

Dificid™ (fidaxomicin) 200 mg Tablets

Optimer Pharmaceuticals

April 5, 2011

Anti-Infective Drugs Advisory Committee of the
Food and Drug Administration

Fidaxomicin

For the Treatment of *C. difficile* Infection

Sherwood Gorbach, MD, FIDSA

Chief Scientific Officer

Optimer Pharmaceuticals

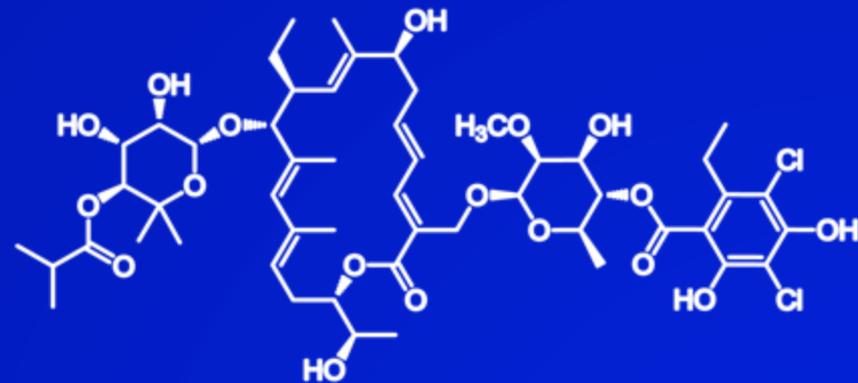
Fidaxomicin

Requested Indication for Adults

- Treatment of *Clostridium difficile* infection (CDI), also known as *Clostridium difficile*-associated diarrhea (CDAD), and for reducing the risk of recurrence when used for treatment of initial CDI

Fidaxomicin – A Safe and Effective Treatment Against *C. difficile* Infection

- Novel antibiotic agent
- First of a new class
 - 18-membered macrocycle
- Narrow spectrum
- Minimally absorbed
- Locally active in GI tract



***C. difficile* Infection and Related Issues**

- *C. difficile* is spore-forming, anaerobic, gram-positive bacillus
- CDI caused by an overgrowth of *C. difficile* in colon
- Overgrowth produces harmful toxins
 - Diarrhea
 - Abdominal pain
 - Pseudomembranous colitis
 - Toxic megacolon
 - Colon perforations
 - Sepsis
 - Death

***C. difficile* Infection is Associated with Antibiotic Use**

- Antibiotics can eradicate beneficial bacteria in gut flora
- *C. difficile* normally resistant to most antibiotics
- Rising incidence of CDI attributed to frequent use of broad-spectrum antibiotics

Recurrence is the Most Important Unmet Need with Current CDI Treatments

- 20-30% Recurrence rate
- Recurrences are serious
 - Hospitalization
 - Death
- Treatment of recurrences is difficult

Phase 3 Studies Demonstrate that Fidaxomicin is Effective and Safe

- Two Phase 3, multi-center, randomized, double-blind, vancomycin controlled clinical studies
- > 1100 subjects
- Positive results for fidaxomicin
 - Non-inferior Clinical Cure rate
 - Significantly superior reduction of Recurrences
 - Significantly superior Global Cure rate
- Well-tolerated
- Safety profile comparable to oral vancomycin

Agenda

The Burden of CDI and the Need for Additional Treatment Options

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Microbiology and Pharmacology

Pamela Sears, PhD

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Efficacy of Fidaxomicin

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Safety of Fidaxomicin in Phase 3 Studies

Michael Corrado, MD, FIDSA

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INC Research

Concluding Remarks

Sherwood Gorbach, MD, FIDSA

The Burden of *C. difficile* Infection and the Need for Additional Treatment Options

Mark A. Miller, MD, FRCPC

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Jewish General Hospital, McGill University

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***C. difficile* Infection in North America**

High Incidence and Variable Severity

- Most common cause of healthcare-associated infectious diarrhea
- Currently 700,000 new cases per year in the U.S.
- Increasing disease incidence
- Spectrum of disease
 - Mild to severe; sometimes fatal
 - Ranges from mild diarrhea to pseudomembranous colitis to overwhelming pan-colitis, perforation and sepsis

Morbidity and Mortality from CDI

- Dehydration and gastrointestinal hemorrhage
- Death rate attributable to CDI
 - Up to 6.9% in outbreaks
 - Up to 15% in frail elderly individuals
- Need for Intensive Care Unit (ICU) in 2-3%
- Emergency bowel surgery and colectomy in 1%
- Incidence of CDI has surpassed MRSA as a complication of health care in the U.S.

