ABSTRACT

In vitro activity of NXL103 (formerly XRP 2868) is an orally active, semisynthetic streptogramin combination (linopristin/flopristin) with potential to treat pathogens associated with community-acquired pneumonia (CAP) and acute bacterial skin and soft tissue infections. NXL103 has also demonstrated activity against resistant organisms, such as community-associated (CA) and healthcare-associated (HA) methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE). We determined its in vitro activity of NXL103 against Gram-positive pathogens and Haemophilus influenzae recently isolated from patients in medical and surgical wards, intensive care units, clinics, and emergency rooms at 15 Canadian hospitals from January to December 2009.

Methods: Antimicrobial susceptibility testing was performed using broth microdilution panels following the recommended CLSI method.

Results: The activity of NXL103 and comparator agents is summarized below.

NXL103 demonstrated potent in vitro activity against pathogens commonly associated with clinical and hospital-acquired MRSA and S. pneumoniae, respiratory tract infections (pneumococcal and macrolide-nonsusceptible S. pneumoniae, S. pyogenes, and H. influenzae), as well as VRE and MRSE.

NXL103 (Linopristin/Flopristin) Activity Against Pathogens Isolated from Patients in Canadian Hospitals: CANDAR 2009

J.A. Karlowsky, P. Lagacé-Wiens, A. Wierzbowski, D.J. Hoban, G.G. Zhanel

University of Manitoba, Health Sciences Centre, Winnipeg, Canada

From January 2009–December 2009, 15 sentinel Canadian hospital laboratories were asked to submit consecutive bacterial pathogens (1 per patient) from blood, respiratory, urine, and wound infections. In total, 5,375 isolates were submitted (4,546 isolates (1,871 Gram-positive, 2,675 Gram-negative) were tested for antimicrobial susceptibilities. Yeasts, non-specified coagulase-negative staphylococci, Streptococcus epidermidis, viridans streptococci, Moraxella catarrhalis, and species with fewer than 10 isolates were not tested for antimicrobial susceptibilities. Isolates were tested for antimicrobial susceptibilities using in-house prepared (Department of Clinical Microbiology, Health Sciences Centre, Winnipeg, Canada) 96-well broth microdilution panels according to CLSI M100-S19 (2009) guidelines. Minimal inhibitory concentrations (MICs) were interpreted using CLSI M100-S19 (2009) guidelines, where available.

DISCUSSION

• Against methicillin-susceptible S. aureus (MSSA), NXL103 demonstrated an MIC of 0.12 µg/mL, with an MIC range of ≤0.03–0.25 µg/mL. Against MRSA, specifically, isolates of healthcare-associated MRSA, NXL103 had a higher MIC of 0.12 µg/mL. Isolates from community-associated MRSA had an MIC of 0.12 µg/mL, identical to MSSA (Table 1).

• NXL103 appeared equally potent against S. aureus and S. epidermidis (Table 1).

• NXL103 showed greater in vitro potency against S. pyogenes (MIC ≤0.03 µg/mL) than against S. pneumoniae (MIC ≥0.12 µg/mL), E. faecalis (MIC ≤0.03 µg/mL), and E. faecium (MIC ≥0.12 µg/mL) (Table 1). S. aureus non-susceptible to clarithromycin or clindamycin (MIC ≥0.5 µg/mL) had NXL103 MICs that were similar to those from clindamycin- or clarithromycin-susceptible isolates (MIC ≤0.12 µg/mL) (Table 1). Concurrent resistance to clarithromycin or clindamycin and oxacillin did not appear to affect NXL103 activity (MIC ≤0.12 µg/mL). NXL103 in vitro activity was also not affected by resistance in other combinations, namely mecA-mediated, antimicrobial agents (data not shown).

• NXL103 was active against H. influenzae (MIC, 1 µg/mL), and demonstrated similar activity against both clarithromycin-susceptible (MIC, 0.5 µg/mL) and non-susceptible isolates (MIC, ≥0.5 µg/mL).

CONCLUSION

NXL103 demonstrates potent in vitro activity against pathogens commonly associated with clinical and hospital-acquired MRSA and S. pneumoniae, respiratory tract infections (pneumococcal and macrolide-nonsusceptible S. pneumoniae, S. pyogenes, and H. influenzae), as well as VRE and MRSE collected from patients attending hospitals across Canada in 2009.

ACKNOWLEDGMENTS

Funding for the CANDAR study was provided in part by the University of Manitoba, National Microbiology Laboratory, and AstraZeneca (Macclesfield, UK). The medical centers (investigators) that participated in CANDAR 2009 are listed at http://www.candar.com/.

REFERENCES