**Acinetobacter baumannii pneumonia (CAP) is among the most common and serious infections requiring systemic antibiotic therapy and is associated with significant morbidity and mortality, despite therapeutic advances.**

**The emergence and spread of respiratory pathogens resistant to antibiotics and other classes of antibiotics has begun to limit therapeutic options for CAP.**

**A macrolide with improved activity, a better safety profile and availability in both intravenous (IV) and oral formulations would be a significant therapeutic advance in the treatment of CAP.**

**Solithromycin (SOLI), a fourth-generation macrolide, with potent in vitro activity against CAP pathogens, including atypical bacteria and macrolide-resistant strains, is being developed in oral and IV formulations.**

**Phase 3 Trials in CAP:**

- **MOXI**, a potent fluoroquinolone, was selected as the comparator because of its proven effectiveness in CAP and the ability to study both oral and IV formulations worldwide with a consistent dose regimen.
- **SOLI** demonstrated clinical non-inferiority to oral moxifloxacin in treating adults with CAP in the outpatient setting (SOLITAIRE-Oral trial).
- **SOLITAIRE IV** was a global non-inferiority trial of IV-to-oral SOLI versus MOXI.

**Methods**

**Study Design:** The SOLITAIRE IV trial was conducted under the new FDA CABP Guidance with clinical outcomes measured using an objective endpoint of early clinical response (ECR) at 72 h post-dose. All 263 patients with confirmed CAP (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.

**Screening Baseline**

<table>
<thead>
<tr>
<th>Day</th>
<th>ECR</th>
<th>End of Treatment (EOT)</th>
<th>Day 7</th>
<th>Short-term Follow-up (SFU)</th>
<th>Day 15</th>
<th>Long-term Follow-up (LFU)</th>
<th>Day 28-32</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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</tr>
</tbody>
</table>

**Microbiological Assessments**

- A variety of techniques were used to enhance the detection of pathogens:
  - blood and sputum culture
  - urinary antigen test (EA) - S. pneumoniae and L. pneumophila
  - serology (4-fold rise in titer at LFU) - L. pneumophila and M. pneumoniae
  - quantitative PCR of nasopharyngeal swabs for S. pneumoniae
  - culture and qPCR of oropharyngeal swabs for M. pneumoniae

**Analysis Populations**

- The ITT (intention-to-treat) population consists of all randomized patients, the mITT (microbiological ITT) population consists of all randomized patients with a baseline pathogen identified, the CE (clinically evaluable) population consists of patients who met inclusion/exclusion criteria and had, with the exception of significant protocol deviations, the ME (microbiologically evaluable) population is the intersection of the ITT and CE populations.

**Primary: Early clinical response (improvement of cough/ dyspnea/ chest pain / pustular production without worsening of any) at 72 h in the ITT population**

**Secondary:** ECR in the mITT, investigator’s assessment of clinical response at SFU visit in the ITTCE-SFU. Additional: clinical response at SFU in the mITT/CE-SFU. By-phenotype treatment outcomes in mITT/CE-SFU visits in mITT/CE-SFU.

**Table 1. Early Clinical Response and Clinical Success at SFU**

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>SOLI (n=158)</th>
<th>MOXI (n=139)</th>
<th>Delta, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ITT Population</strong></td>
<td>79.3 (344/443)</td>
<td>79.7 (342/434)</td>
<td>-0.46 (-1.61, 5.52)</td>
</tr>
<tr>
<td><strong>MOXI Population</strong></td>
<td>80.3 (139/171)</td>
<td>79.7 (121/152)</td>
<td>+1.6 (1.08, 10.95)</td>
</tr>
<tr>
<td><strong>ESR Population</strong></td>
<td>86.3 (136/159)</td>
<td>86.3 (136/159)</td>
<td>+3.8 (5.16, 12.67)</td>
</tr>
<tr>
<td><strong>Successful SFU</strong></td>
<td>84.6  (367/434)</td>
<td>86.6 (380/429)</td>
<td>+2.0 (4.80, 8.09)</td>
</tr>
<tr>
<td><strong>SOLI</strong></td>
<td>82.2 (133/164)</td>
<td>81.0 (132/165)</td>
<td>+1.2 (3.32, 13.37)</td>
</tr>
</tbody>
</table>

**Table 2. SOLI was non-inferior to MOXI in both the ITT and mITT populations.**

**Figure 3: Solithromycin MIC distribution among S. pneumoniae**

**Table 3. By-phenotype Treatment Outcomes at Clinical Success at SFU and Outcome for MIC for selected CAP bacteria (ME-SFU population)**

**Figure 1: Microbiological Diagnoses (mITT population)**

**Table 4. Solithromycin MIC distribution for macrolide-resistant S. pneumoniae by genotype**

**References**