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Fidaxomicin is a Superior Treatment to Vancomycin for Recurrent *Clostridium Difficile* Infection

Angela Mathison

St. Catherine University
FIDAXOMICIN IS A SUPERIOR TREATMENT TO VANCOMYCIN FOR RECURRANT CLOSTRIDIUM DIFFICILE INFECTION

Abstract

Clostridium difficile has been historically viewed as a hospital acquired infection. However, the emergence of community acquired infection in low risk populations, the identification of new risk factors, detection of a hypervirulent strain of C. difficile, and increasing mortality have changed the epidemiology if this infection. Current standards of treatment have come into question due to increasing recurrence rates and treatment failures, possible resistance of Metronidazole, and concerns surrounding Vancomycin resistant enterococci (VRE). Fidaxomicin, a narrow-spectrum macrolide, is the first drug approved by the FDA in 20 years for the treatment of C. difficile infection. It has shown good in vitro and in vivo activity, has similar clinical cure rates, lower recurrence rates, and higher global cure rates compared to Vancomycin in non-hypervirulent strains and similar efficacy in all outcomes in the hypervirulent strain. Overall, Fidaxomicin appears to be a reasonable second line treatment option for recurrent C. difficile infection in patients who have failed to respond to treatment under the current guidelines.

Keywords: Clostridium difficile, Fidaxomicin, Vancomycin
**Introduction**

*Clostridium difficile* (*C. difficile*), an opportunist gram positive, anaerobic, spore-forming bacillus, is the most widely recognized cause of infectious diarrhea with a high healthcare cost burden (McFarland, 2008). There are two primary virulence factors found in *C. difficile* infections, toxin A and toxin B (Warny, et al., 2005). These toxins bind to surface proteins in the intestinal epithelial cells and disrupt the cytoskeleton resulting in a rounding of the cell, opening of the tight junction between cells and a subsequent fluid release resulting in diarrhea (McFarland, 2008; Noren, 2010). Toxin A is unique in that it also induces apoptosis of the cells (McFarland, 2008). Depending on the virulence of the toxin and the host response, *C. difficile* can cause a wide array of symptoms ranging from mild, watery diarrhea to life threatening conditions including: fulminant pseudomembranous colitis, toxic mega colon, bowel perforation, septic shock and death (LoVecchio & Zacur, 2011; McFarland, 2008). Higher incidence rates, changing epidemiology, the emerging hypervirulent strain and apparent decreased efficacy of current treatment options have piqued much interest into the cause and transmission of *C. difficile* as well as renewed interest in the pursuit of new treatments for this disease.

**Incidence of C. difficile**

The rates of *C. difficile* have been climbing in the last 15 years with a dramatic rise in mortality. The CDC reports an eight-fold increase in the number of deaths due to *C. difficile* from 1999 to 2006 (Xu, Kochanek, Murphy & Tejada-Vera, 2010). In 2006, *C. difficile* was added to the rankable causes of death and is listed as one of the 20 leading causes of death for the
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elderly accounting for nearly 92% of all deaths from C. difficile (Xu, Kochanek, Murphy & Tejada-Vera, 2010). This is in part due to the changing epidemiology of C. difficile infection.

Historically, the populations at greatest risk for contracting C. difficile have been those with traditional risk factors which include: previous antibiotic exposure, advanced age, co-morbid conditions, feeding tubes, immune suppression/compromise, previous episode of C. difficile infection, mucosal damage from chemotherapy or radiation, and hospitalizations (LoVecchio & Zacur, 2011; Freeman, et al., 2010; Noren, 2010). However, there have been increasing reports of C. difficile in atypical populations. Multiple reports have described a growing number of C. difficile infections emerging in the community in persons without the classic risk factors, including recent exposure to antibiotics, which have been implicated in the acquisition of this infection in children, peripartum women and young adults (Khanna, Pardi, Aronson, Kammer & Baddour, 2012; Kuntz, Chrischilles, Pendergast, Herwaldt & Polgreen, 2011; McFarland, 2008). It has been postulated that shorter inpatient lengths of stay have led to community identification of nosocomial infections (Prabaker & Weinstein, 2011).