***C. difficile* Infection is Moving into the Community**

- Affecting otherwise healthy adults, peripartum women, and children
- No recent history of hospital admission
- No recent antibiotic use

True Cure of *C. difficile* Infection is Elusive

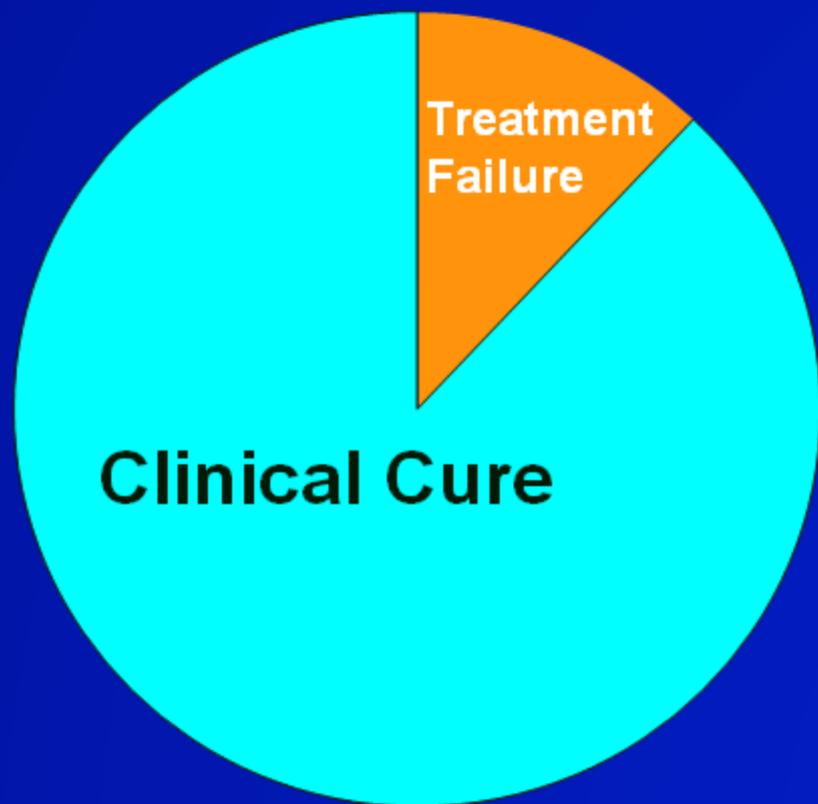
- Cure of CDI is assessed at the end of 10 days of therapy
- However, recurrences may occur, usually within 4 weeks following therapy

Unique Aspect of *C. difficile* Infection

Frequent Recurrences after Treatment

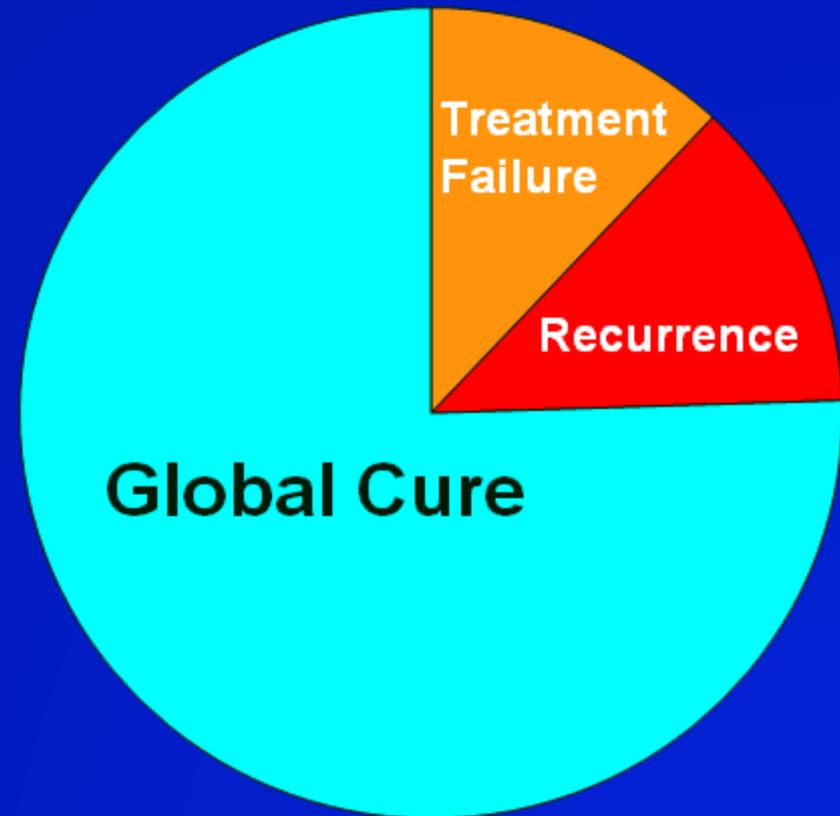
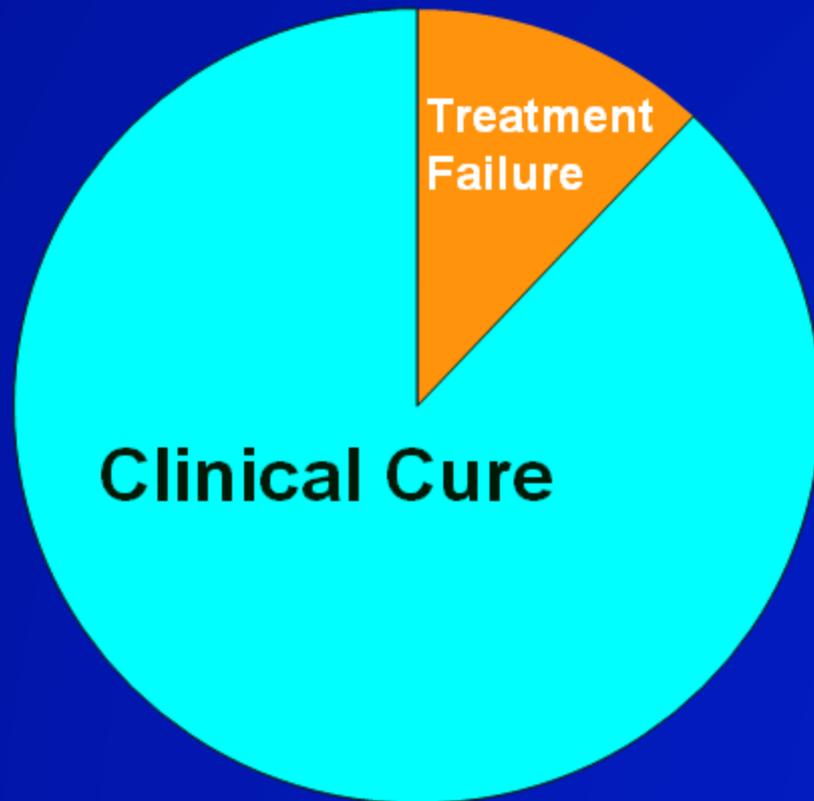
- Re-appearance of the symptoms and signs of CDI after successful treatment
- Overall recurrence rate of 20-30%; higher in the elderly
- After 1 recurrence, likely to get further recurrences

