**Abstract**

Objective: New antimicrobials administered as monotherapy or in combinations that are active against multidrug-resistant Enterobacteriaceae are needed. A new siderophore carbapenem, BAL30072 (P), is a novel monosaccharide antibiotic with potent activity against MDR isolates and is currently in phase 1 clinical development in combination with meropenem (MER). In these studies, a known synergistic effect between MER and SFM was demonstrated against a range of multidrug Gram-negative bacteria.

Methods: In vivo mice were infected intraperitoneally with 2×10⁷ CFU of an E. coli strain harboring a plasmid encoding blaoxy and SFM-resistant blaKPC-3. BAL30072 was administered intraperitoneally at 0.3 mg/kg every 8 h or intravenously at 3 mg/kg every 12 h in combination with SFM (2:1, 1:1 or 1:2) during 24 h post-infection. Efficacy was determined as the reduction of the bacterial burden in the kidney and thigh.

Results: Meropenem and BAL30072 were well tolerated at the doses administered. The combination of meropenem and SFM at the ratio 2:1 showed the largest improvements in efficacy compared to monotherapy or the combination at the ratio 1:2. The combination of meropenem and SFM at the ratio 1:2 was the least effective combination of the two antimicrobials. The combination of meropenem with SFM at the ratio 1:1 was the most effective combination of the two antimicrobials. The combination of meropenem with SFM at the ratio 1:1 was the most effective combination of the two antimicrobials.

Conclusions: The combination of meropenem and BAL30072 in combination increased the treatment efficacy window against all strains suggesting a synergistic interaction. The largest improvements in efficacy were observed with the combination meropenem and BAL30072. The antimicrobial activity is driven predominantly by one agent of the combination and that can be predicted using in vitro synergy assays. These data suggest the combination of meropenem and BAL30072 could be a feasible treatment option for MDR Gram-negative bacteria.

**References**


**Acknowledgements**

This project has been funded in whole or 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/BAHRA) under contract No. HHSN272201300010C.