Efficacy of Lefamulin Versus Moxifloxacin in Adults With Community-Acquired Bacterial Pneumonia: Results of the Lefamulin Evaluation Against Pneumonia (LEAP) 1 and LEAP 2 Double-Blind Noninferiority Phase 3 Clinical Trials

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Purpose

- Among the leading causes of hospitalization and infection-related death in the United States.1
- Approximately 1 in 3 patients with community-acquired bacterial infections (CABIs) develop CABP.2
- Bacterial resistance to commonly used antibiotics is increasing, and healthcare systems are becoming overwhelmed.3
- Resistance is associated with increased duration of hospital stay and cost.4
- Bacterial resistance is a major contributor to hospital acquired infections and healthcare costs, estimated to exceed $10 billion annually in the United States.5
- There is an unmet need for new antibiotic agents.
- The LEAP 1 and LEAP 2 studies evaluated the efficacy and safety of lefamulin (LEF) compared with moxifloxacin (MOX) as monotherapy for the treatment of CABP.

Methods

- Study Design: Both studies were prospective, randomized, double-blind, double-dummy, phase 3 trials.4
- Patients were randomized to either LEF or MOX.4
- LEF was administered orally (p.o.) or intravenously (i.v.) at a dose of 150 mg every 12 hours (q12h) for 5–7 days.4
- MOX was administered at a dose of 400 mg i.v. every 24 hours (q24h) on day 1 followed by 400 mg p.o. or 400 mg i.v. every 12 hours (q12h) for 5–7 days.4
- Both studies were conducted in North America, South America, Europe, and Asia.4
- The LEAP 1 study was conducted from June 2016 to January 2017, and the LEAP 2 study was conducted from November 2016 to July 2017.4

Results

- **Patients**: A total of 1200 patients with CABP were enrolled: 602 in LEAP 1 and 598 in LEAP 2.2
- **Baseline Characteristics**: The demographic and baseline characteristics were similar in both studies.2
- **Clinical Efficacy**: LEF was noninferior to MOX in CABP outcomes (Figure 3B).2
- **Clinical Efficacy by Subpopulations**: LEF was noninferior to MOX across all subpopulations.2
- **Other Findings from LEAP 1 and LEAP 2 Pooled Analyses**: LEF was noninferior to MOX in the pooled CE population (Figure 3A).2

Conclusions

- LEF demonstrated high ECR and IACR rates and was found to be noninferior for both endpoints to standard of care comparator MOX.2
- Response rates remained high across pneumonia severities as assessed by PORT risk class and baseline variables.2
- LEF was generally safe and well-tolerated regardless of the route of administration (i.v. only, i.v.-to-oral, oral only).2
- LEF may provide a valuable i.v. and oral monotherapy alternative to fluoroquinolones or macrolides for empirical treatment of CABP in adults.2

References

4. E1006 (CHEST 2019 LEAP 1_2_Efficacy) - CHEST Poster #1006. CHEST Annual Meeting 2019: October 19–23, New Orleans, LA, USA

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Figure 3. Pooled (A) Early Clinical Response and (B) Investigator Assessment of Clinical Response Success Rate

Table 1. Demographics and Baseline Characteristics (ITT Population)

Table 2. Pooled Results of PORT Risk Class

Table 3. Baseline Response rates for criteria for success or improvement (≥4 mmHg increase in SpO2 ≥3 points on Day 30)

Table 4. Baseline Response rates for criteria for success or improvement (≥4 mmHg increase in SpO2 ≥3 points on Day 30)