Clinical Cure = Cure at End of Treatment



Global Cure = Clinical Cure – Recurrence

“Global Cure” of CDI is cure at the end of therapy AND no recurrence of disease



Unique Aspect of *C. difficile* Infection

Recurrences May be Serious

- Recurrences may
 - Vary in severity
 - Continue repeatedly for months or years
 - Require hospitalization

Treatment of Recurrences is Variable and Frustrating

- Oral vancomycin
 - Repeated courses
 - Tapering courses
 - “Pulsed” doses
- Various probiotics
- Off-label use of rifaximin
- Intravenous immune globulin (IVIG)
- Fecal transplant

Current Treatment Options are Limited

- Oral vancomycin
 - Only approved treatment for CDI in the U.S.
- Oral metronidazole
 - Off-label use for CDI in the U.S.

Drawbacks of Vancomycin

- Recurrence rate of 20-30%
- Broad spectrum of activity at gut concentrations disrupts normal gut flora
- Dosing usually 4 times daily
- Increases risk of colonization with vancomycin resistant *Enterococcus* (VRE)
- Increases risk of emerging of vancomycin intermediate *Staphylococcus aureus* (VISA)

Drawbacks of Metronidazole

- Lower cure rate in severe CDI, compared to vancomycin
- Broad spectrum activity disrupts normal gut flora
- Fully absorbed orally; numerous adverse effects
- Cannot be used for long duration (for multiple relapses) due to neurotoxicity

Attributes of an Ideal Treatment for *C. difficile* Infection

- Safe and well-tolerated oral therapy
- Convenient treatment regimen
- Non-absorbable, working directly in the gut
- Narrow spectrum, potent, bactericidal activity
- Minimal disruption of normal gut flora
 - Does not promote VRE colonization
- Low potential of resistance development

Attributes of an Ideal Treatment for *C. difficile* Infection (continued)

- Rapid resolution of CDI symptoms
- High and reliable efficacy in the presence of concomitant antibacterials
- High cure rate at end of treatment
- High cure rate for severe CDI
- Low recurrence rate post-treatment

Microbiology and Pharmacology of Fidaxomicin

Pamela Sears, PhD

Executive Director of Biology and Preclinical Science
Optimer Pharmaceuticals

Overview

- Microbiology
 - Mode of Action
 - Spectrum
 - Resistance
- Pharmacology
 - Absorption
 - Fecal concentration
 - Drug-drug interactions

Unique Mechanism of Action

- Inhibition of transcriptional initiation by bacterial RNA polymerase
- Inhibits transcription
 - *C. difficile* enzyme IC₅₀ ~1 μM
- Lack of cross-resistance with other classes of antibacterials
- Distinct from macrolides and rifamycins

Fidaxomicin is a Narrow Spectrum Drug

- High activity against *C. difficile*
 - MIC₉₀ 0.25 µg/mL
- Moderate activity against other Gram positive organisms
 - *Staphylococcus* MIC₉₀ 2 µg/mL
 - *Enterococcus* MIC₉₀ 8 µg/mL
 - Including vancomycin-resistant species
 - Low potential for VRE colonization
- No activity vs. Gram negative bacteria or yeast

Attributes of Fidaxomicin

- Bactericidal effect against *C. difficile*
 - Time dependent
 - Not concentration dependent
- Post Antibiotic Effect (PAE) of ~10 hours
 - Supports twice daily dosing

Resistance Development Expected to be Slow for Fidaxomicin

- Resistance infrequent in the laboratory
 - Frequency of Spontaneous Resistance $< 4 \times 10^{-9}$
 - 14 passages to reach plateau of 2 $\mu\text{g}/\text{mL}$
- Phase 3 studies
 - All subjects had susceptible strains at baseline and end of therapy
 - One subject had isolate at recurrence with MIC value of 16 $\mu\text{g}/\text{mL}$ (reduced susceptibility)

