SOLITAIRE-IV: Results of a Phase 3 IV to Oral Trial in Adults with Community-acquired Bacterial Pneumonia comparing Solithromycin to Moxifloxacin

Conference: ATS 2016

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Background/Rationale: A new macrolide, with IV and oral formulations and activity against resistant strains, would meet a critical need for the treatment of community-acquired bacterial pneumonia (CABP). Resistance rates of *S. pneumoniae* to older macrolide antibiotics approach or exceed 50% in the United States, which has led to an increased use of fluoroquinolones for CABP.

Methods: Solitaire-IV was a Phase 3, randomized, double-blind, multi-center study to evaluate the efficacy and safety of IV to oral solithromycin compared to IV to oral moxifloxacin in the treatment of adults with CABP. All patients received IV study drug on Day 1, and could be switched to oral study drug if criteria were met, or remain on IV for 7 once-daily doses. Patients randomized to moxifloxacin received 400 mg IV or PO QD; those randomized to solithromycin received 400 mg IV, 800 mg PO on the first oral dosing day, and 400 mg PO on subsequent days for a total of 7 doses.

Results: 863 patients were enrolled from 147 sites in 22 countries; 434 patients were randomized to solithromycin and 429 were randomized to moxifloxacin. 44% of patients were ≥65 years of age and 21% of patients had a history of COPD or asthma. PORT scores were balanced between treatment arms; in the solithromycin treatment arm 24.4% of patients were PORT II, 45.2% PORT III, 30.0% PORT IV, and 0.5% PORT V.

In the intent-to-treat (ITT) population, solithromycin met the primary objective of statistical non-inferiority (NI, 10% margin) compared to moxifloxacin in early clinical response (ECR, Day 3 to 5) rate. Solithromycin also met the secondary objectives of comparable success to moxifloxacin at the short-term follow-up visit (SFU, 5 to 10 days after treatment) in the ITT population and NI at ECR in the microbiological-ITT (mITT) population.

Study Populations	Solithromycin ITT n=434;mITT n=173	Moxifloxacin ITT n=429;mITT n=153	Difference	95% confidence intervals
ITT – ECR rate	79.3%	79.7%	-0.46	-6.1%, 5.2%
ITT – SFU success	84.6%	88.6%	-4.02	-8.8%, 0.8%
mITT – ECR rate	80.3%	79.1%	1.26	-8.1%, 10.6%

Five (16.9% solithromycin; 5.4% moxifloxacin) and discontinuations due to adverse events (4.6% solithromycin; 3.7% moxifloxacin.2%) solithromycin patients and 7 (1.6%) moxifloxacin patients died during the study. Serious adverse events () were comparable between treatment arms. Infusion-related adverse events were observed more frequently in solithromycin patients and were mostly mild to moderate and rarely treatment-limiting. Other adverse events were comparable between treatment arms. One event of *C. difficile* colitis occurred in a moxifloxacin patient.

Conclusion: IV to oral solithromycin is non-inferior to IV to oral moxifloxacin and is a promising new monotherapy, with the flexibility of IV and oral dosage formulations, for the treatment of CABP.

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