SOLITAIRE-IV: A Phase 3 IV to Oral Trial Evaluating Solithromycin in Adults with Community-Acquired Bacterial Pneumonia

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Background: Macrolides have been a preferred class of antibiotics in the treatment of community-acquired bacterial pneumonia (CABP) because of their specific spectrum of activity, including against pneumococcus and atypical pathogens such as *Legionella pneumophila* and *Mycoplasma pneumoniae*. Solithromycin is a new macrolide with both intravenous (IV) and oral (PO) formulations and exhibits potent activity against resistant *Streptoccocus pneumoniae*, other typical, and atypical bacterial respiratory pathogens. Oral solithromycin was non-inferior to moxifloxacin in treating adults with CABP in the outpatient setting (SOLITAIRE-Oral trial).

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 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 receive IV for 7 once-daily doses. Patients 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. Patients randomized to moxifloxacin received 400 mg IV or PO once-daily.

Efficacy was evaluated at Day 3 to 5 (Early Clinical Response; ECR) and Day 12 to 17 (Short-term Follow-up; SFU). Success at ECR was based upon improvement in 2 (without worsening in any) of 4 cardinal symptoms of CABP – cough, dyspnea, sputum production, and chest pain; success at SFU was based on the Investigator's assessment of clinical success.

Results: A total of 863 patients were enrolled from 147 sites in 22 countries; 434 patients were randomized to solithromycin and 429 were randomized to moxifloxacin. Patients were primarily treated as inpatients, with 44% of patients ≥65 years of age and 21% having 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.

Solithromycin was non-inferior to moxifloxacin in the ITT population in ECR (79.3%; 79.7%) and SFU success rates (84.6%; 88.6%). Solithromycin was also non-inferior to moxifloxacin in the mITT population (38% of ITT) in ECR rate (80.3%; 79.1%). The most common pathogens identified were *S. pneumoniae*, *M. pneumoniae*, *Staphylococcus aureus*, *Legionella* spp., and *Haemophilus influenzae*. By-pathogen responses were comparable between treatment arms.

Five (1.2%) solithromycin patients and 7 (1.6%) moxifloxacin patients died. Serious adverse events (6.9% solithromycin; 5.4% moxifloxacin) and discontinuations due to adverse events (4.6% solithromycin; 3.7% moxifloxacin) were comparable. Infusion-related adverse events, mostly mild, were more common in solithromycin patients; other adverse events were comparable between treatment arms. One moxifloxacin patient had *C. difficile* colitis.

Conclusion: IV to oral solithromycin is a promising new monotherapy for empiric treatment of adults with CABP.

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