LEFAMULIN EFFICACY AND SAFETY IN ADULTS WITH COMMUNITY-ACQUIRED BACTERIAL PNEUMONIA: POOLED ANALYSIS OF THE LEFAMULIN EVALUATION AGAINST PNEUMONIA (LEAP) 1 AND LEAP 2 TRIALS IN PATIENTS WITH MULTILOBAR OR UNILOBAR PNEUMONIA

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Purpose:

Pneumonia with multilobar infiltration is associated with early treatment failure, delayed resolution, and prolonged hospitalization. The pleuromutilin antibiotic lefamulin (LEF) is approved for intravenous (IV) and oral use in adults with community-acquired bacterial pneumonia (CABP) based on the results of 2 noninferiority phase 3 trials, LEAP 1 and LEAP 2. In both trials, patients were stratified according to pneumonia severity as indicated by their PORT risk class. To investigate the efficacy/safety of LEF in patients with CABP who have or may be at risk for severe pneumonia, pooled data from LEAP 1 and 2 were analyzed in patients based on presence of unilobar vs multilobar infiltrates.

Methods:

In LEAP 1, adults with CABP (PORT risk class III–V; ≥25% required to have PORT risk class IV–V) received IV LEF 150 mg every 12 hours (q12h) for 5–7 d or moxifloxacin (MOX) 400 mg every 24 hours (q24h) for 7 d, with optional IV-to-oral switch. In LEAP 2, adults with CABP (PORT risk class II–IV; ≥50% required to have PORT risk class III–IV) received oral LEF 600 mg q12h for 5 d or MOX 400 mg q24h for 7 d. Exclusion criteria included recent hospitalization for ≥2 d, life expectancy ≤3 mos, pleural empyema, or noninfectious cause of pulmonary infiltrates. In this post hoc pooled analysis, early clinical response (ECR) at 96±24 h after first study drug dose and investigator assessment of clinical response (IACR) at test of cure (TOC; 5–10 d after last dose) were assessed in the microbiological intent-to-treat population (ie, all randomized pts with ≥1 CABP-causing baseline pathogen). Treatment-emergent adverse events (TEAEs) were also assessed.

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Results:

Among patients randomized to LEF (*n*=343) or MOX (*n*=333), 468 (69%) had unilobar infiltrates and 208 (31%) had multilobar infiltrates. Compared with patients with unilobar pneumonia, those with multilobar pneumonia were more likely to be aged ≥65 y (37% vs 47%, respectively), have a history of asthma/chronic obstructive pulmonary disease (16% vs 21%) or smoking (41% vs 47%), or have PORT risk class IV–V (16% vs 25%); the most frequently identified baseline pathogen in both groups was *Streptococcus pneumoniae* (≥60%). Patients treated with LEF or MOX had high and similar ECR (unilobar: LEF 92%, MOX 94%; multilobar: LEF 85%; MOX 90%) and IACR success (unilobar: LEF 86%, MOX 89%; multilobar: LEF 77%, MOX 80%) rates. The most common TEAEs were gastrointestinal, with similar rates across groups for LEF (unilobar 14%; multilobar 10%) and MOX (unilobar 9%; multilobar 11%).

Conclusions:

LEF efficacy was high for patients with unilobar or multilobar pneumonia and comparable to that with MOX, and TEAE profiles were similar.

Clinical Implications:

LEF is an alternative to fluoroquinolones for treating CABP in patients with multilobar pneumonia who have or may be at risk for severe pneumonia.

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