**Efficacy and Safety of Lefamulin Versus Moxifloxacin for *Legionella pneumophila* in Patients With Community-Acquired Bacterial Pneumonia: Pooled Results From the Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Phase 3 Clinical Trials**


Medstar Washington Hospital Center, Washington, DC, USA; Nabriva Therapeutics US, Inc., King of Prussia, PA, USA; Nabriva Therapeutics GmbH, Vienna, Austria; Das Consulting, Guerneville, CA, USA; Olive View-UCLA Medical Center, Los Angeles, CA, USA; UC Davis School of Medicine, Sacramento, CA, USA; Summa Health, Akron, OH, USA

**INTRODUCTION & PURPOSE**

- Antimicrobial resistance among *Legionella pneumophila* strains is a growing concern.
- Lefamulin, a novel macrolide antibiotic, has demonstrated activity against *L. pneumophila*.
- The European Medicines Agency coprimary endpoints (FDA secondary endpoints) were investigator assessment of early clinical response and microbiological response.

**METHODS**

**Study Design**

- Randomization: LEAP 1 (LEF: 646; MOX: 646); LEAP 2 (LEF: 364; MOX: 364)
- Follow-up: 7 days after last dose
- Safety outcomes: 60 days after last dose

**RESULTS**

- **TABLE 1**: Demographics and Baseline Characteristics
  - **Patients and Baseline Characteristics**
    - *Legionella pneumophila* was detected in the majority of patients.
    - Baseline characteristics were generally similar across treatment groups.

- **TABLE 2**: Treatment-Emergent Adverse Events
  - **TEAEs** reported for the microITT population.
  - No significant differences were observed between treatment groups.

- **TABLE 3**: TEAE System Organ Classes Reported by SOC
  - Respiratory, thoracic, and cardiovascular disorders were the most common adverse events.

- **Table 4**: Pathogen Distribution for Patients With *L. pneumophila* at Baseline (Pooled microITT Population)
  - High rates of identification of *S. pneumoniae* were observed.

- **Figure 1**: LEAP 1 and LEAP 2 Study Design

- **Figure 2**: Diagnostic Model for patients With *L. pneumophila* at Baseline (Combined Treatment Groups)
  - The model included serology and urinary antigen test as diagnostic modalities.

- **Figure 3**: Pathogen Distribution for Patients With *L. pneumophila* at Baseline (Pooled microITT Population) (Combined Treatment Groups)
  - Distribution of pathogens overlaps among treatment groups.

- **Figure 4**: (A) Early Clinical Response and (B) Microbiological Response of Patients With *L. pneumophila* at Baseline (Pooled microITT Population)
  - Similar rates of response were observed between treatment groups.

**CONCLUSIONS**

- Lefamulin demonstrated efficacy and safety in treating patients with community-acquired bacterial pneumonia caused by *L. pneumophila*.
- Further studies are warranted to evaluate its role in the treatment of *L. pneumophila* infections.

**REFERENCES**

- National Kidney Foundation categories of renal impairment based on baseline central laboratory serum creatinine. When baseline central laboratory serum creatinine was not available, local serum creatinine results were used. Renal impairment categories are: normal [CrCl ≥90 mL/min], mild [CrCl of 60 to <90 mL/min], moderate [CrCl of 30 to <60 mL/min].

**ACKNOWLEDGMENTS**

- The authors thank the following individuals for their contributions to the study design and conduct: Drs. Jennifer Schranz, Lisa Goldberg, Susanne Paukner, Anita F. Das, Gregory J. Moran, Christian Sandrock, Thomas M. File Jr., Elizabeth Alexander, Steven P. Gelone.
- The authors also thank the patients and study sites who participated in the trials.

**DISCLOSURES**

- The authors have declared no competing interests.

---

**IDWeek 2019: October 2–6, Washington, DC, USA**

**Table 1**: TEAE System Organ Classes Reported by SOC

<table>
<thead>
<tr>
<th>Safety</th>
<th>Leptomeningeal disorders</th>
<th>Nervous System disorders</th>
<th>Gastrointestinal disorders</th>
<th>Respiratory, thoracic, and cardiovascular disorders</th>
<th>Dermatological disorders</th>
<th>Vascular disorders</th>
<th>Psychiatric disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Legionella pneumophila</em></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>BIAS</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

**Table 2**: Treatment-Emergent Adverse Events

<table>
<thead>
<tr>
<th>TEAE Leading to Death</th>
<th><em>Legionella pneumophila</em></th>
<th><strong>Primary</strong></th>
<th><strong>Secondary</strong></th>
<th><strong>Tertiary</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Clinical response</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Microbiological response</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>BIAS</strong></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>