Lefamulin (Pleuromutilin-Class Antibiotic) Is an Empiric, Monotherapeutic Option for Community-Acquired Bacterial Pneumonia Caused by Staphylococcus pneumoniae, Including Drug-Resistant Strains

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INTRODUCTION & PURPOSE
- Community-acquired bacterial pneumonia (CAP) is associated with substantial morbidity and mortality, and antibiotic resistance is a major public health issue. Multiple antibiotic-resistant pathogenic bacteria have emerged in the US, as well a variety of extended-spectrum β-lactamase-producing bacteria that are associated with antibiotic-resistant infections.
- Staphylococcus pneumoniae and Staphylococcus aureus are increasingly resistant to antibiotics such as penicillin and cephalosporins. Multidrug-resistant S. pneumoniae poses a serious threat to public health and healthcare systems.
- Several community-acquired bacterial pneumonia (CABP) pathogens have been implicated in CAP, including those resistant to antibiotics of various classes such as cephalosporins, β-lactams, and penicillins.

PATIENTS & METHODS
- Study Design and Efficacy in LEAP 1 & LEAP 2
- Patients were randomized to receive oral lefamulin 600 mg q12h for 5 days or oral moxifloxacin 400 mg q24h for 7 days. The primary endpoint was IACR at TOC.
- In the two global phase 3 studies, LEAP 1 and LEAP 2, lefamulin, the first pleuromutilin, showed high clinical response rates that were comparable to a respiratory drug class that is currently the standard of care.

RESULTS (Overall pooled LEAP trial program)
- Lefamulin demonstrated clinical efficacy across all clinical endpoints achieving non-inferiority between lefamulin and moxifloxacin.
- The FDA and EMA have approved lefamulin for the treatment of CABP.

METHODS (continued)
- Multi-drug resistance was defined as resistant to ≥ 2 of the following: oral cephalosporins, macrolides, macrolide resistance-modifying agents, clindamycin, and erythromycin.
- We evaluated the ECR and IACR for both lefamulin and moxifloxacin in the microtiter plate broth dilution assay and as well as various subgroups of patients based on the resistance phenotypes of their S. pneumoniae pathogens.

RESULTS (S. pneumoniae cohort)
- The overall cure rate was 83.3% in patients who received ≥1 dose of study drug; TOC=test of cure; ITT=intent to treat (all randomized patients); NR=not reached; MPA=multiple pathogen analysis; BIO=bi-dose regimen
- The European Medicines Agency (EMA) coprimary endpoints (FDA secondary endpoints) were IACR at the TOC and ECR at ≤7 days after the last dose of study drug.

CONCLUSIONS
- In the two global phase 3 studies, LEAP 1 and LEAP 2, the first pleuromutilin, showed high clinical response rates that were comparable to a respiratory drug class that is currently the standard of care.
- Evaluating S. pneumoniae isolates from these studies, we found trends in vitro activity for both lefamulin and moxifloxacin across multidrug-resistant, penicillin-resistant, and multidrug-resistant strains.
- Combining this in vitro, clinical success rates were also high and similar between lefamulin and moxifloxacin across S. pneumoniae isolates including those resistant subgroups.
- Given it is indicated as a short course 5-day oral therapy, it has targeted activity against the most common clinical isolates of S. pneumoniae, as well as its multidrug-resistant forms, and its ability to be quickly transitioned of care with both the oral form and formulation across multidrug-resistant, penicillin-resistant, and multidrug-resistant strains.

REFERENCES

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