P0802
Poster Session III
C. difficile: antimicrobial susceptibility and treatment

IN VITRO ACTIVITY OF MCB3681 AGAINST CLOSTRIDIUM DIFFICILE STRAINS

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Objectives: *Clostridium difficile* infections (CDIs) have increased significantly world-wide during the last decade. CDI and in particular recurrent CDI are associated with high morbidity, mortality and a lot of healthcare-associated costs. The recommended first line oral treatments for CDI are not optimal in the treatment of recurrent CDIs. MCB3681 is a novel oxazolidinone-quinolone hybrid molecule active against aerobic and anaerobic Gram-positive bacteria. MCB3837, the prodrug of MCB3681, is administered i.v. and may offer a new treatment of CDI. Therefore, its activity against *C. difficile* has been studied.

Methods: One hundred fourteen *C. difficile* strains were collected from 67 patients and analyzed for the presence of *C. difficile* toxin B by the cell cytotoxicity neutralization assay, genes for toxin A, toxin B, binary toxin and *Tcd*C deletion by PCR. All strains were also PCR-ribotyped. The *in-vitro* activity of MCB3681 is compared with cadazolid, fidaxomicin, vancomycin, metronidazole, tigecycline, ciprofloxacin, moxifloxacin, linezolid and clindamycin. MICs were determined by the agar dilution method according to the CLSI guidelines using *Bacteroides fragilis* ATCC 25285 and *C. difficile* ATCC 700057 as control strains.

Results: All 114 isolates were positive for toxin B, toxin A and B genes. In addition, 13 of the 114 isolates were positive for binary toxin gene. Thirty-two different ribotypes were identified. The most common ribotypes were 020 (14.9%), 014/077 (8.8%), 078/126 (7%), 001 (6.1%) and 026 (6.1%). No strain of ribotype 027 was found. All 114 isolates were sensitive to MCB3681 (0.008-0.5 mg/L), cadazolid (0.064-0.5 mg/L), fidaxomicin (0.008-0.125 mg/L), metronidazole (0.125-2 mg/L), vancomycin (0.125-1 mg/L) and tigecycline (0.032-0.25 mg/L). Three isolates were resistant to linezolid (8 mg/L), 12 isolates were resistant to moxifloxacin (8-32 mg/L), 87 isolates were resistant to clindamycin (8-256 mg/L) and 107 isolates were resistant to ciprofloxacin (8-256 mg/L). Three strains were quinolone-, clindamycin- and linezolid-resistant. No association between toxins A, B and binary toxin, ribotypes and the sensitivity to MCB3681 could be found.

Conclusions: MCB3681 demonstrated high *in-vitro* activity against *C. difficile* strains with MICs which were comparable or lower than the MICs of cadazolid, fidaxomicin, metronidazole and vancomycin. Its prodrug MCB3837 may offer an alternative for i.v. treatment of CDI.