Hypervirulent Strain

Complicating the epidemiology of this disease is the emergence of a hypervirulent strain of C. difficile, B1/NAP1/027 (McFarland, 2008). This hypervirulent strain has been implicated in multiple epidemic outbreaks in Canada and the United States since 1999. The B1/NAP1/027 strain can produce 16 times more toxin A and 23 time more toxin B than non-epidemic strains, is resistant to fluoroquinolones, and has higher morbidity and mortality rates than non-epidemic strains (LoVecchio & Zacur, 2012; McFarland, 2008; Warny, et al., 2005). To date, this
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A hypervirulent strain of C. difficile has been identified in 40 states in the U.S. as well as epidemic outbreaks in countries globally (Freeman, et al., 2010; Gerding, 2010).

Risk Factors

Exposure to high risk antibiotics remains the primary risk factor for C. difficile acquisition. Historically, the antibiotic most strongly implicated in the induction of C. difficile infection was clindamycin (Freeman, et al., 2010). However, more recently many other antibiotics have come into favor as the cause for C. difficile as the use or misuse of these medications continues to rise. All antibiotics have the potential to interrupt the normal flora of the bowel thereby altering the effectiveness of competitive exclusion and increasing the susceptibility of patients to C. difficile contraction (LoVecchio & Zacur, 2012; McFarland, 2008). Preservation of the normal flora, mainly comprised of the Clostridium and Bacteroides groups as well as Lactobacillus, and Bifidobacterium is important to maintain competitive exclusion (Noren, 2010). The fluoroquinolones specifically have been attributed to the increasing rates of C. difficile (Freeman, et al., 2010; McFarland, 2008; Noren, 2010).

In addition to antibiotic exposure, several other risk factors have been identified including age (>65), compromised immune system and comorbid conditions (Freeman, et al., 2010; LoVecchio & Zacur, 2012; McFarland, 2008). The number of hospitalizations and lengths of stay have also been identified as contributing risk factors (Freeman, et al, 2010; McFarland, 2008). More recently new sources of susceptibility for C. difficile have been described including animals and food, the use of feeding tubes, and the use of proton pump inhibitors, the latter of
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which remains highly controversial (Freeman, et al, 2010; Gerding, 2010; LoVecchio & Zacur, 2012; McFarland, 2008; Noren, 2010).

Current Standards of Treatment

LoVecchio & Zacur (2011) describe the properties that pharmacologic therapy for C. difficile should possess including: oral administration ability, high activity levels in the colon, low systemic absorption and preservation of normal flora in the colon. Current guidelines call for discontinuing the offending agent and instituting antimicrobial therapy with oral Metronidazole or Vancomycin (Cohen, et al., 2010). These are the only two drugs recommended for therapy but Metronidazole has high systemic absorption with low fecal concentration whereas Vancomycin has poor systemic absorption and high levels of fecal concentration (Cohen, et al., 2010).

According to the Infectious Diseases Society of America (IDSA) guidelines, Metronidazole is the first line treatment for mild-moderate disease but is not approved by the Food and Drug Administration (FDA) for use in C. difficile and its efficacy appears to be declining (Cohen, et al., 2010; McFarland, 2008; Miller, 2010). Interestingly, Metronidazole has also been given a specific black box warning stating “Unnecessary use of the drug should be avoided. Its use should be reserved only for conditions for which it is approved” (FDA, 2010). For first recurrence of infection, repeating treatment with the initial choice of drug is recommended. However, if Metronidazole fails, is poorly tolerated, or contraindicated, second line treatment is Vancomycin (Cohen, et al., 2010). Repeated recurrences call for use of Vancomycin only in tapered or pulse dosing as Metronidazole has the “potential for cumulative neurotoxicity”
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(Cohen, et al., 2010, p. 433). However, even with Vancomycin high rates of failure and recurrence have been described which may be, in part, due to colonization with VRE and the emergence of B1/NAP1/027 (Choi, et al., 2011; LoVecchio & Zacur, 2012; Prabaker & Weinstein, 2011; Tannock, et al., 2010).

Metronidazole is more cost-effective but has a higher systemic absorption than Vancomycin which may be the reason for treatment failures with this therapy. Others have suggested that *C. difficile* has become resistant to therapy with Metronidazole (Freeman, et al., 2010; McFarland, 2008; Miller, 2010). However, recurrence rates ranging from 5-47% have been described with current treatment options (Choi, et al., 2011; LoVecchio & Zacur, 2012; McFarland, 2008). Current standards of treatment have come into question due to the high rates of treatment failure and recurrence.

