Combination Therapy for *Clostridium difficile* Infection at an Academic Medical Center

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INTRODUCTION

- *Clostridium difficile* (*C. difficile*): an anaerobic, spore-producing bacillus
- Outbreaks of severe *C. difficile* infections (CDI) were seen in North America and parts of Europe in early 2000s, and were accompanied by high mortality rates
  - Outbreaks correlated with the spread of a hypervirulent strain known as B1/NAP1/027
  - B1/NAP1/027 strain has mutations that allow for increased production of toxins A and B
- Current guidelines for treatment of initial CDI recommend metronidazole for mild-moderate infection, oral vancomycin for severe initial infections, and oral vancomycin with or without intravenous (IV) metronidazole for severe, complicated infection
- Recommendations for combination therapy are currently based on limited data and expert opinion and do not address the influence of the B1/NAP1/027 hypervirulent strains

SPECIFIC AIMS

- Determine significant factors associated with the use of combination oral vancomycin and metronidazole as initial therapy for moderate to severe *C. difficile* associated diarrhea (CDAD)
- Determine the incidence of non-response, recurrence, relapse, and rate of complications of CDI treated with combination of metronidazole and vancomycin versus vancomycin alone over a one-year period by treatment and strain type (i.e., NAP1/B1/027)
- Compare the incidence of 7-day and 30-day all-cause mortality in patients with moderate to severe CDAD disease prescribed vancomycin only or combination metronidazole plus vancomycin as initial therapy

Table 1. Subject Demographics (N = 85)

		Combination Therapy (N = 55)	Vancomycin Only (N = 30)	p-value
Mean (SD)				
Age, years		63 (18)	65 (19)	0.654
Weight, kg		74 (24)	67 (19)	0.157
Number (%)				
Female sex		34 (62)	16 (53)	0.448
Race	**White**	30 (55)	21 (70)	0.206
	White, Hispanic	18 (33)	8 (27)	
	Black	4 (7)	0 (0)	
Admitted to ICU on Day 0		20 (36)	11 (36)	-
Median (Range)				
Total Length of Stay, days		12 (3 – 265)	11 (3 – 60)	0.295

Figure 1. CDI Response, Failure, and Recurrence Rates by Treatment Group

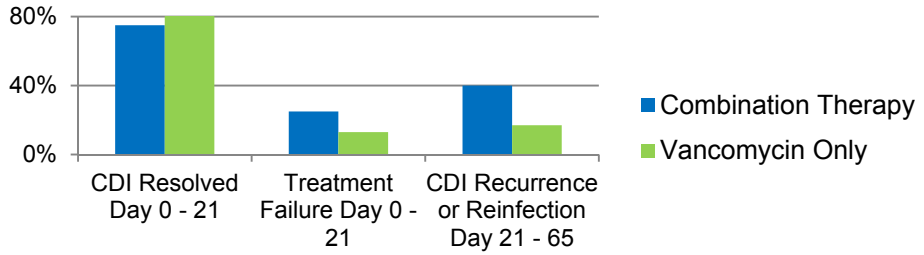

Table 2. CDI Outcomes

	Combination Therapy (N = 55)	Vancomycin Only (N = 30)
Number (%)		
Dehydration on Day 1	18 (33)	4 (13)
Abdominal Surgery	4 (7)	0 (0)
Ileus	3 (5)	1 (3)
Pseudomembranous colitis	6 (11)	1 (3)
Megacolon	1 (2)	0 (0)
7-day All-Cause Mortality	3 (5)	1 (3)
30-day All-Cause Mortality	5 (9)	2 (7)

METHODS

- IRB approved, retrospective electronic medical record review

Inclusion criteria

- Adult patients ≥ 18 years of age
- Admitted to an academic medical center between April 2010 and March 2011
- Treated for CDAD with either oral vancomycin monotherapy or oral vancomycin and metronidazole (IV and/or oral) combination therapy

Exclusion criteria

- Received a combination of metronidazole and oral vancomycin for more than 0% but less than 80% of the first 10 days of therapy
- Received less than 48 hours of prescribed CDAD therapy
- Inpatient for less than 72 hours and discharged alive

DATA ANALYSIS

- Calculated for all treatment groups, based on strain type:
  - Rates of 7-day and 30-day all-cause mortality
  - Rates of incidence of non-response, recurrence, relapse, and rate of complications of CDI
- Continuous data analyzed by calculating means and standard deviations and compared using an independent t-test with the *a priori* α level at 0.05
- Categorical data to be compared using chi-square analysis with the *a-priori* α level at 0.05

CONCLUSION

While not statistically significant, subjects who received a combination of oral vancomycin and metronidazole had higher rates of clinical failure and recurrence than subjects who received vancomycin monotherapy