Lefamulin Is Noninferior to Moxifloxacin in Adults With Community-Acquired Bacterial Pneumonia: Phase 3 Lefamulin Evaluation Against Pneumonia (LEAP 1) Study

Thomas File,1 Lisa Goldberg,2 Anita Das,3 Carolyn Sweeney,4 John Saviski,5 Steven P. Gelone,6 Elisey Seltzer,7 George H Talbot,8 Leanne B. Gasink9

1Summa Health, Akron, OH, USA; 2Nabriva Therapeutics US, Inc., King of Prussia, PA, USA; 3Das Consulting, Guerneville, CA, USA; 4EGS Consulting, Ardmore, PA, USA; 5Talbot Advisors LLC, Anna Maria, FL, USA

INTRODUCTION

Community-acquired pneumonia (CAP) causes significant morbidity, mortality, and a substantial burden on healthcare systems worldwide. The estimated incidence of CAP ranges from 1.7 to 7.6 cases per 1,000 person-years in Europe and the United States on an annual basis.1 In CAP, community-acquired pneumonia (CAP) – usually defined as any lower respiratory infection occurring in an individual without a neutropenic status or a history of chronic lung disease – accounts for 90% of cases.2

Nabriva Therapeutics

METHODOLOGY

Study Design

LEAP 1 was a phase 3, double-blind, active-controlled, double-dummy, 2-stage study to evaluate infected adults with CAP treated with lefamulin + moxifloxacin vs moxifloxacin + linezolid or matching placebo. Primary endpoints were investigator assessment of clinical response (IACR) and early clinical response (ECR) at EOT. Patients were randomized to receive lefamulin or moxifloxacin plus linezolid or matching placebo.

METHODS (continued)

RESULTS (continued)

RESULTS

The 807 patients enrolled, 2% were randomized to receive lefamulin and 27% to receive moxifloxacin plus linezolid. (Table 1)

Patients

Patients were randomized to one of three study drug arms for CAP: Lefamulin Pneumonia Research Network (LPRN) class II trial: 101/305 (33.5%) were eligible.

Early Clinical Response and Investigator Assessment of Clinical Response

• For the ECR primary endpoint, lefamulin was noninferior to moxifloxacin plus linezolid (83.1% vs 78.2% ECR; Difference: –4.9% [90% CI –12.3% to 2.5%]; p = 0.18). (Figure 3)

Clinical Efficacy by PORT Classification

• Lefamulin demonstrated noninferiority to moxifloxacin for the mITT primary endpoint; IACR was classified as successful if the signs and symptoms of CAP resolved or improved ≥ 2 days’ therapy, and the patient did not require ≥ 2 additional antibacterial treatments for CAP during the study. IACR was classified as unsuccessful if the patient required ≥ 2 additional antibacterial treatments for CAP during the study. (Table 2)

CONCLUSIONS

In this phase 3 study in CAP, lefamulin demonstrated high response rates for ECR and IACR that were noninferior to the comparator, moxifloxacin plus linezolid at ≤ 7 days of therapy. Response rates were high across pneumonia severities as assessed by PORT scores. Lefamulin shows promise as an empiric and targeted monotherapy with an ITT-to-TTC visit for the treatment of CAP in adults.

REFERENCES

6. 2013. US