Poster #P1836

Gut Microbiome Diversity and Bacterial Taxonomic Group Changes in Healthy Volunteers Receiving Oral Omadacycline or Vancomycin

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BACKGROUND

- Omadacycline is an aminomethylcycline tetracycline available in both intravenous and oral formulations and is currently approved for community-acquired bacterial pneumonia and acute bacterial skin and skin structure infections
- Previous in vitro studies have demonstrated its potent activity against *Clostridioides difficile* including hypervirulent strains (ribotype 027) with low minimal inhibitory concentration compared to currently available agents (e.g., vancomycin, fidaxomicin) and in vivo studies also showed favorable outcomes of omadacycline in *C. difficile* infectious models[1,2]
- Preclinical data collectively suggest that omadacycline may be a candidate for an anti-C. difficile agent, however there has not been a clinical study of omadacycline conducted in humans

OBJECTIVE

To characterize gut microbiome changes in healthy adult volunteers given oral omadacycline or vancomycin

METHODS

Inclusion Criteria

- Healthy adults aged between 18 and 40 years
- No significant past medical history and antibiotic use in the past 90 days prior to enrollment

Study Design/Sample Collection

- Subjects were randomized to receive 10 days of either oral omadacycline (450 mg daily on day 1 and 2 followed by 300 mg daily on remaining days) or oral vancomycin (125 mg daily)
- Stool samples were collected at baseline, during antibiotic days (day 1 to 10), and follow-up visits (day 13-14 and day 30-32)

Stool DNA Extraction

- Stool DNA extraction was performed using the MagAttract Power Microbiome Kit protocol (Qiagen)

Quantitative PCR and Microbiome Analysis

- qPCR was performed on specific microbial families using the Qubit 4 Fluorometer (Thermo Fisher Scientific)
- The V4 region of the 16S ribosomal RNA gene was amplified and sequenced using the Illumina MiSeq and sequencing yielding >5,000 reads per sample were used for operational taxonomic unit clustering using the CLC Genomics Workbench (version 22.0.2, Qiagen)
- All statical analyses and data visualization were performed using R software (version 4.2.1)

