28th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES
Madrid, Spain
21 – 24 April 2018

# P0619 In Vitro activity of lefamulin against bacterial pathogens collected from patients with community- or hospital-acquired respiratory tract infections: 2016 SENTRY data from Europe

Susanne Paukner*[1], Helio S. Sader[2], Rodrigo E. Mendes[2], Robert Flamm[2], Steve Gelone[3]

*[1]Nabriva Therapeutics GmbH, Vienna, Austria*, *[2]JMI Laboratories, North Liberty, United States*, *[3]Nabriva Therapeutics Inc., King of Prussia, United States*

**Background:** Lefamulin is the first semi-synthetic pleuromutilin antibiotic for IV and oral use in humans and has recently completed a Phase 3 trial for the treatment of community-acquired bacterial pneumonia (CABP) in adults where it demonstrated non-inferiority to moxifloxacin +/- linezolid. Lefamulin effectively and selectively inhibits bacterial translation by binding to the peptidyl transferase center via four H-bonds and other interactions resulting in an "induced fit". CABP is a leading cause of infectious death worldwide and increasing resistance complicates its treatment. This study investigated the activity of lefamulin and comparators against a contemporary set of bacterial respiratory pathogens collected in Europe.

**Materials/methods:** Isolates (n=1,183, 1/patient) were collected in Europe (18 countries, 35 sites) from community-acquired respiratory tract infections (83.9%) and pneumonia from hospitalized patients (16.1%) as part of the SENTRY Surveillance Program. Lefamulin and comparators were tested by CLSI broth microdilution methods and susceptibility was determined using the EUCAST (2017) breakpoints.

**Results:** Lefamulin displayed potent antibacterial activity against this collection of respiratory pathogens (99.2% of isolates inhibited at concentrations ≤1 mg/L). Lefamulin was the most active compound against *Streptococcus pneumoniae* ($MIC_{50/90}$ of 0.06/0.12 mg/L), and its activity was not affected by resistance to other antibiotic classes. *S. pneumoniae* isolates were susceptible to levofloxacin (98.2%) and ceftriaxone (88.1%), whereas 22.2% and 19.9% of isolates were resistant to macrolides and tetracycline, respectively. Lefamulin also showed potent activity against *Staphylococcus aureus* ($MIC_{50/90}$ of 0.06/0.12 mg/L), *Haemophilus influenzae*, ($MIC_{50/90}$ of 0.5/1 mg/L, 20.4% of ß-lactamase producing) and *Moraxella catarrhalis* (0.06/0.12 mg/L, 96.5% β-lactamase positive).

**Conclusions:** Lefamulin demonstrated potent *in vitro* activity against a contemporary collection of respiratory pathogens from Europe. Lefamulin was active regardless of resistance phenotype to other antibiotic classes including macrolides, β-lactams, tetracyclines or fluoroquinolones. These data support the continued clinical development of lefamulin for the treatment of CABP or other respiratory tract infections.

***In vitro* activity of lefamulin and comparators.**

| | | $MIC_{50/90}$ [mg/L] | | | | | |
|---|---|---|---|---|---|---|---|
| **Organism** | **N** | **Lefamulin** | **Amoxi/Clav** | **Ceftriaxone** | **Azithromycin** | **Levofloxacin** | **Tetracycline** |
| *S. pneumoniae* | 772 | 0.06/0.12 | ≤0.03/2 | 0.03/1 | 0.06/>32 | 1/2 | ≤0.25/>8 |
| Penicillin non-susceptible | 221 | 0.06/0.12 | 1/>4 | 0.5/2 | 8/>32 | 1/1 | 0.5/>8 |
| Macrolide resistant | 171 | 0.06/0.12 | 0.5/>4 | 0.5/2 | >32/>32 | 1/2 | >8/>8 |
| *S. aureus* | 110 | 0.06/0.12 | ND | ND | 0.5/>32 | 0.25/>4 | ND |
| *H. influenzae* | 216 | 0.5/1 | 0.5/2 | 0.004/0.015 | 0.5/1 | 0.015/0.03 | 0.5/1 |
| *M. catarrhalis* | 85 | 0.06/0.12 | 0.12/0.25 | 0.25/0.5 | 0.015/0.03 | 0.06/0.06 | 0.25/0.5 |