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Abstract (poster session)

Effective treatment of simulated Clostridium difficile infection with a shortened course (4 day) of oritavancin in a human gut model

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Objectives: We previously demonstrated that oritavancin (ORI) is effective as a treatment of clindamycin induced Clostridium difficile infection (CDI) in a human gut model, and may be more effective than vancomycin (V) due to apparent increased activity against spores, and prevention of recurrence of toxin production. We compared the efficacy of a shortened dosing period (4 d) of ORI vs V for the treatment of CDI within the gut model. Methods: A 3-stage chemostat human gut model was inoculated with pooled faeces (5 healthy elderly volunteers). Clindamycin (CLIN, 33.9 mg/L qid for 7d) was dosed to induce CDI by C. difficile ribotype 027 (NAP1/BI). Following CDI induction, 2x 4-day dosing regimens were used: ORI (64 mg/L) bid; or V (125 mg/L/) qid. CD total viable counts (TVC), spore counts (SP), toxin titres, and gut microflora components were measured throughout Results: CLIN instillation induced CD germination and high level toxin production in V and ORI models. CD TVC decreased to SP by 5d post V, whereas both TVC and SP were undetectable by 2d post-ORI. Toxin titres reduced to undetectable levels by 12d post-V vs 5d post ORI. There was evidence of recurrence of CD germination and high level toxin production, 20d after V instillation ceased. Conversely, low levels of toxin (titre of >2) were observed without detectable germination in the ORI model: SP remained undetectable in the ORI model for the remainder of the experiment, but TVC were detectable at the limit of detection. Lactose fermenters and enterococci decreased (~4 and ~ 3 log10 cfu/ml reduction respectively), and B. fragillis group increased (~4 log10 cfu/ml increase) following V treatment. Enterococci and clostridia decreased following ORI treatment (~5 and ~ 3 log10 cfu/ml reduction respectively). Conclusions: As with 7d dosing regimens, ORI was superior to V in reducing TVC counts and SP below the limits of detection. ORI reduced SP counts whereas V did not. There was clear evidence of recurrence in the V model. These data support previous conclusions that ORI may be an effective treatment for CDI, even when administered over only four days. The confirmed observation of ORI effects on SP recovery represent a potential advantage over other CDI treatments.