RESULTS

Figure 1. Proportional Phyla Changes Between Antibiotic Groups

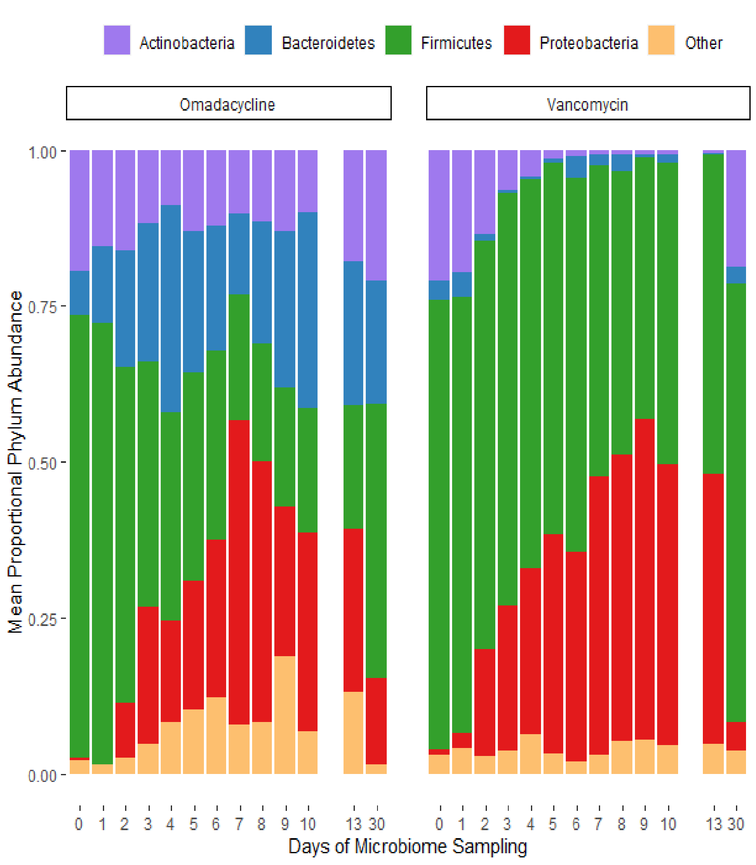


Figure 2. qPCR Analysis on a Bacterial Group

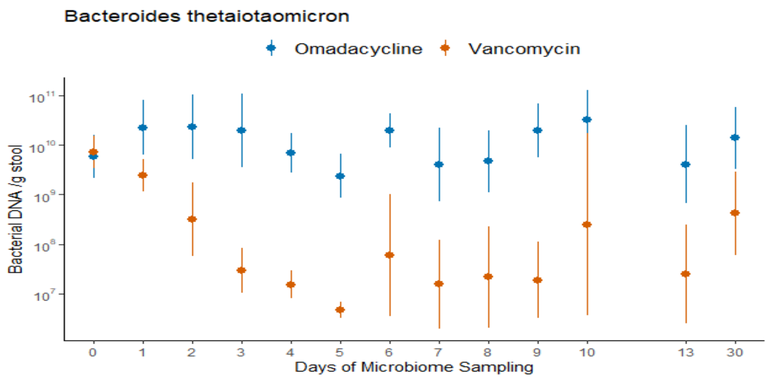


Figure 3. Alpha-Diversity Changes

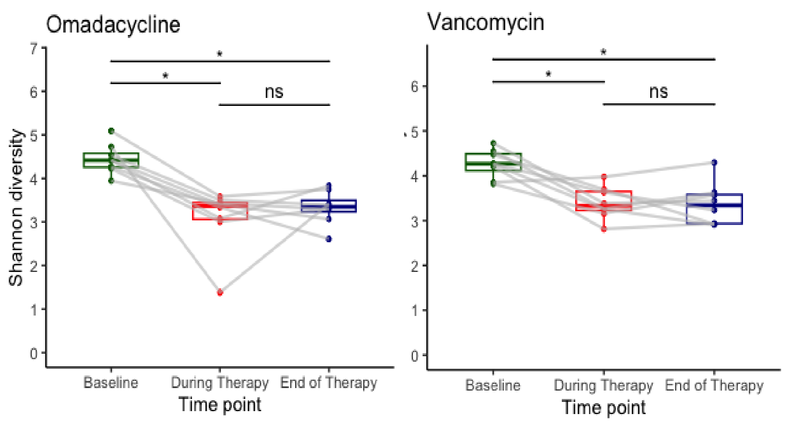
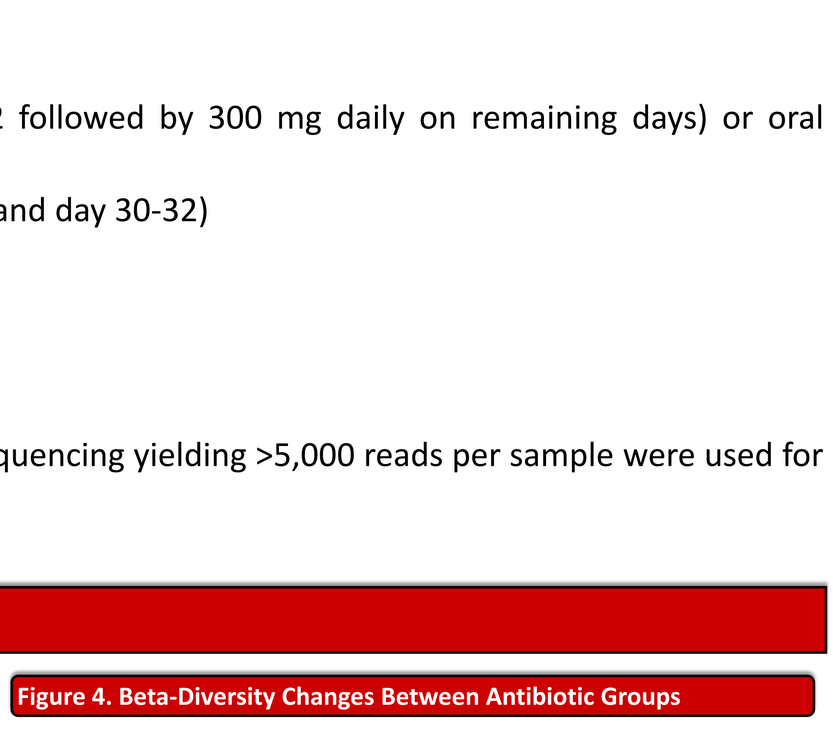


Figure 4. Beta-Diversity Changes Between Antibiotic Groups



CONCLUSIONS

- Overall, both omadacycline and vancomycin resulted in microbiome diversity changes in healthy adult subjects
- However, the degree of those changes were distinct in those given omadacycline compared to vancomycin
- Further functional microbiome studies are warranted to elucidate these findings

FUNDING

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REFERENCES

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.