

Activity of SPR206 and Comparator Compounds against Enterobacterales Isolates Responsible for Infections in Hospitals in Europe and Adjacent Regions

RE Mendes¹, HS Sader¹, SJR Arends¹, N Cotroneo², IA Critchley², M Castanheira¹

¹ JMI Laboratories, North Liberty, IA, USA; ² Spero Therapeutics, Cambridge, MA, USA

Introduction

- The proportion of isolates producing extended-spectrum β -lactamases (ESBLs) has increased in both hospital and nosocomial settings worldwide. This increased frequency challenges empiric treatment of serious infections and may promote the use of more potent antimicrobial agents, such as carbapenems.
- This scenario helped potentialize the emergence and dissemination of Gram-negative multidrug-resistant (MDR) pathogens in recent decades, including carbapenem-resistant Enterobacterales, for which treatment options are often limited.
- SPR206 is a next-generation polymyxin under clinical development to treat pneumonia, bloodstream, and urogenital tract infections caused by Gram-negative MDR pathogens.
- The *in vitro* activity of SPR206 and comparators was monitored against Gram-negative pathogens causing infection in European hospitals during 2021 as part of the SENTRY Antimicrobial Surveillance Program.
- We report the activity of SPR206 and comparators against Enterobacterales from European countries and adjacent regions.

Results

- *E. coli* (425 isolates) and *K. pneumoniae* (425) were the most common pathogens, followed by *Enterobacter cloacae* species complex (213), *Citrobacter* spp. (121), *K. oxytoca* (110), *Serratia marcescens* (106), *K. aerogenes* (65), *P. mirabilis* (60), *Morganella morganii* (60), and 8 other species/groups (29) (data not shown).
- Overall, SPR206 and colistin had MIC₅₀ results of 0.06 mg/L and 0.25 mg/L against Enterobacterales, respectively, including those isolates intrinsically resistant to polymyxins (Tables 1 and 2). Indole-positive Proteaceae, *Proteus* spp., and *Serratia* spp., which are intrinsically resistant to polymyxins (MIC, >8 mg/L), had elevated SPR206 MICs of >8 mg/L (data not shown). Including these organisms, SPR206 (MIC_{50/90}, 0.06/0.25 mg/L) and meropenem (MIC_{50/90}, 0.03/0.06 mg/L) showed the lowest MICs against this subset, followed by colistin (MIC_{50/90}, 0.25/0.5 mg/L) and ceftazidime-avibactam (MIC_{50/90}, 0.12/0.5 mg/L) (Table 2).
- In general, *E. coli* isolates were susceptible to various agents tested, such as colistin (99.8% susceptible), ceftazidime-avibactam (100% susceptible), piperacillin-tazobactam (90.6% susceptible), ceftolozane-tazobactam (99.1% susceptible), and the carbapenems (100% susceptible) (Table 2). However, 21.6% were classified to presumptive ESBL enzymes, which was reflected in decreased susceptibilities to ceftazidime (21.6% non-susceptible), ceftriaxone (20.7% non-susceptible), and a treonam (21.6% non-susceptible).
- SPR206 (MIC_{50/90}, 0.06/0.25 mg/L) and colistin (MIC_{50/90}, 0.25/0.5 mg/L) showed the lowest MICs against *K. pneumoniae* (Table 2). Colistin (92.9% susceptible) and ceftazidime-avibactam (98.6% susceptible) were active against *K. pneumoniae*.