The rates of recurrence and treatment failures, increasing morbidity and mortality, systemic absorption, few treatment options and emergence of the hyper virulent strain have raised concern regarding the current treatment options. Optimer Pharmaceuticals has recently received FDA approval for Fidaxomicin, a narrow spectrum macroligyclic antibiotic, for the treatment of mild to moderate *C. difficile* infections and is the first drug to be approved for use in *C. difficile* in 25 years (Peterson, 2011). The aim of this study is to review the available evidence to determine whether fidaxomicin for the treatment of mild to moderate *clostridium difficile* infection improves cure rates and decreases the episodes of recurrence as compared to vancomycin.

**Fidaxomicin Versus Current Standard of Treatment**
Minimum inhibitory concentrations (MIC) are crucial in determining the efficacy of a medication. A low MIC indicates the lowest concentration of a drug that will inhibit the growth of the bacteria in question. In the case of *C. difficile* infection, the MIC against both *C. difficile* and the normal bacterial flora become important to understand as preservation of the normal flora is an important component of efficacious treatment.

In 2004, two quasi-experimental studies were published assessing the in vitro activity of Fidaxomicin (formerly known as OPT-80) against several hundred anaerobic intestinal bacteria. MICs were measured in both of these studies and compared to multiple other antibacterial agents including Vancomycin and Metronidazole. Table 1 summarizes the findings of Fidaxomicin, Vancomycin, and Metronidazole against *C. difficile*, all *clostridium* species, *bacteroides fragilis*, *lactobacillus* and *bifidobacteria*. Both studies showed good activity for Fidaxomicin, Vancomycin, and Metronidazole against *Clostridium* species but with varying MIC ranges between studies (Credito & Appelbaum, 2004; Finegold, et al., 2004). Superior activity of Fidaxomicin against *C. difficile* was shown in both studies. Credito & Appelbaum (2004) found that Fidaxomicin had superior activity against *C. difficile* and all *clostridium* species versus Vancomycin and Metronidazole, was equivalently active against *lactobacillus*, *bifidobacteria*, and had less activity against *bacteroides fragilis* than the two current recommended medications. This would presumably result in higher preservation of normal gut flora in vivo.

In contrast, Finegold, et al. (2004) found that Fidaxomicin was only superior to Vancomycin in certain *clostridium* species, specifically *clostridial* clusters I and XI (including *C.*
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difficile), had more activity against lactobacillus and bifidobacteria than Metronidazole but not Vancomycin, and markedly less activity against the bacteroides group and clostridial clusters XIVa, XI, and XIII than either Vancomycin or Metronidazole. Of note is the variation in the MICs reported between studies. Finegold, et al. (2004) used a Wadsworth agar dilution technique whereas Credito & Appelbaum (2004) used a Brucella agar with sheep blood. This difference in technique may account for the variation in MIC results. However, the results of both studies support the narrow-spectrum activity of Fidaxomicin which is a desirable trait for antimicrobial therapy for C. difficile.

The in vivo efficacy of Fidaxomicin was evaluated in two small open-label Phase 2A randomized dose-finding trials in which authors tested fecal samples of patients for spared normal bacterial flora after treatment with Fidaxomicin versus Vancomycin. The return of normal flora, specifically clostridial clusters XIVa and IV, increased during and after treatment with Fidaxomicin but was not statistically significant (p>0.05), whereas Vancomycin reduced the population of these clusters as well as bifidobacteria with statistical significance (p<0.05) (Tannock et al., 2010). This study also reported a statistically significant increase in lactobacilli and enterococci in the Vancomycin treatment group (p<0.05) which was “coincident with the decrease in proportions of clostridial clusters and bifidobacteria” (Tannock, et al., 2010, p. 3357). In another study, Fidaxomicin was reported to suppress C. difficile (no p-value given) and lower recurrence (p=0.03) when compared to Vancomycin with no alteration in bacteroides (p=0.11-0.56) (Louie, et al., 2009). While the latter outcome was not statistically significant, in the Vancomycin treatment group alteration in bacteroides was significant (p=0.03) (Louie, et al., 2009).
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In an additional Phase 2, dose-finding, randomized, open-label study by Louie, et al. (2009), plasma and fecal levels of Fidaxomicin were measured to assess systemic absorption and colonic retention of the drug. Plasma levels were found to be less than 20ng/ml in all subjects receiving the 200mg twice daily dosing and a high fecal concentration of 1433 ± 975 μg/ml (Louie, et al., 2009). These results were supported in their Phase 3 clinical trial which showed mean plasma concentrations of 22.8 ± 26.5 ng/ml and mean fecal concentrations of 1225 ± 759.0 μg/g (Louie, et al., 2011). These studies did not compare Fidaxomicin levels against Vancomycin levels. While no statistical significance was reported, this is clinically significant as effective treatment for C. difficile must have low systemic absorption and high fecal concentrations to be effective.