Fidaxomicin

Minimal Absorption

- Predominantly confined to the gut
- Excretion in urine < 1%
- Excreted in the feces > 99%

Low Systemic Exposure after Oral Dosing in Healthy Subjects

Pharmacokinetic Parameters Single 200 mg Dose

	Fidaxomicin N=6	OP-1118 N=6
C_{max} (ng/mL)	9.9 ± 3.96	17.6 ± 4.73
T_{max} (hr)	1.8 (1.0, 8.0)	1.8 (1.0, 8.0)
AUC_{0-t} (ng-hr/mL)	69.5 ± 18.3	136 ± 26.2

Note: T_{max} presented as median and range; all other data presented as mean ± Standard Deviation.

Low Systemic Exposure after Oral Dosing in Subjects with CDI

Fidaxomicin Concentration 3-5 hours	Phase 3 200 mg (ng / mL)	Phase 1 200 mg (ng / mL)	Phase 1 400 mg (ng / mL)
Day 1	N=312	N=6	N=28
Mean (SD)	22.8 (26.7)	5.2 (2.4)	3.6 (2.0)
Range	0.4 – 197	3.0 – 9.7	0.5 – 8.9
Day 10	N=100		
Mean (SD)	28.5 (33.4)	NA	NA
Range	0.3 - 191		

NA = Not Applicable

Fidaxomicin has a Favorable Fecal PK Profile for Treating *C. difficile* Infection

Fecal Concentration at EOT

Fidaxomicin
N=175
($\mu\text{g/g}$)

OP-1118
N=172
($\mu\text{g/g}$)

**Fidaxomicin
Fecal conc./MIC₉₀**
N=175

Mean (SD)

1397 (1019)

834 (617)

5588 (4076)

Range

5.0, 7630

63.4, 4170

20, 30520

Fidaxomicin has no Significant Drug Interactions in Clinical Studies

- CYP450
 - Not significantly metabolized
 - Weak inhibition
- No significant interaction with drugs that are CYP substrates
 - Omeprazole, midazolam, warfarin
- Fidaxomicin is a P-glycoprotein (P-gp) substrate
 - Increased plasma concentrations with cyclosporine (C_{\max} 5.2 → 26.9 ng/mL)
- Fidaxomicin is P-gp inhibitor
 - No meaningful interaction with digoxin

Microbiology and Pharmacology Summary

- Bactericidal activity against *C. difficile*
- Minimal impact on normal gut flora
- Prolonged post-antibiotic effect (PAE)
- Distinct mechanism of action
- No cross resistance
- Minimally absorbed: low plasma concentrations
- Achieves concentrations well above the MIC₉₀ in feces
- No significant drug interactions identified in clinical studies

