Antimicrobial Synergistic Effect of a New Anti-Gram-Positive Agent Tested In Combination with a Polymyxin Derivative against Gram-Negative Pathogens, Including ESKAPE Group Organisms

RE MENEDES,1 PR RHOMBERG,1 A LEE1, T LISTER,2 TR PARR JR,3 M VAARA3, RK FLAMM4
1JMI Laboratories, North Liberty, Iowa, USA; 2Spero Therapeutics, Cambridge, Massachusetts, USA; 3Northern Antibiotics, Espoo, Finland

Background: Gram-negative pathogens displaying a multidrug-resistant (MDR) phenotype have become common. Combination therapy is often used to obtain greater potency and therapeutic success when treating infections caused by Gram-negative species.

Materials and Methods: This study was a new agent against Acinetobacter baumannii and Enterobacteriaceae clinical isolates

Results: MICs for comparators applied CLSI/EUCAST/FDA criteria. Tested in combination with SPR741 at a fixed concentration of 8 μg/mL. Interpretation of isolate susceptibility were selected and tested for susceptibility by CLSI methods. SPR719 was ≤0.015/0.03 μg/mL) displayed the lowest MICs, followed by colistin (MIC50/90, 0.12/0.25 μg/mL) against A. baumannii species intrinsically resistant to polymyxin. This study evaluated a new approach combining a novel gram-positive agent (a gyrase inhibitor) and a gram-negative agent (a polymyxin-like) for the treatment of infections caused by Gram-negative species.

Conclusions: • SPR719/SPR741 showed potent activity against A. baumannii and Enterobacteriaceae species. • The investigational agent SPR719 tested in combination with the polymyxin-like agent SPR741 showed excellent activity against carbapenem-resistant strains. • This study was obtained for further investigations warranted for potential evaluation in a multi-drug resistant setting.

Acknowledgements: • Thank you to all the sponsors at Spero Therapeutics who supported the study. • The limitations of this study are acknowledged.