

CONTROL ID: 828630 **CATEGORY:** CLINICAL PRACTICE **PRESENTATION TYPE:** AGA Institute Oral **PRESENTER:** Stuart Johnson **PRESENTER (E-MAIL ONLY):** sjohnson@lumc.edu

Abstract TITLE: Randomized Clinical Trial (RCT) in Clostridium difficile Infection (CDI) Confirms Superiority of Fidaxomicin over Vancomycin **AUTHORS (LAST NAME, FIRST NAME):** Johnson, Stuart^{1,2}; Crook, Derrick³; Cornely, Oliver A.⁴; High, Kevin P.⁵; Miller, Mark⁶; Gorbach, Sherwood L.⁷ **INSTITUTIONS (ALL):** 1. Infectious Diseases, Loyola U. Medical Center, Maywood, IL, United States.
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ABSTRACT BODY: Background: The usual treatments of CDI, metronidazole or vancomycin (VAN), have cure rates of 80-90% but 20-30% experience a relapse. This phase 3 RCT compared fidaxomicin (FDX), a first-in-class bacteriocidal macrocyclic antibiotic, with VAN in treatment of CDI.

Methods: Eligible patients had acute CDI symptoms and a positive stool toxin test. Patients received oral FDX (200 mg twice daily) or oral VAN (125 mg 4 times daily) for 10 days. Primary end point was clinical cure. Secondary end points were CDI recurrence (diarrhea and positive stool toxin test within 4 wks after treatment), and global cure (clinical cure with no recurrence).

Results: This RCT comprised 535 subjects with 524 available for safety, 509 for modified Intent-To-Treat (mITT), and 451 for Per Protocol (PP) analyses. Europe (39%), USA (30%) and Canada (31%) contributed subjects from 100 clinical sites. All data are given for the PP population; the mITT population was similar in all instances. The primary non-inferiority endpoint of cure was met with 91.7% cured vs. 90.6% (FDX vs VAN, respectively). Recurrence was seen in 12.8% vs. 25.3% (FDX vs VAN, respectively, $P = 0.002$). Global cure was noted in 79.6% vs. 65.5% (FDX vs VAN, respectively, $P < 0.001$). Concomitant antibiotics (CAs) to treat infections other than CDI were given to 59% of patients during CDI treatment. Those who received CAs had a lower cure rate (86.1% with CAs vs 98.4% without, $P < .001$), a higher recurrence rate (23.9% with CAs vs 8.1% without, $P < .001$), and lower global cure rate (59.8% with CAs vs 90.3% without, $P < .001$). For those given CAs, FDX treatment was associated with lower recurrences (17.6% FDX vs 29.5% VAN, $P = .027$) and higher global cures (67.5% FDX vs 53.4% VAN, $P = .020$) but no difference in cures. FDX was well tolerated with an adverse event profile similar to that of VAN.

Conclusions: This RCT found equivalent cure rates with FDX and VAN but significantly fewer relapses and higher global cures. A previously reported RCT of identical design revealed the same findings. CAs had a deleterious effect on lowering cures and global cures and increasing relapses; however, FDX therapy significantly improved the relapse rate and global cures in the CA group. A total of 1100 CDI subjects in 2 RCTs have established the potential benefits of FDX in CDI treatment even when concomitant antibiotics are administered.

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Disclosure Status The following authors have completed their 2010 DDW disclosure: Stuart Johnson: Disclosure completed Derrick Crook: No Answer. Oliver Cornely: No Answer. Kevin High: No Answer. Mark Miller: No Answer. Sherwood Gorbach: No Answer.