Efficacy of Fidaxomicin

Sherwood Gorbach, MD, FIDSA

Chief Scientific Officer

Optimer Pharmaceuticals

Clinical Development Program

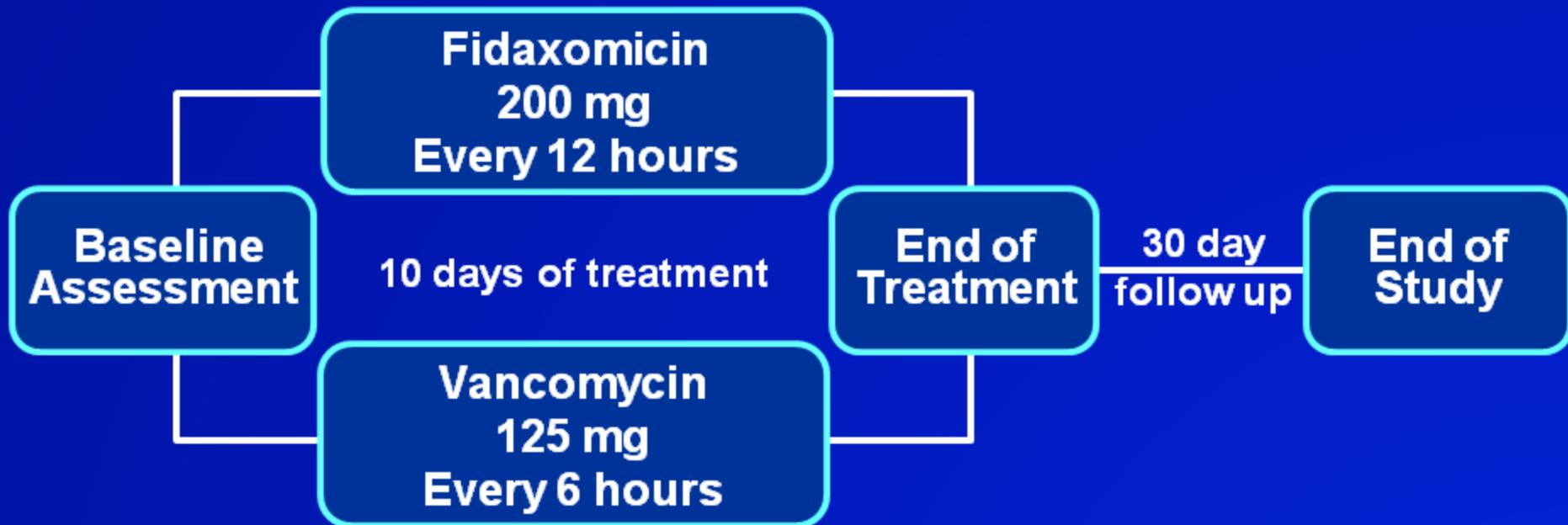
Phase 1 and 2

- Food effect
- Bioavailability
- Drug-drug interaction
- Dose finding

Phase 3

- Study 003
- Study 004

Phase 3, Multicenter, Randomized, Double-blind Studies



Key Inclusion Criteria

- 16 years or older
- Diarrhea
 - > 3 unformed bowel movements in prior 24 hours
- Confirmed diagnosis of CDI
 - Toxin A or B in the stool
- Maximum 24 hours of pre-treatment allowed
 - Vancomycin or metronidazole

Key Exclusion Criteria

- Life expectancy < 72 hours
 - Megacolon, Ileus
- Ulcerative colitis
- Crohn's disease
- Drugs used to treat diarrhea
- Drugs effective in treating CDI
 - e.g., bacitracin, fusidic acid
- No exclusions for laboratory value abnormalities
- Not excluded: cancer, leukemia, renal failure, ICU subjects

Co-Primary Study Population Modified Intent-to-Treat (mITT)

- Confirmed diagnosis of CDI
 - > 3 UBMs in the 24 hours prior to randomization

AND

- Positive toxin assay

AND

- At least one dose of study medication

Co-Primary Study Population Per Protocol (PP)

- Included in the mITT

AND

- Treatment
 - ≥ 3 complete days for failure

OR

- ≥ 8 complete days for cure

AND

- An End of Treatment (EOT) clinical evaluation

AND

- No major protocol violation

Study 003 Population Disposition

Fidaxomicin

Vancomycin

Enrolled and
Randomized
N=629

Randomized
N=306

Randomized
N=323

Toxin not positive, 11
No diarrhea, 4
No study drug, 2

17

16

Toxin not positive, 6
No diarrhea, 6
No study drug, 4

mITT
N=289

mITT
N=307

21

27

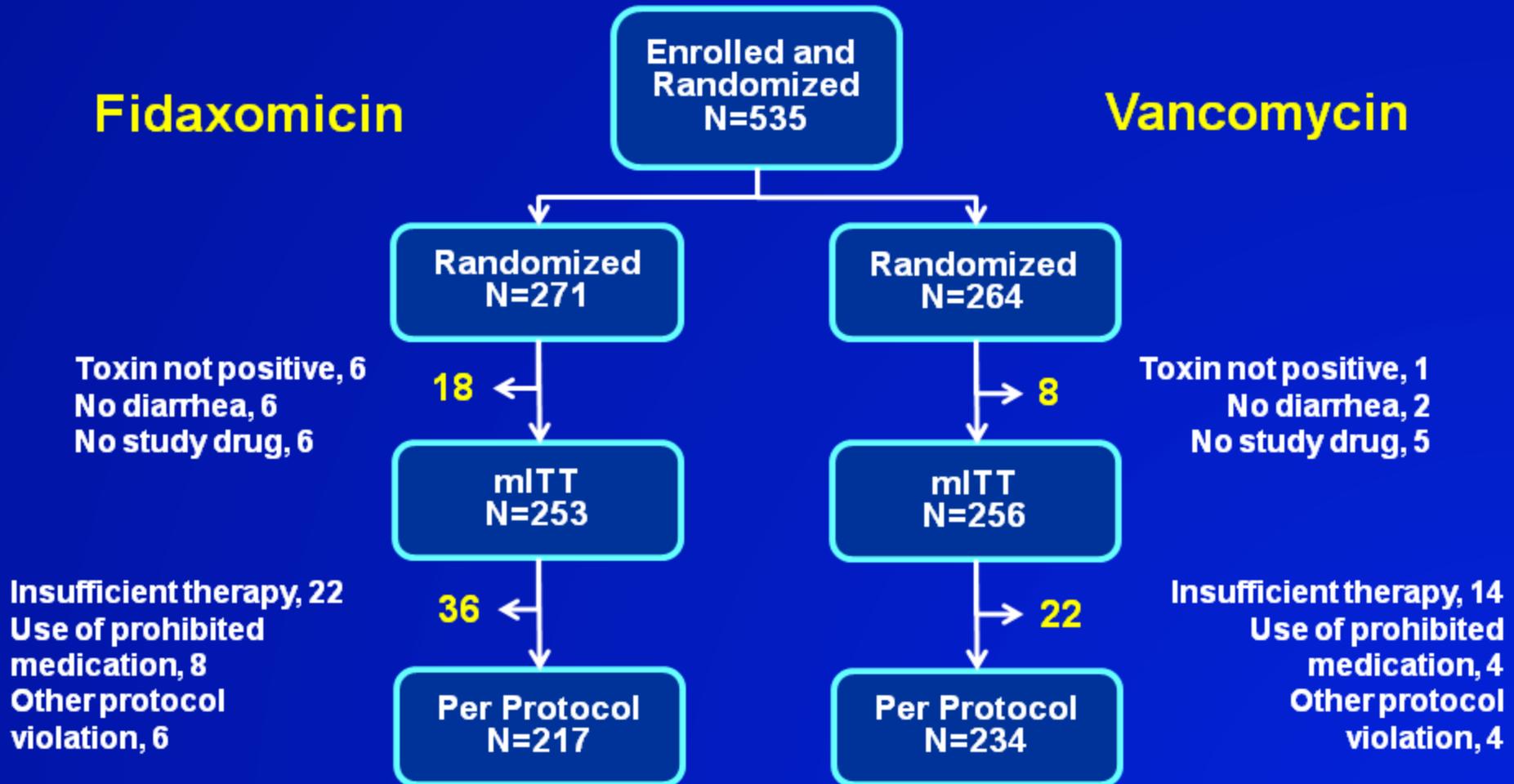
Insufficient therapy, 21
Insufficient evaluation, 1
Use of prohibited
medication, 3
Other protocol
violation, 2

