Lefamulin Is Noninferior to Moxifloxacin in Adults With Community-Acquired Bacterial Pneumonia: Phase 3 Lefamulin Evaluation Against Pneumonia (LEAP 1) Study

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**INTRODUCTION**

Community-acquired pneumonia (CAP) causes significant morbidity, mortality, and a substantial economic burden. A meta-analysis of 163,596 patients from 20 countries outside the United States found that patients with CAP had a 30-d mortality of 17.4%, and 11.2% of patients required mechanical ventilation.

**METHODS**

**Study Design**

Patients who were 18 years old with community-acquired bacterial pneumonia (CABP) (Pneumonia Outcomes Research Team (PORT) risk class III–IV, n = 326) were randomized to receive lefamulin 150 mg intravenously (IV) every 12 hours (q12h) or moxifloxacin 400 mg IV q24h for 3 to 5 days. Patients were stratified by predefined signs of infection, and randomly assigned to a 1:1:1 ratio based on predefined signs of infection. Patients were randomized via telephone to receive lefamulin 150 mg q12h or placebo within 24 h of the initiation of antibacterial treatment.

**Patients**

- **Patients (n = 273):** Lefamulin 149 (54.6%) patients, placebo 124 (45.4%).
- **Mean age, y:** 65 ± 12 years.
- **Sex: Male:** 150 (54.9%); **Female:** 123 (45.1%)
- **BMI, kg/m²:** 25.6 ± 4.3.
- **Clotting status:** Normal: 169 (62.1%); Impaired: 104 (37.9%)
- **Renal status:** Normal: 247 (89.9%); Impaired: 26 (9.5%)
- **Baseline pathogen detected:** Streptococcus pneumoniae: 134 (48.7%); **S. aureus:** 175 (63.8%)

**RESULTS**

- **Randomization:** 149 (54.6%) patients received lefamulin 150 mg q12h or placebo within 24 h of the initiation of antibacterial treatment.
- **Baseline characteristics:** The mean age was 65 ± 12 years, and 54.9% were male. Lefamulin was noninferior to moxifloxacin in terms of investigator assessment of clinical response (ITT) and ITT.
- **Early clinical response (ECR):** 149 (54.6%) patients received lefamulin 150 mg q12h or placebo within 24 h of the initiation of antibacterial treatment.
- **Primary endpoint:** Lefamulin was noninferior to moxifloxacin in terms of investigator assessment of clinical response (ITT) and ITT.

**CONCLUSIONS**

Lefamulin demonstrated noninferiority to moxifloxacin in terms of the primary endpoint, investigator assessment of clinical response (ITT), and ITT. Lefamulin shows promise as an empiric and targeted monotherapy with an acceptable safety profile in patients with CABP. The study was supported by Nabriva Therapeutics.