A new weapon against the super-tough C diff bacteria tested in phase-one human trial

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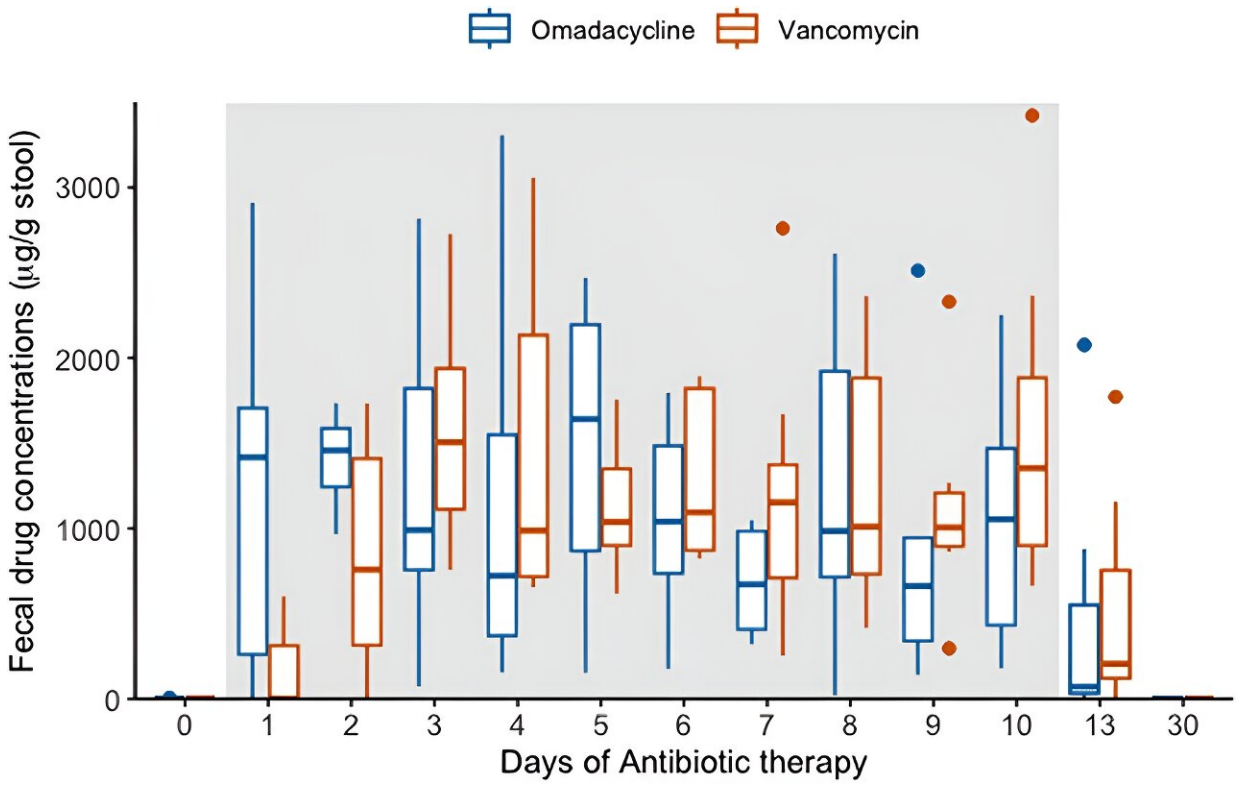

Fecal drug concentrations of omadacycline and vancomycin. Credit: *The Journal of Infectious Diseases* (2023). DOI: 10.1093/infdis/jiad537

In a phase-one human clinical trial, a University of Houston pharmacist researcher has demonstrated that a newer generation tetracycline antibiotic, called Omadacycline, may be a promising tool in combating

the resilient bacteria Clostridioides difficile (C diff), which causes an infection often picked up in hospitals. C diff brings on diarrhea and colitis, an inflammation of the colon, and is responsible for nearly 500,000 infections annually in the United States.

The fight against C diff takes its toll internally, including a significant disruption of gut microbiota, usually by broad-spectrum antibiotics, leading to loss of colonization resistance to C difficile. Omadacycline demonstrated a low likelihood of causing C diff in clinical trials, but no one understood why.

Kevin Garey, Robert L. Boblitt Endowed Professor of Drug Discovery at the UH College of Pharmacy, assessed the pharmacokinetics and gut microbiome effects of oral Omadacycline in comparison to Vancomycin, another possible C diff drug. Vancomycin is used to treat C diff but is not good at eliminating it over the long-term. Garey's team investigated whether Omadacycline, given orally, achieves high concentration in the gut and the effect on the gut microbiome, the healthy bacteria that lives in the colon.

"Our research shows off the coolness of the microbiome. Omadacycline caused a distinctly different effect on the microbiome than Vancomycin. This could explain why Omadacycline is a safe drug to give to patients at high risk for C diff infection.

"This could become a new method in drug development to see if antibiotics are not only killing the bacteria causing infections (the bad bugs) but not causing harm to the beneficial microbes that live in our body (the good bugs)," said Garey, whose results were published in the *Journal of Infectious Diseases*. "I would hope that this becomes a normal part of the antibiotic drug development process."

In the study, 16 healthy volunteers tolerated Omadacycline with no

safety differences compared to the other antibiotic. A rapid initial increase in fecal concentration of Omadacycline was observed compared to Vancomycin, with maximum concentrations achieved within 48 hours. Rapid increase is a good thing—it means the active drug is getting to the site of the infection faster.

"Both the Omadacycline and Vancomycin groups showed significant changes in their microbiomes when we looked at how diverse they were internally (alpha diversity). However, when we compared the changes between the two groups (beta diversity), they were noticeably different from each other," reported Garey.

More information: Jinhee Jo et al, Fecal Pharmacokinetics and Gut Microbiome Effects of Oral Omadacycline versus Vancomycin in Healthy Volunteers, *The Journal of Infectious Diseases* (2023). DOI: 10.1093/infdis/jiad537

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