Per Protocol
N=268

Per Protocol
N=280

Insufficient therapy, 17
Insufficient evaluation, 1
Use of prohibited
medication, 1
Other protocol
violation, 2

Study 004 Population Disposition



Primary Endpoint – Clinical Cure

- Unformed Bowel Movements (UBM)
 - ≤ 3 UBMs for two consecutive days

OR

- Marked reduction in the number of UBMs at end of therapy

AND

- No CDI therapy required within two days of completion of study medication

Primary Analysis

Clinical Cure Evaluation

- Co-primary populations
 - Per Protocol
 - mITT
- Analysis
 - Non-inferiority (NI)
 - NI margin of 10% for Clinical Cure rate
- Success requires NI in both populations

Sensitivity Analysis of Clinical Cure

- Sensitivity analysis: only bowel movements
 - ≤ 3 unformed bowel movements for 2 consecutive days
- Non-inferiority analysis

Secondary Endpoint Recurrence

- Re-establishment of diarrhea following Clinical Cure
 - UBM frequency greater than at EOT

AND

- Toxin A or B

AND

- Retreatment with *C. difficile* anti-infective therapy
- Superiority analysis

Exploratory/Secondary Endpoint Global Cure

- Clinical Cure achieved

AND

- No recurrence during 30 day follow-up

- Superiority analysis

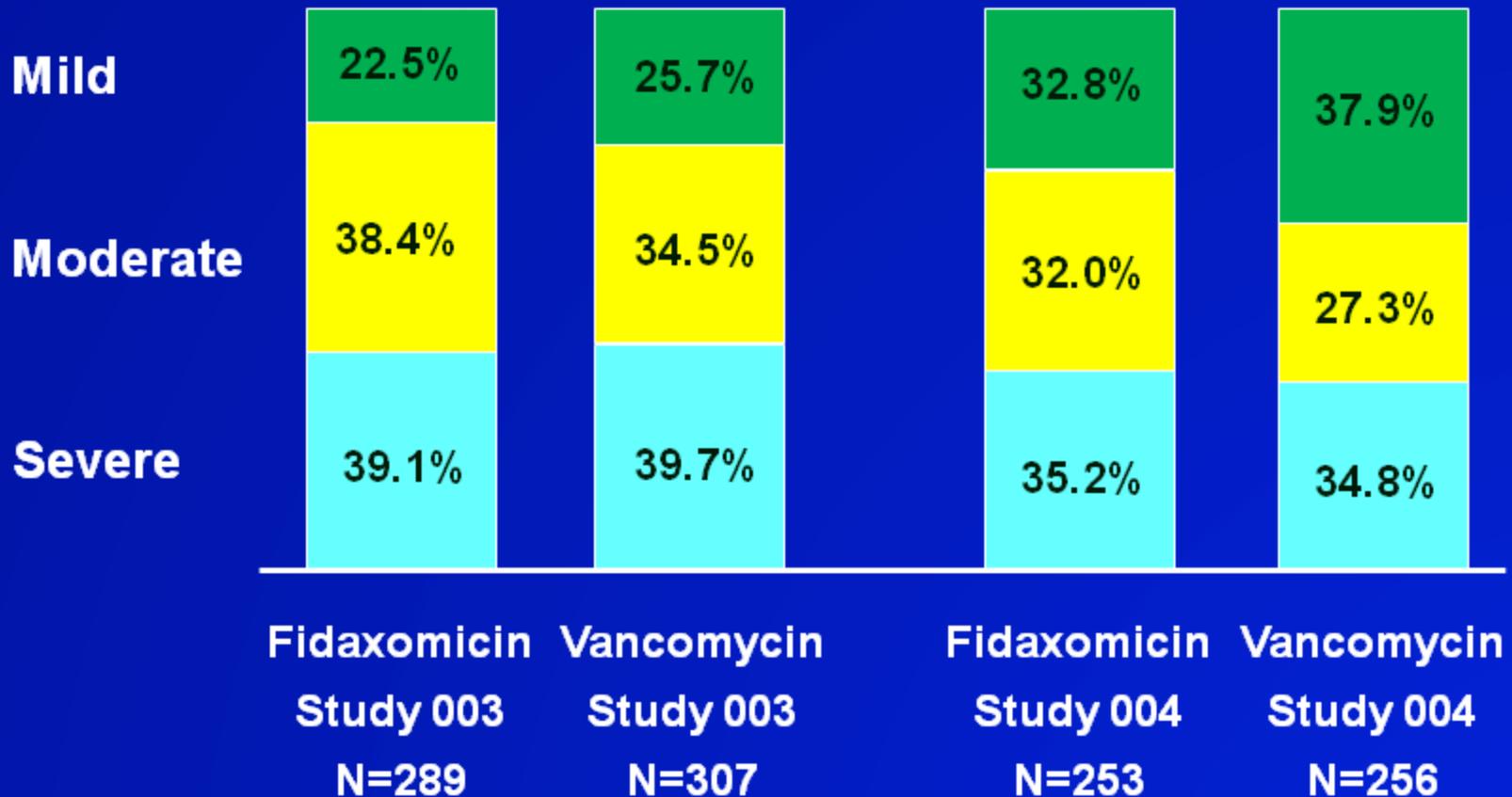
Similar Baseline Demographics (mITT)

