P0241

Paper Poster Session I

New antibacterial drugs

Comparing the effects of SMT19969, vancomycin and fidaxomicin on sporulation of several *Clostridium difficile* ribotypes

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Objectives: SMT19969 (SMT) is a novel antimicrobial under clinical development for *Clostridium difficile* infection (CDI) that is associated with minimal impact on host gut microbiota. CDI is the leading cause of antibiotic associated diarrhoea, is associated with significant morbidity and mortality and imparts a significant financial and patient welfare burden on the healthcare system. Recurrent infection is a particular concern with at least 25% of patients experiencing recurrent disease after an initial episode. Treatment options are limited and currently only metronidazole, vancomycin (VAN) and fidaxomicin (FDX) are routinely used. *Clostridium difficile* is capable of producing endospores and these spores are the transmissive agent, leading to outbreaks and persistent contamination of the environment and play a role in recurrent disease. In this study we assessed the effect of SMT, VAN and FDX on sporulation of several relevant ribotypes of *C. difficile*.

Methods: *C. difficile* strains 630 (ribotype 012), DH196 (ribotype 027) and EK28 (ribotype 078) were used in this study. Sporulation was assessed at 0.5, 1, 5 and 10 x MIC of SMT, FDX or VAN and compared to drug free controls. Sporulation was measured by growing 630, DH196 and EK28 in rich media (BHIS) with corresponding antibiotics and plating heat resistant and non-heat resistant CFUs at 0, 24, 48, 72 and 96 hours onto BHIS + taurocholate (TC). Data reported are the means (±SE) of triplicate runs. The results are presented as % of cells forming spores.

Results: SMT, FDX and VAN all resulted in a dose dependent inhibition of sporulation which was particularly apparent at 10x MIC. VAN and FDX were markedly less effective against strains DH196 (ribotype 027) and 630 (ribotype 012) respectively compared to other strains tested. SMT showed significant reductions particularly against the ribotype 027 strain DH196 (15.8% and 9.2% of cells forming spores at 1x MIC and 10x MIC respectively compared to 100% with drug free controls).

Conclusion: SMT and FDX showed superior reductions in sporulation compared to VAN. The effect of all three drugs was strain dependent. The reduction in sporulation may result in a reduced spore load in the GI tract of CDI patients which may impact on rates of recurrent disease. These data support the continued clinical development of SMT for CDI.