Microbiological Diagnoses from a Recent Community-Acquired Bacterial Pneumonia (CABP) Trial – Solitaire-IV

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Background: CABP is the most common cause of death from infectious disease in the US, and most patients do not have a microbiological diagnosis established. Solithromycin (SOLI) is a 4th generation macrolide with potent activity against CABP pathogens, including macrolide-resistant strains. Solitaire-IV was a global Phase 3 non-inferiority trial of IV-to-oral SOLI versus moxifloxacin (MOXI) in the treatment of CABP.

Methods: The trial was conducted under the new FDA CABP Guidance with clinical outcomes measured using an objective endpoint of early clinical response (ECR) at 72 hours post-dose. 863 patients with confirmed CABP (PORT II to IV) were randomized between January 2014 and July 2015 to receive IV SOLI or MOXI on Day 1 and were permitted to switch to oral dosing on subsequent days.

A variety of techniques were used to enhance the detection of pathogens including 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), culture and PCR of oropharyngeal swabs for *M. pneumoniae*, and quantitative PCR of nasopharyngeal swabs for *S. pneumoniae*.

Results: SOLI was non-inferior to MOXI in ECR in the microbiological intent-to-treat (mITT) population (80.3% vs 79.1%; 95% Confidence Interval: -8.1, 10.6). The most frequently identified pathogens were *S. pneumoniae* (18%), *M. pneumoniae* (8%), and *H. influenzae, S. aureus,* and *L. pneumophila* (all 4%). The rate of macrolide resistance in *S. pneumoniae* was 27% and SOLI maintained activity against these isolates with MICs ≤1 mg/L. SOLI MICs were generally lower than MOXI and the macrolide azithromycin (AZI) among Gram-positive and atypical pathogens, while MOXI MICs were lower for Gram-negative pathogens.

	MIC90		
Pathogen (N)	AZI	SOLI	MOXI
***S. pneumoniae* (98)**	>32	0.06	0.12
Macrolide-resistant* *S. pneumoniae* (26)	>32	0.5	0.12
***S. aureus* (37)**	>32	0.12	2
***H. influenzae* (35)**	2	2	0.06
***M. pneumoniae* (26)**	0.0005	≤0.000032	0.125

*Defined as resistance to AZI or erythromycin by CLSI

Conclusion: SOLI is a new macrolide with potent activity against typical and atypical CABP pathogens, including macrolide-resistant ones, and shows promise as a new macrolide for in-patient and outpatient treatment of CABP.

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