Clinical cure and recurrence

Clinical efficacy of Fidaxomicin versus Vancomycin was reported in three studies, two large randomized control trials and a systematic review. Initial clinical cure, recurrence and global cure were reported in both trials. Global cure was not reported in the systematic review. The studies are summarized in Table 2 with demographics and interventions outlined in Table 3.

Clinical cure.

Clinical cure was defined by the authors as resolution of diarrhea which is maintained until 2 days after treatment completion (Louie, et al., 2011; Mullane, et al., 2011). Fidaxomicin clinical cure rates were found to be non-inferior to Vancomycin in all three studies. Drekonja, et al. (2011) reported no significant difference between Fidaxomicin and Vancomycin, giving no p-value. When given with a concomitant antibiotic, Fidaxomicin was found to have higher clinical
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cure than Vancomycin (p=0.04) but the clinical cure rate in the presence of high-risk concomitant antibiotics did not reveal a statistical significance (p=0.09) (Mullane, et al., 2011). One study reported clinical cure rates in Fidaxomicin for the modified intention to treat (mITT) and per protocol (PP) groups as non-inferior to Vancomycin “with a lower boundary of the 97.5% CI for the difference in cure rates of -3.1...[and] -2.6 percentage points” respectively (Louie et al., 2011).

Recurrence.

Recurrence rates were reported by all three studies. Clinical recurrence was defined in the randomized control trials as the reappearance of symptoms (more than three unformed stools per day) within 4 weeks after completion of therapy, C. difficile toxin A or B, or both in stool, and treatment requirement for infection (Louie, et al., 2011; Mullane, et al., 2011). Louie, et al. (2011) reports statistically significant lower recurrence rates with Fidaxomicin in both the mITT group (p=0.005) and the PP group (p=0.004). This study did show similar rates of recurrence between Fidaxomicin and Vancomycin on the B1/NAP1/027 hyper virulent strain which was not statistically significant (p=0.93) (Louie, et al., 2011). Administration of Fidaxomicin with concomitant antibiotics, was found to have increased recurrence rates but it did not reach statistical significance (p=0.48) and in conjunction with high risk antibiotics the difference in rate of recurrence between Fidaxomicin and Vancomycin was not statistically significant (p=0.54) (Mullane, et al., 2011). In a systematic review, Drekonja, et al. (2011) found that the overall recurrence rate for Fidaxomicin was lower than Vancomycin (p=0.005).

Global Cure.
Global cure is defined as “clinical cure with no recurrence” (Mullane, et al, 2011). Two studies reported results for global cure. Louie, et al. (2011) reports a statistically significant global cure rate for Fidaxomicin in both the mITT and PP groups with p=0.006 for both groups. In a study evaluating cure rates with concomitant antibiotic use, global cure rate was statistically significant (p=0.02) except when adjunctive high risk antibiotics were used (p=0.18) (Mullane, et al., 2011).

Strengths/Limitations

The studies conducted by Louie, et al. (2011) and Mullane, et al. (2011) were both double-blind randomized control trials. This approach has strong rigor, lends itself to generalizability and has strong external validity due to the “natural” setting. The remaining studies were quasi-experimental with quite small samples sizes which weakens the generalizability and external validity of these studies. Additionally, no study reported power analysis or effect size which further weakens their external validity. The results of these studies must be interpreted with caution. Bias is a major concern with each of the studies evaluated as it was either funded by Optimer pharmaceuticals, the manufacturer of Fidaxomicin, or written by an investigator employed by said manufacturer. The systematic review provides the strongest form of evidence and lessens the bias that may be present in the other studies.

Discussion

Fidaxomicin is the first antibiotic to be approved by the FDA for treatment of C. difficile in 20 years. It has good in vitro and in vivo efficacy, has been shown to be non-inferior to Vanco in clinical trials, in both epidemic and non-epidemic strains, and appears to significantly
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decrease the rate of recurrent infection. Additionally, it meets the criteria for effective
treatment of C. difficile: It is given orally, has low systemic absorption, high fecal concentrations
and preserves the normal bacterial flora of the bowel, which the current treatments do not.

