



Comment on ‘Cefiderocol, a New Siderophore Cephalosporin for the Treatment of Complicated Urinary Tract Infections Caused by Multidrug-resistant Pathogens: Preclinical and Clinical Pharmacokinetics, Pharmacodynamics, Efficacy and Safety’

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Dear Editors,

We read with interest the paper by Lee et al., which reviewed the in vitro, in vivo, and clinical data on cefiderocol [1]. However, we would like to address and highlight for your readers, the inaccurate characterization of all-cause mortality (ACM) in the APEKS-NP (NCT03032380, EudraCT 2016-003020-23) clinical trial and the subsequent conclusion drawn from this mischaracterization.

APEKS-NP was specifically designed to assess mortality in the nosocomial pneumonia patient population. Furthermore, APEKS-NP met its primary endpoint of non-inferiority. ACM in the cefiderocol arm was 12.4% versus 11.6% in the high-dose meropenem arm with a treatment difference of 0.8% [95% CI – 6.6 to 8.2] demonstrating that cefiderocol was non-inferior to high-dose meropenem in critically ill patients with nosocomial pneumonia caused by a broad range of Gram-negative bacteria, including *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and Enterobacteriaceae [2, 3]. APEKS-NP subsequently served as the basis of approval by the US Food and Drug Administration (FDA) for use of cefiderocol in hospital-acquired

and ventilator-acquired pneumonias (HAP/VAP) due to susceptible Gram-negative microorganisms, and supported removal of the restriction of limited or no alternative treatment options, and limited safety and efficacy data statements from the cefiderocol label [4].

From these results, Lee et al. draw the conclusion that cefiderocol should be limited only to the treatment of cUTI from Gram-negative bacteria [1]. Our organization, as well as the FDA and European Medicines Agency, examined these results and concluded that cefiderocol can be used in patients with cUTI and HAP/VAP as evidenced by cefiderocol’s current FDA-approved indication as well as the pathogen-focused indication in the European Union [4, 5].

Thank you for the opportunity to respond to Lee et al. We hope this letter helps clarify the design, results and interpretation of APEKS-NP and cefiderocol’s place in therapy.

Declarations

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Conflict of interest Andrew Koren and Andreas Karas are employees of Shionogi Inc. Roger Echols is a consultant for Shionogi and received a consultancy fee for his services.

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