Tebipenem In vitro Activity against a Collection of Pathogens Responsible for Urinary Tract Infections in the US

R.E. Mendes1, I.A. Crichtle2, N. Cotonero2, J.M. Streit1, H.S. Sader1, M. Castanheira3
1JMI Laboratories, North Liberty, IA, USA 2Spero Therapeutics, Cambridge, MA, USA

Introduction

- Enterobacteriaceae—especially Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis—are widely implicated in urinary tract infection (UTI).
- Many oral agents are used to manage UTIs, but their clinical usefulness has been compromised by the increased prevalence of extended-spectrum β-lactamase (ESBL) and carbapenemases. The rising prevalence of these enzymes (3) has prompted interest in alternatives (4).
- Tebipenem is an oral carbapenem, one of the few in development for oral use (5).

Materials and Methods

Bacterial organisms

- A total of 5,372 Enterobacteriaceae collected from 52 medical centers in 9 US Census Divisions were recovered from urine samples during the 2010–2012 STEWIRD Surveillance Program and included in the study.
- Bacterial identification was confirmed by standard algorithms supported by matrix-assisted laser desorption ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany).

Susceptibility testing

- Isolates were tested for susceptibility by broth microdilution following the Clinical and Laboratory Standards Institute (CLSI) M07-18 guidelines.
- From four broth microdilution panels were manufactured by JMI Laboratories (North Liberty, IA, USA) and contained calibrated Mueller-Hinton broth, E. coli, K. pneumoniae, and P. mirabilis, and MIC results were analyzed separately, and presumptively characterized as ESBL producers.
- Quality assurance was performed by sterile checks, colony counts, and testing CLSI recommended quality control reference strains.

Results

- E. coli comprised 65.4% of all Enterobacteriaceae pathogens included in the study and associated with UTI, followed by K. pneumoniae (14.2%) and P. mirabilis (6.6%) (Table 1).
- Other pathogens comprised 25 species or species groups (13.7%).
- In general, tebipenem (MIC90 0.015–0.06 µg/mL) and ertapenem (MIC90 0.06–1 µg/mL) showed susceptibility rates >90% against E. coli isolates with susceptible production of β-lactamase (Table 2).

Conclusions

- Tebipenem displayed potent activity against Enterobacteriaceae pathogens causing UTI among patients in the US. The in vitro potency of oral tebipenem was similar to that of the intravenous ertapenem.
- In general, these data showed compelling activity of oral agents used for treating UTIs. These data support the development of tebipenem as an oral option for management of UTIs in the US.

Acknowledgements

This research was supported by a contract by Spero Therapeutics, Inc. and funded in part with federal funds from the Department of Health and Human Services: Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No. HHS0125201800012C.

References


Contact

R.E. Mendes
JMI Laboratories
1654 Brink Road, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: r.mendes@jmilabs.com

To obtain a PDF of this paper: Scan the QR code or visit this link: https://www.jmila.com/data/posts/ESBL2021_JMI_SperoTherapeutics_US.pdf

Figure 1. Rates of non-susceptibility for amoxicillin-clavulanic acid, cefazolin (predicts nonsusceptibility to oral cephalosporins), levofloxacin, and trimethoprim-sulfamethoxazole (TMP-SMX) against E. coli (Figure 1A), K. pneumoniae (Figure 1B), and P. mirabilis (Figure 1C). Criteria as published by CLSI (2021).

Figure 2. Distribution by US Census region of E. coli and K. pneumoniae clinical isolates with MIC results of ≥2 µg/mL for cefazolin, aztreonam, and/or ceftazidime, and presumptively characterized here as ESBL producers.