

# Detection of Pneumococcal Pneumonia in a Phase 3 Trial Comparing Oral Solithromycin versus Oral Moxifloxacin for Treatment of Community-acquired Bacterial Pneumonia in Adults

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**Background:** *Streptococcus pneumoniae* (Spn) is the most common pathogen associated with community acquired bacterial pneumonia (CABP). However, the detection of Spn in CABP patients can be challenging due to difficulties in quality sputum collection, low recovery of isolates from specimens that must be transported over distances to microbiology laboratories, and the low sensitivity of urinary antigen tests. In this global Phase 3 trial to evaluate the efficacy and safety of solithromycin compared to moxifloxacin in the treatment of CABP in adults, multiple microbiological and diagnostic methods were utilized to identify Spn.

**Methods:** Patients had acute onset of radiologically confirmed CABP with consistent clinical signs and symptoms. Spn was identified as an etiologic agent on the basis of blood or sputum culture, urine antigen testing (UAT; BINAX), sputum multiplex PCR (Curetis) and quantitative Spn PCR of nasopharyngeal (NP) swabs. The NP swab PCR assay targeted the Spn-specific *lytA* gene and a threshold of 1000 CFU/mL (determined by receiver operating characteristic curve analysis) was used to differentiate between nasopharyngeal colonization and pneumococcal pneumonia.

**Results:** 860 subjects were enrolled from 16 countries; not all patients had specimens available for analysis. Spn was the most frequently identified pathogen in the trial (23%). Pneumococcal bacteremia was diagnosed in 15 patients and 28 patients were positive by UAT. Spn was cultured from sputum meeting diagnostic criteria in 55 patients. Pneumococcal pneumonia was identified by NP swab PCR in 133 (15.5%) patients. The overlap of NP swab PCR with more traditional diagnostic modalities is shown in Table 2. NP swab PCR positivity overlapped with blood cultures (67%) and UATs (46%) more frequently than sputum culture did with either (33% and 18%, respectively).

**Conclusion:** The use of quantitative PCR of NP swabs in this Phase 3 trial significantly increased the rate of identification of Spn as the cause of CABP. Diagnosis by NP swab PCR was better correlated with blood culture, sputum culture and UAT, than any of these more traditional diagnostic methods were with one another.