016	NA	0.004 - 0.125

Conclusion: SOLI is a new macrolide with activity against typical and atypical CABP pathogens, including macrolide-resistant ones. Using traditional and molecular methods, 54% of patients in the trial had a bacterial pathogen identified. Culture and serology confirmed many of the results from molecular methods, which supplemented the overall bacterial identification in this oral CABP trial, the first to use the new FDA guidance.

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