

# Results from a Phase 3 trial in Moderate to Moderately Severe Community Acquired Bacterial Pneumonia (CABP) Treated As Outpatients With a New Oral Macrolide, Solithromycin

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**Background/Purpose:** Macrolides are sometimes used in monotherapy but more often with a cephalosporin for CABP. Pneumococcal macrolide resistance is now at >40% (US). We report the results of an outpatient Phase 3 study with oral solithromycin (soli) a 4th generation macrolide that had sufficient potency to be tested in monotherapy in comparison to moxifloxacin (moxi) in CABP.

**Methods:** Patients with CABP, PORT Risk II-IV (NCT#01756339) were double-blind randomized (1:1) to oral soli (5 days) or oral moxi (7 days). Evaluations were performed on Day 4 for early clinical response (ECR), Day 7, Day 12-17 short term follow up (SFU) visit, and Day 28. ECR was defined as improvement in at least 2 of 4 cardinal symptoms (cough, chest pain, dyspnea, sputum production) without worsening in any. Investigators assessed success at SFU. Primary objectives were demonstration of non-inferiority (10% NI margin) in ECR (intent-to-treat (ITT) population) and in success at SFU (ITT and clinically evaluable (CE) populations).

**Results:** 860 patients from 16 countries were randomized (ITT population), 90% met key protocol criteria (CE population). 50.7% of soli patients had PORT III/IV disease (11.3% PORT IV), vs. 48.6% of moxi patients (8.8% PORT IV). Soli was non-inferior to moxi in the ITT population in ECR (78.2% vs. 77.9%) and SFU success (84.5% vs. 86.6%) and in the CE-SFU population (88.1% vs. 91.3%). ECR success was higher among soli patients  $\geq$  age 75 (83.9% vs 69.8%, n=125). Soli had safety comparable to moxi in occurrence of adverse events (AEs) (36.6% vs 35.6%), study-drug related Aes (10.1% vs 12.5%), Serious AEs (6.6% vs 6.3%; none attributed to study drug) and deaths (1.4% vs 1.4%). Grade 4 ALTs (>8xULN) were observed in 5 moxi patients and 2 soli patients (without symptoms or bilirubin elevation). Two episodes of *C. difficile* diarrhea were diagnosed in moxi recipients. 15 patients had *S. pneumoniae* (Spn) bacteremia; treatment was successful in the majority, with equal success rates (soli vs moxi). Among all Spn patients, treatment was successful at SFU in 85.3 % (soli) and 87.3 % (moxi) of patients. 100% success at SFU was observed in all soli patients with macrolide-resistant Spn at SFU.

**Conclusion:** Oral soli was non-inferior to moxi for treatment of CABP. Safety outcomes were comparable, although moxi was associated with more Grade 4 ALT elevation and *C. difficile* diarrhea.