Fidaxomicin appears to be a reasonable alternative therapy for recurrent C. difficile but
not for initial treatment. As the only randomized control studies that have been published were
conducted by Optimer Pharmaceuticals, bias is a concern. Large, independent trials are
warranted to provide a clearer picture of its overall efficacy against C. difficile and superiority in
treatment versus Vancomycin.

Additionally, pharmacoeconomics cannot be disregarded when choosing therapy. In a
review of this new drug, Grant (2011) reports wholesale pricing of Fidaxomicin much higher
than Vancomycin for a 10-day course of treatment ($2,800 versus $1,061 respectively). Retail
pricing shows Fidaxomicin is $3,260.19 for a 10-day course as opposed to Vanco which is $1,365
and Metronidazole is markedly less expensive than either of these drugs at $27 for a 10-day
course (N. Bidinger, personal communication, April 2, 2011). It may be reasonable to offset the
concern of cost with decreased recurrence rates in those patients who experience recurrent
infection. However, this will prohibit many providers from prescribing and will not be covered
under health insurance plans requiring, at minimum, a pre-authorization for coverage.

For health care providers, prudent prescription of antimicrobial agents is of utmost
importance in preventing the contraction of C. difficile. If a high-risk antimicrobial must be used,
such as Clindamycin or a fluoroquinolone, signs and symptoms of C. difficile should be included
in the counseling of patient, such as more than three watery stools a day, abdominal cramping,
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fever, nausea, and dehydration so the offending agent can be discontinued and treatment for the infection can be instituted early (Mayo Clinic, 2010).

Polymerase chain reaction (PCR) testing is generally used to assess the presence of *C. difficile* in stool. This test is rapid, with high sensitivity and specificity (Cohen, et al., 2010). However, current guidelines report that more data is still needed on PCR testing before an official recommendation will be issued for use of PCR (Cohen, et al., 2010). Rather, guidelines state that identification of the infection should be obtained using an enzyme immunoassay test (EIA) to screen followed by a toxinogenic culture for confirmation (Cohen, et al., 2010). The IDSA guidelines support this method as an “interim recommendation” pending more data on sensitivity and support stool culture as the gold standard but acknowledge that “stool culture is not clinically practical because of its slow turnaround time” (Cohen, et al., 2010, p.9).

If recurrent *C. difficile* is diagnosed with failed response to current treatment guidelines, Fidaxomicin is a reasonable next line therapy. Patients should be counseled on duration of treatment (10 days of twice daily dosing), side effects of the medication including abdominal pain, nausea and vomiting, anemia, and neutropenia, as well as the more serious side effects of bowel obstruction and gastrointestinal hemorrhage (FDA, 2011). Follow-up should occur after therapy and with any progression of disease symptoms, non-resolution of symptoms, and recurrence of infection.
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Table 1. In vitro activity of Fidaxomicin, Vancomycin and Metronidazole against select bacterial isolates

<table>
<thead>
<tr>
<th>Study</th>
<th>Bacterial group</th>
<th>Antimicrobial agent</th>
<th>MIC$_{50}$</th>
<th>MIC$_{90}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finegold, et al (2004)</td>
<td><em>C. difficile</em></td>
<td>Fidaxomicin</td>
<td>0.12</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole</td>
<td>0.25</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td><em>All clostridium species</em></td>
<td>Fidaxomicin</td>
<td>0.062</td>
<td>128</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole</td>
<td>≤0.5</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>Miscellaneous gram-positive</td>
<td>Fidaxomicin</td>
<td>1</td>
<td>32.0</td>
</tr>
<tr>
<td></td>
<td>non-spore-forming rods</td>
<td>Vancomycin</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><em>Includes lactobacillus and</em></td>
<td>Metronidazole</td>
<td>4.0</td>
<td>&gt;128</td>
</tr>
<tr>
<td></td>
<td><em>bifidobacteria</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Bacteroides fragilis</em></td>
<td>Fidaxomicin</td>
<td>256</td>
<td>1024</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
<td>64</td>
<td>128</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Credito, et al (2004)</td>
<td><em>C. difficile</em></td>
<td>Fidaxomicin</td>
<td>≤0.016</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
<td>0.5</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole</td>
<td>≤0.125</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td><em>All clostridium species</em></td>
<td>Fidaxomicin</td>
<td>≤0.016</td>
<td>0.25</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
<td>0.25</td>
<td>2.0</td>
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<td></td>
<td></td>
<td>Metronidazole</td>
<td>≤0.125</td>
<td>2.0</td>
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<td>Fidaxomicin</td>
<td>0.25</td>
<td>16.0</td>
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<td>16.0</td>
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<td></td>
<td><em>Includes lactobacillus and</em></td>
<td>Metronidazole</td>
<td>2.0</td>
<td>&gt;16.0</td>
</tr>
<tr>
<td></td>
<td><em>bifidobacteria</em></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td><em>Bacteroides fragilis</em></td>
<td>Fidaxomicin</td>
<td>64.0</td>
<td>&gt;128</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vancomycin</td>
<td>&gt;16.0</td>
<td>&gt;16.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Metronidazole</td>
<td>0.25</td>
<td>1.0</td>
</tr>
</tbody>
</table>

