

**INTRODUCTION AND PURPOSE**

Community-acquired bacterial pneumonia (CABP) is associated with considerable morbidity and mortality worldwide and is the number one cause of death from infectious disease in the US [1]. Due to the rising threat of microbial resistance, along with concerns over antibiotic tolerability and impact on intestinal microbiota, new CABP treatments are needed.

Solithromycin (CEM-101), a 4th generation macrolide, is being developed as oral, intravenous, and pediatric suspension formulations for the treatment of CABP. Solithromycin has potent antibacterial activity against "typical" and "atypical" CABP pathogens, including macrolide-resistant strains. Solithromycin has limited activity against anaerobic gram negative flora and is therefore not expected to have the risk of C. difficile infection often associated with fluoroquinolones and broad-spectrum β-lactams antibiotics. Solithromycin was definitively negative in a thorough QT study [2].

Moxifloxacin, being available in IV and oral formulations was chosen as the comparator for both Phase 3 trials. Azithromycin could not be used as the comparator since it is not approved in monotherapy for PORT II-IV pneumonia.

The purpose of this Phase 3 trial was to evaluate the safety and efficacy of oral solithromycin compared to oral moxifloxacin in the treatment of adult patients with CABP.

**METHODS**

**Results (Continued)**

**Primary objective and endpoint (for FDA)**
- Non-Inferiority (NI) in Early Clinical Response (ECR) rate in the ITT population
  - Improvement at 72 hours (+12/-36) in at least two of the following symptoms: chest pain, cough, difficulty with sputum production, and dyspnea, without worsening in any

**Primary objective and endpoint (for EMA)**
- NI in success rate at SFU (short term follow-up visit, 5 to 10 days after end of therapy) in the ITT and clinically-evaluable (CE) populations
- Success or failure as determined by the investigator

**Secondary objectives**
- NI in early clinical response rate at 72 (+12/-36) hours in the pooled mITT population from the two Phase 3 trials
- NI in early clinical response rate at 72 (+12/-36) hours in the individual study mITT population
- Safety and tolerability of oral solithromycin vs oral moxifloxacin

**RESULTS (Continued)**

### Treatment Emergent Adverse Events

| Event | Solithromycin (N=424) | Moxifloxacin (N=432) | p-value
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<thead>
<tr>
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<tbody>
<tr>
<td>Headache</td>
<td>4.5%</td>
<td>2.5%</td>
<td>---</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4.2%</td>
<td>6.5%*</td>
<td>---</td>
</tr>
<tr>
<td>Nausea</td>
<td>3.5%</td>
<td>3.9%</td>
<td>---</td>
</tr>
<tr>
<td>Emesis</td>
<td>2.4%</td>
<td>2.3%</td>
<td>---</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2.1%</td>
<td>1.6%</td>
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<tr>
<td>ALT** - Grade 3</td>
<td>4.6%</td>
<td>2.1%</td>
<td>---</td>
</tr>
<tr>
<td>Grade 4</td>
<td>0.5%</td>
<td>1.2%</td>
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* p≤0.05 vs solithromycin
** No patient in either arm of the study developed treatment emergent elevation of both ALT and bilirubin that met Hy's Law criteria. Observed ALT elevations were reversible and asymptomatic.

### Study Outlines and Visit Schedule

**Study Outline**
- 1:1 randomization of 860 CABP patients to oral solithromycin (5 days) or oral moxifloxacin (7 days)
- Stratified by geographic region, by history of asthma and/or COPD, and by PORT score (vs SIIV)
- PORT II severity pneumonia capped at 50%. PORT IV enrollment limited to PII score < 100

**Enrollment Criteria**
- Acute onset or worsening of at least 3 of 4 cardinal symptoms: cough, dyspnea, chest pain, and sputum production
- Must have fever or hypothermia, and/or physical examination findings consistent with CABP
- Chest radiograph with lobar or patchy parenchymal pulmonary infiltrates
- Pneumonia should not be hospital or health care associated; no long-acting antibiotic use during the prior 7 days

**Visit Schedule**
The schedule of visits is outlined in the diagram below. All patients were followed through to the Long-term Follow-Up (LFU) visit for all cause mortality.

### Study Populations and Subgroups

| Event | Solithromycin | Moxifloxacin | p-value
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Intent to Treat Population (ITT)</td>
<td>426</td>
<td>434</td>
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<tr>
<td>PORT II</td>
<td>259 (49.1%)</td>
<td>223 (51.4%)</td>
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<tr>
<td>PORT IV</td>
<td>168 (36.9%)</td>
<td>173 (38.8%)</td>
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### Safety Outcomes

- Solithromycin demonstrated an acceptable safety and tolerability profile, comparable to moxifloxacin
- No SAEs attributed to Solithromycin