	Study 003		Study 004	
	Fidaxomicin N=289	Vancomycin N=307	Fidaxomicin N=253	Vancomycin N=256
Female (%)	56.7	55.0	58.9	62.9
Race (%)				
White	87.9	86.3	92.1	92.6
Black	10.4	10.7	6.7	6.6
Asian	1.4	2.3	0.8	0.4
Other	0.3	0.7	0.4	0.4
Hispanics (%)	4.2	1.6	7.1	7.8
Age (yrs)				
Median	61.0	64.0	67.0	65.0
Range	18, 94	19, 94	18, 94	19, 93

Similar Baseline Characteristics (mITT)

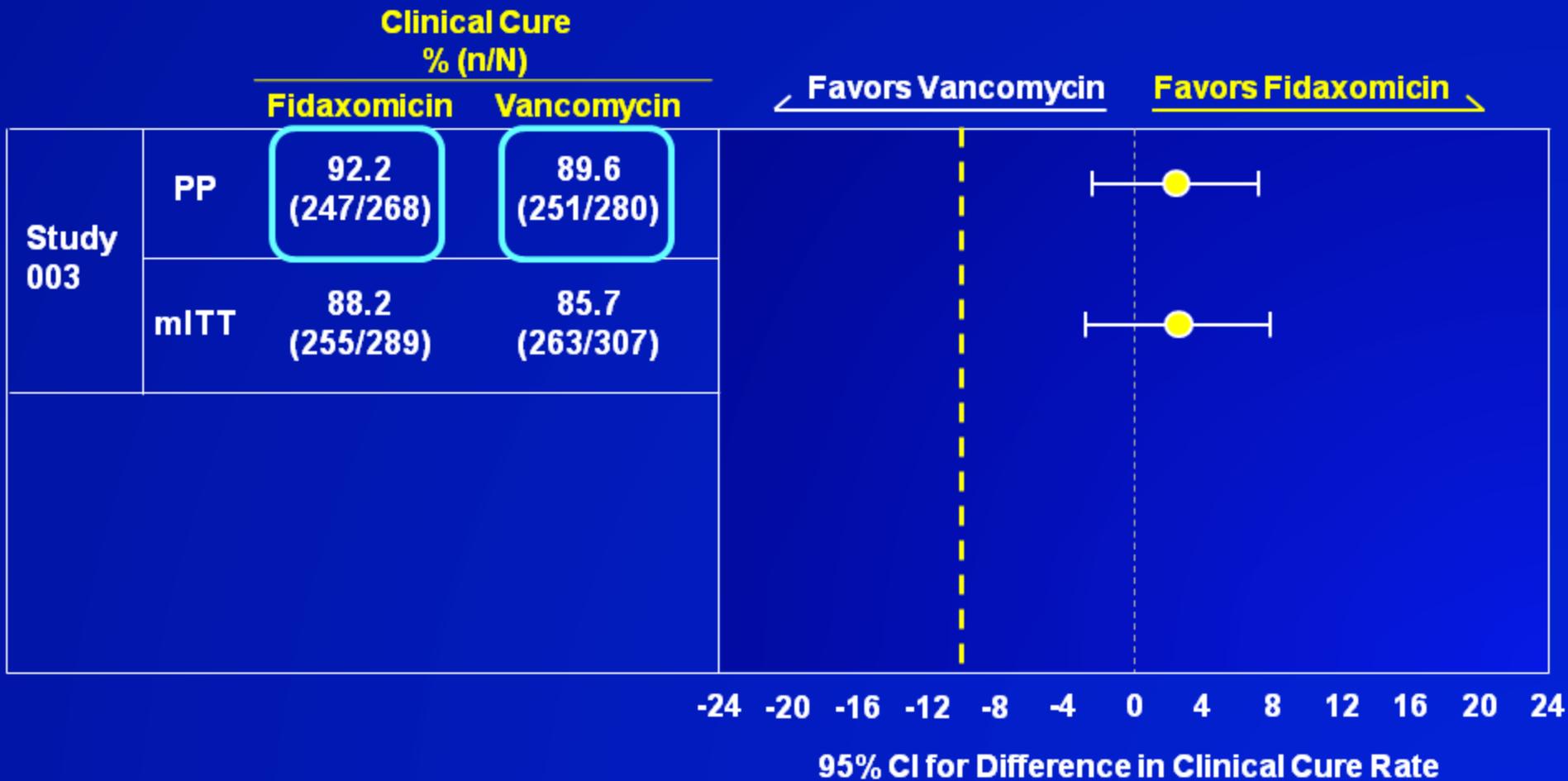
	Study 003		Study 004	
	Fidaxomicin N=289	Vancomycin N=307	Fidaxomicin N=253	Vancomycin N=256
Inpatient (%)	58.1	60.6	69.2	67.2
Prior Episode (%)				
None	83.4	82.4	84.2	85.9
Single	16.6	17.6	15.8	14.1
Daily Unformed Bowel Movements				
Median	7.0	6.0	6.0	6.0
Range	4, 32	4, 50	4, 30	3.3, 30
Prior Use of <i>C. difficile</i> Antibiotics within 24 hours (%)	38.9	39.7	38.7	37.9
BI strain (%)	37.6	38.5	33.2	33.2

