LEFAMULIN EFFICACY IN ADULTS WITH COMMUNITY-ACQUIRED BACTERIAL PNEUMONIA (CABP) IS UNAFFECTED BY OBESITY: POOLED ANALYSIS OF THE LEFAMULIN PHASE-3 CLINICAL TRIAL PROGRAM

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Purpose:

According to the CDC, 42.4% of American adults in 2018 were obese (body mass index [BMI]>30) and 9.2% were morbidly obese (BMI>40). Given this prevalence, it is important to understand pharmacokinetics and clinical outcomes for new therapies in the obese population. Lefamulin (LEF) is a pleuromutilin antibiotic recently approved as monotherapy for the treatment of CABP and pharmacokinetic modeling has suggested no correlation between exposure and body weight. The clinical efficacy of LEF vs moxifloxacin (MOX) in adults with CABP within the Lefamulin Evaluation Against Pneumonia (LEAP)1 and LEAP2 phase-3 clinical trial programs was assessed in relationship to BMI categories.

Methods:

The global, prospective, randomized, double-blind, non-inferiority, phase-3 trials that compared the efficacy and safety of LEF IV/oral 5–7days (LEAP1) or oral LEF 5days (LEAP2) to MOX IV/oral 7days (LEAP1) or MOX oral 7days (LEAP2) in adults with CABP were analyzed. Primary outcomes for both trials were early clinical response (ECR) 96±24hours after treatment start and investigator assessment of clinical response (IACR) 5–10days after last dose (test of cure; TOC). For this analysis patients were stratified by BMI into the following categories: Healthy-Weight, BMI<25; Overweight, BMI 25-<30; Obese, BMI 30-<40; Morbidly Obese, BMI≥ 40. Clinical outcomes were evaluated for both LEF and MOX across BMI categories.

Results:

Among the 1289 patients included in the pooled LEAP trials, 554 (43.0%) were healthy weight, 442 (34.3%) were overweight, 262 (20.3%) were obese, and 31 (2.4%) were morbidly obese. Median age, history of chronic obstructed pulmonary disease/asthma, and smoking history was relatively similar across BMI categories; obese and morbidly obese patients were more likely to have comorbidities such as chronic heart failure (11.1% and 38.7%), diabetes (21% and 32.3%), and hypertension (50% and 67.7%), as compared with the respective rates in the healthy weight group (6%, 3.6%, 14.1%). In each category, patients treated with LEF had high and similar ECR rates to MOX (healthy weight 86% vs 90.5%; overweight 90% vs 91.5%; obese 94.7% vs 88.5%; and morbidly obese 92.9% vs 94.1%). IACR success rates were also comparable to MOX (healthy weight 79% vs 86%; overweight 86.1% vs 88%; obese 91.6% vs 88.6%; and morbidly obese 92.9% vs 76.5%).

Conclusion:

Consistent with *in silico* pharmacokinetic modeling, data from the pooled LEAP analyses suggest that LEF was a highly efficacious monotherapeutic treatment of CABP, regardless of BMI category.

Clinical Implications:

LEF represents an alternative to fluoroquinolones for treating CABP in patients with a range of BMIs as typically encountered in normal clinical practice.