MIC$_{50}$ - MIC at which 50% of isolates tested were inhibited
MIC$_{90}$ – MIC at which 90% of isolates tested were inhibited
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Table 2. Efficacy of Fidaxomicin versus Vancomycin in clinical cure rates, recurrence, and global cure rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Clinical cure</th>
<th>Recurrence</th>
<th>Global cure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drekonja, et al (2011)</td>
<td>no significant difference</td>
<td>p=0.005</td>
<td>not reported</td>
</tr>
<tr>
<td>Louie, et al (2009)</td>
<td>mITT group -3.1 percentage points</td>
<td>p=0.005</td>
<td>p=0.006</td>
</tr>
<tr>
<td></td>
<td>PP group -2.6 percentage points</td>
<td>p=0.004</td>
<td>p=0.006</td>
</tr>
<tr>
<td>Mullane, et al (2011)</td>
<td>With any CA antibiotic P=0.04</td>
<td>p=0.048</td>
<td>p=0.02</td>
</tr>
<tr>
<td></td>
<td>With high-risk antibiotic p=0.09</td>
<td>p=0.54</td>
<td>p=0.18</td>
</tr>
</tbody>
</table>

mITT: modified intention to treat group
PP: per protocol group
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Table 3. Demographics and interventions of studies examining the efficacy of Fidaxomicin versus Vancomycin in clinical cure rates, recurrence, and global cure rates

<table>
<thead>
<tr>
<th>Author</th>
<th>Purpose</th>
<th>Sample</th>
<th>Research Design</th>
<th>Measures</th>
<th>Intervention Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drekojna, et al (2011)</td>
<td>To determine whether among adults with C. Diff, treatment with certain antibiotics compared with others results in differences in initial cure, recurrence, and harms</td>
<td>1324 subjects</td>
<td>Systematic Review</td>
<td>Fecal samples</td>
<td>IV: Fidaxomicin Vancomycin Flagyl Other Antibiotics DV: Initial Cure Recurrence</td>
</tr>
<tr>
<td>Mullane, et al (2011)</td>
<td>To study the effects of concomitant antibiotics on response to fidaxomicin and vancomycin</td>
<td>999 subjects 584 female 415 male 393 outpatient 606 inpatient 481 fidaxomicin 518 vancomycin</td>
<td>Double Blind RCT</td>
<td>Fecal samples</td>
<td>IV: Fidaxomicin Vancomycin DV: Clinical cure Recurrence Global cure</td>
</tr>
</tbody>
</table>

mITT: modified intention to treat; PP: pre protocol; IV: independent variable; DV: dependent variable RCT: Randomized control trial
References


FIDAXOMICIN IS A SUPERIOR TREATMENT TO VANCOMYCIN FOR RECURRENT CLOSTRIDIUM DIFFICILE INFECTION


Gerding, D.N. (2010). Global epidemiology of Clostridium difficile infection in 2010. Infection Control and Hospital Epidemiology, 31F(S1), S32-S34.


Tannock, G.W., Munro, K., Taylor, C., Lawley, B., Young, W., Byrne, B.,... & Louie, T. (2010). A new macrocyclic antibiotic, fidaxomicin (OPT-80), causes less alteration to the bowel microbiota of *Clostridium difficile*-infected patients than does Vancomycin. *Microbiology, 156*, 3354-3359. doi: 10.1099/mic0.042010-0

