A Functional OMICS Evaluation of Omadacycline to Understand Anti-*Clostridioides difficile* Protective Effects

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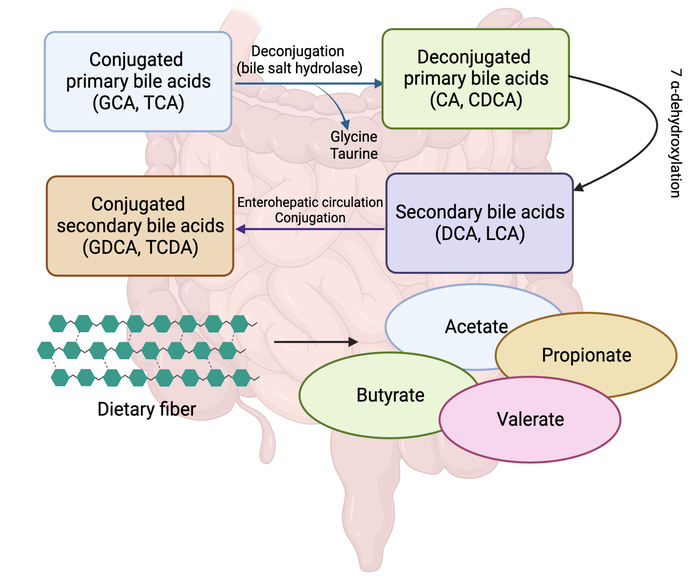
BACKGROUND & OBJECTIVE

- Omadacycline, an aminomethylcycline tetracycline analog with potent *in vitro* activity against *C. diffcile* (CD) and a low propensity for CD infection (CDI) in clinical trials[1,2]
- Bile acids and short-chain fatty acids (SCFAs) play an important role in overall gut microbial health
- This study aimed to compare bile acid and SCFA changes in healthy volunteers given oral omadacycline versus vancomycin



Created by Jinhee Jo via Biorender
GCA: Glycocholic acid, TCA: Taurocholic acid, CA: Cholic acid, CDCA: Chenodeoxycholic acid, DCA: Deoxycholic acid, LCA: Lithocholic acid, GDCA: Glycodeoxycholic acid, TCDA: Taurolithocholic acid

METHODS

Study design

- Healthy subjects aged 18-45 years were randomized to receive 10 days of oral omadacycline or vancomycin (125 mg four times daily)
- Stool samples were collected at baseline, during antibiotic days (day 1 to 10), and follow-up visits on (day 13-14 and day 30-32)

Bile acid and SCFA analysis

- Stool samples collected at baseline, during therapy, and end of therapy were used
- Targeted bile acids and SCFA quantification were performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS)
- The final concentration of each metabolome was normalized by corresponding stool sample weight

