IN VITRO ACTIVITY OF FIDAXOMICIN (OPT-80) AND COMPARATOR ANTIMICROBIAL AGENTS AND REA TYPING OF *CLOSTRIDIUM DIFFICILE* RECOVERED DURING A NORTH AMERICAN CLINICAL TRIAL.

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Background: With the ever-increasing prevalence of *C. difficile* infection (CDI) and the ongoing search for new therapies, it has been recognized that certain strain genotypes are associated with the severity of the disease and its recurrence. As reference lab for a recent large clinical trial comparing fidaxomicin with vancomycin, we received fecal specimens collected at pre-therapy (Pre) and at failure (Fr) or recurrence (Rc) from CDI patients across North America. We determined the MICs and REA types and compared the results for strains found in the Pre specimens with those from Fr and Rc.

Methods: Of 631 specimens cultured, we isolated 503 strains of *C. difficile*—434 from Pre, 12 from Fr and 57 from Rc occurring within 4 weeks after treatment. Using the CLSI agar dilution reference method, all isolates were tested for susceptibilities against the two study drugs, FDX and vancomycin (VAN), as well as metronidazole (MTZ), moxifloxacin (MFX) and rifaximin (RFX). Isolates were sent to Dr. Gerding's lab for restriction endonuclease analysis (REA) genotyping.

Results: BI was the most prevalent type, comprising 38.8% of all strains (195/503), with 66.7% (8/12) in the Fr group and 36.8% (21/57) in the Rc group. Other prominent REA types present in the Pre isolates were Y (7.4%), G (7.2%), J (5.6%) and K (3.7%); all except Y were also found in the Rc/Fr group, with J at 11.5% (8/69) and K at 4.3% (3/69). Thirty five % of the Pre strains were non-specific REA types, and 4 were non-typable. MICs (μg/mL) for FDX, VAN and MTZ were ≤0.004 – 0.5, 0.25 – 4, and 0.03 – 4, respectively, for all isolates and had no apparent bearing on cure or Fr/Rc. RFX-R (MIC >256 μg/mL) was present in 8.2% of all strains including 16.4% (32/195) of BI, 3.1% 1/32 of J, and 25% (5/20) of K. The REA Type K had the highest rate of RFX-R at 18.8% (3/16) from the Pre specimens, and 66.7% (2/3) in Rc. MFX-resistance at ≥8μg/mL was found in 47.2% 211/447 of all strains tested, including 88.6% (156/176) of BI, 53% (16/30) of J, and 100% (12/12) of K, but only 10.3% (3/29) of G and 9.7%

(3/31) of Y types. All but 2 RFX-R strains were also resistant to MFX, but not vice versa. Many strains in the Rc/Fr group were the same types as in Pre, and 11 did not have *C. difficile* isolated from Pre with which to compare, but of the remainder 19% (11/58) were new types, including 4 BI, 2 J, 1 G, and 4 non-specified REA

Conclusions: The BI type was the most prevalent in this study and most often associated with failure and recurrence. Resistance to RFX was higher in Fr/Rc isolates. MFX-R was highest in the BI and K strains.