LB6. Oral Lefamulin Is Safe and Effective in the Treatment of Adults With Community-Acquired Bacterial Pneumonia (CABP): Results of Lefamulin Evaluation Against Pneumonia (LEAP 2) Study

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Background. Lefamulin, a first in class pleuromutilin, is being developed as an IV and oral formulation for treating CABP. The second of phase 3 Lefamulin Evaluation Against Pneumonia studies, LEAP 2 (NCT02813694; EudraCT 2015-004782-92) evaluated oral and IV 5-day regimens, and is presented here. LEAP 2 complements the positive results from LEAP 1, an IV-to-oral switch study in patients with PORT Risk Class III-V.

Methods. In this multicenter, randomized, double-blind, double dummy study, patients with CABP were randomized to oral lefamulin 600 mg q24h for 5 days or 400 mg q24h for 7 days. Adults with PORT Risk Class II–IV were eligible (≥50% were to have PORT Risk Class III or IV). The US FDA primary endpoint was early clinical response (ECR) (96 ± 24 h after first dose) in the intent-to-treat (ITT) population. The EMA primary endpoints were investigator assessment of clinical response (IACR) at test of cure (TOC) (5–10 days after last dose) in the modified ITT (mITT) and clinically evaluable (CED) populations. For FDA and EMA endpoints, noninferiority was concluded if the lower limit of the two-sided 95% CI was greater than –10% (Figure 1).

Results. A total of 738 patients were randomized (n = 370 lefamulin, n = 368 moxifloxacin). Five days of lefamulin was noninferior to 7 days of moxifloxacin for both FDA and EMA primary endpoints (Figure 2). Lefamulin was efficacious regardless of PORT Risk Class (ECR responder rates for PORT II, III, and IV: 91.8% [168/183], 91.0% [132/145], and 85.0% [34/40] for lefamulin; 93.1% [176/189], 90.2% [120/133], and 85.7% [36/42] for moxifloxacin, respectively). Both agents demonstrated similar ECR responder and IACR success rates across baseline CABP pathogen susceptibilities. Rates of serious adverse events (SAEs) and AEs leading to discontinuation were low and similar between groups. Most frequently reported AEs were gastrointestinal, the majority of mild severity with few discontinuations.

Conclusion. Five-day oral lefamulin demonstrated noninferiority for both FDA and EMA efficacy endpoints vs. 7-day oral moxifloxacin. Both agents were safe and generally well tolerated. Lefamulin shows promise as an oral monotherapy with a complete spectrum of antibacterial activity compared against CABP pathogens.

Disclosures. E. Alexander, Nabriva: Employee and Shareholder, Salary and Stock Options. L. Goldberg, Nabriva: Employee, Employee Stock Options and Salary. A. Das, Acheson: Consulting, Consulting fee. Captive: Consulting, Consulting fee. Contracef: Consultant, Consulting fee. Paratech: Consultant, Consulting fee. Tuberculosis: Consultant, Consulting fee. Wahtok: Consultant, Consulting fee. Theravance: Consultant, Consulting fee. Zavante: Consultant, Consulting fee. Utility: Consultant, Consulting fee. Former Employee of Nabriva: Employee, Salary. Nabriva: Consultant, Consulting fee. G. J. Moran, Nabriva: Scientific Advisor, Consulting fee. C. Sandrock, Nabriva: Consultant, Consulting fee. L. B. Gasink, Former Employee of Nabriva: Employee, Salary. P. Spera, Nabriva: Employee and Shareholder, Salary. C. Sweeney, Nabriva: Employee, Stock Options and Salary. S. Paulenk, Nabriva: Employee and Shareholder, Salary. W. W. Wicha, Nabriva: Employee and Shareholder, Salary. J. Schranz, Nabriva: Employee and Shareholder, Salary.

LB7. Contract Tracing Investigation Following First Case of Andes Virus in the United States

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