RESULTS

Figure 1. Metagenomic analysis between antibiotic groups

Figure 1 was previously presented at ECCMID2023

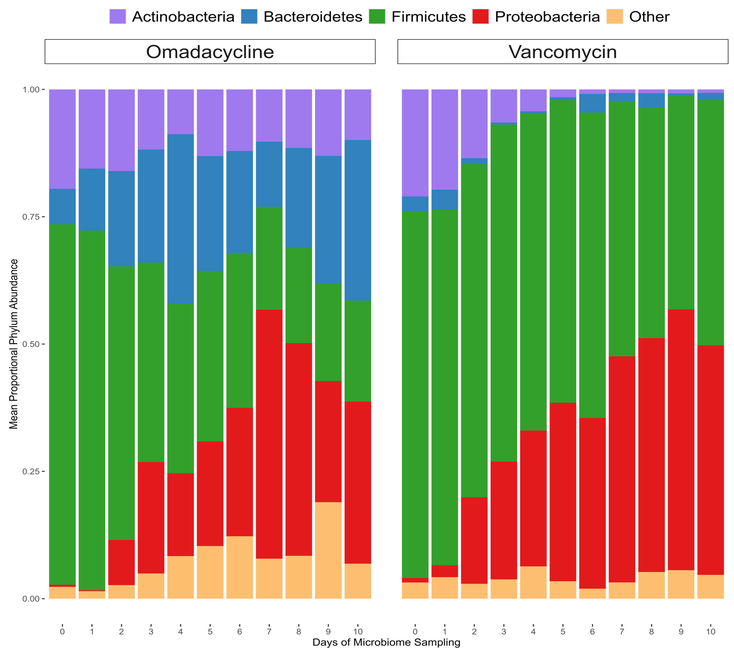


Figure 2. Bile acid changes between antibiotic groups

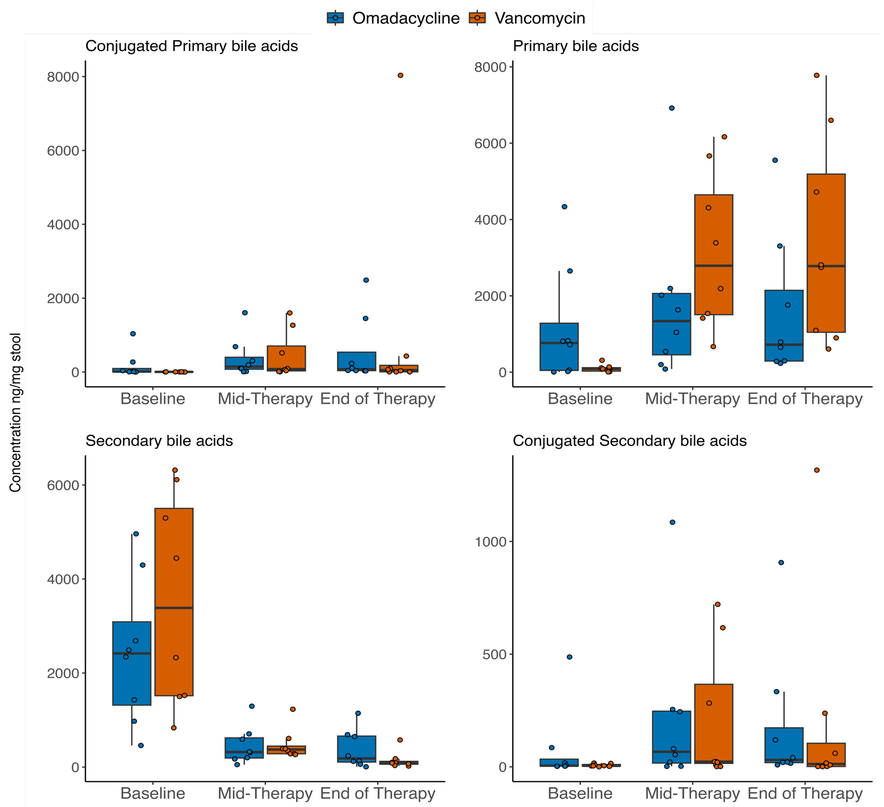
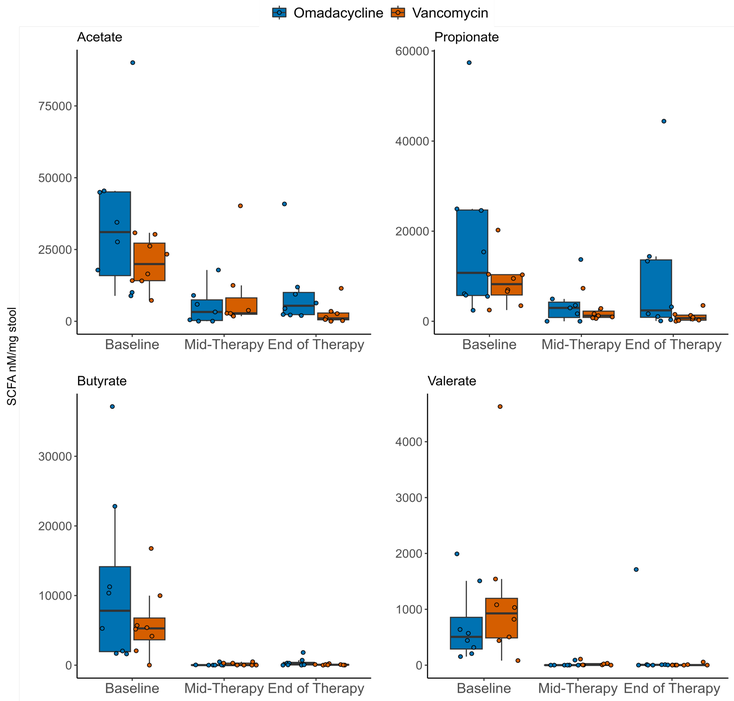


Figure 3. SCFA changes between groups



CONCLUSIONS

- Overall, subjects given omadacycline exhibited differing changes in bile acids and SCFAs compared to those given vancomycin. These observed changes may be correlated with their distinctive post-antibiotic microbiome composition
- This study may provide a framework to better understand the anti-*C.difficile* effects of omadacycline however larger studies are needed

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REFERNCES

1. Begum K, et al. In vitro activity of omadacycline, a new tetracycline analog, and comparators against *Clostridioides difficile*. *Antimicrob Agents Chemother*. 2020;64(8):e00522-20.
2. Moura IB, et al. Omadacycline gut microbiome exposure does not induce Clostridium difficile proliferation or toxin production in a model that stimulates the proximal, medial, and distal human colon. *Antimicrob Agents Chemother*. 2019;63(2):e01581-18.