Adequate Representation of Subjects with Mild, Moderate and Severe CDI



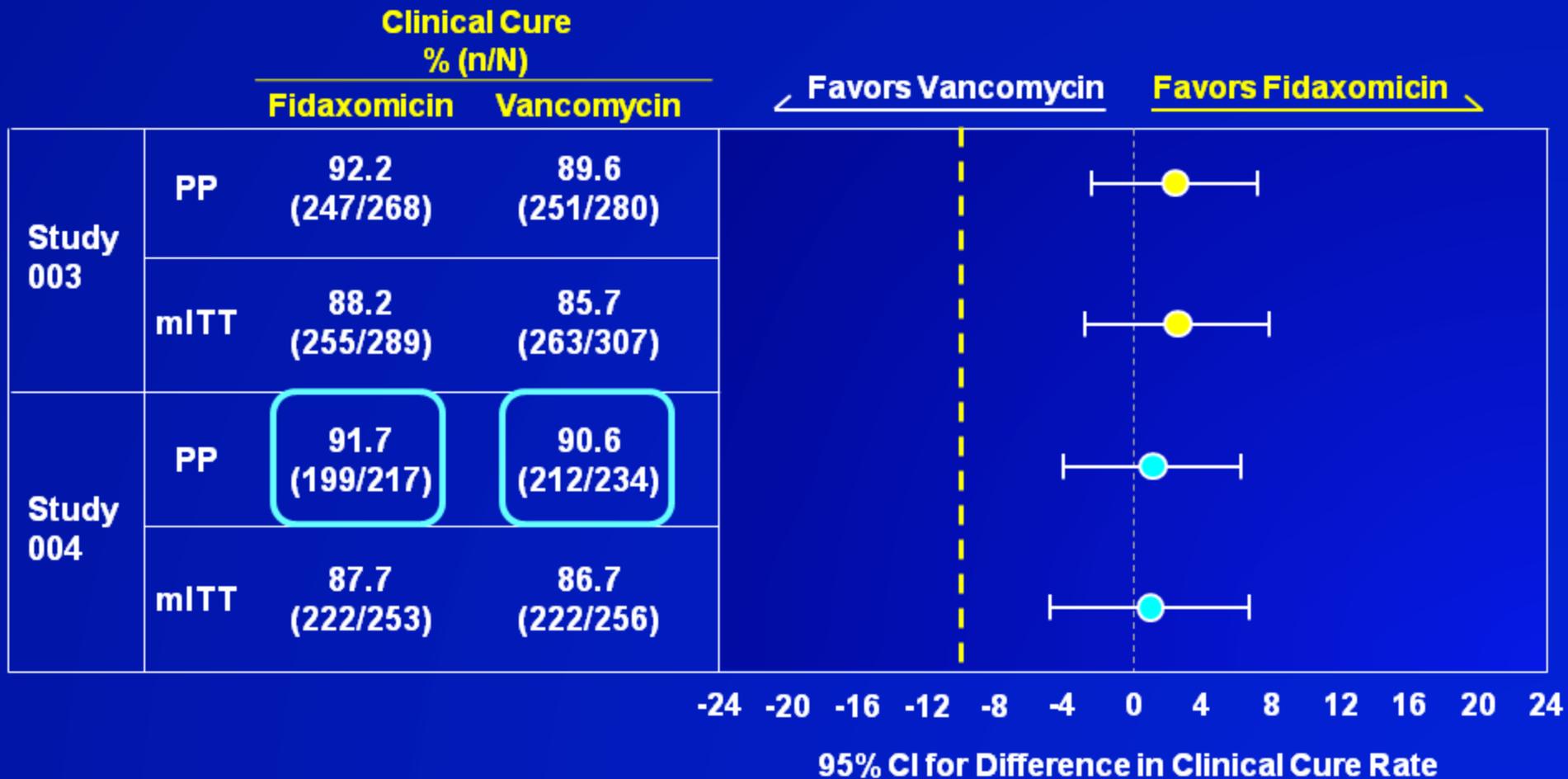
Primary Endpoint – Clinical Cure

Fidaxomicin Non-inferior to Vancomycin



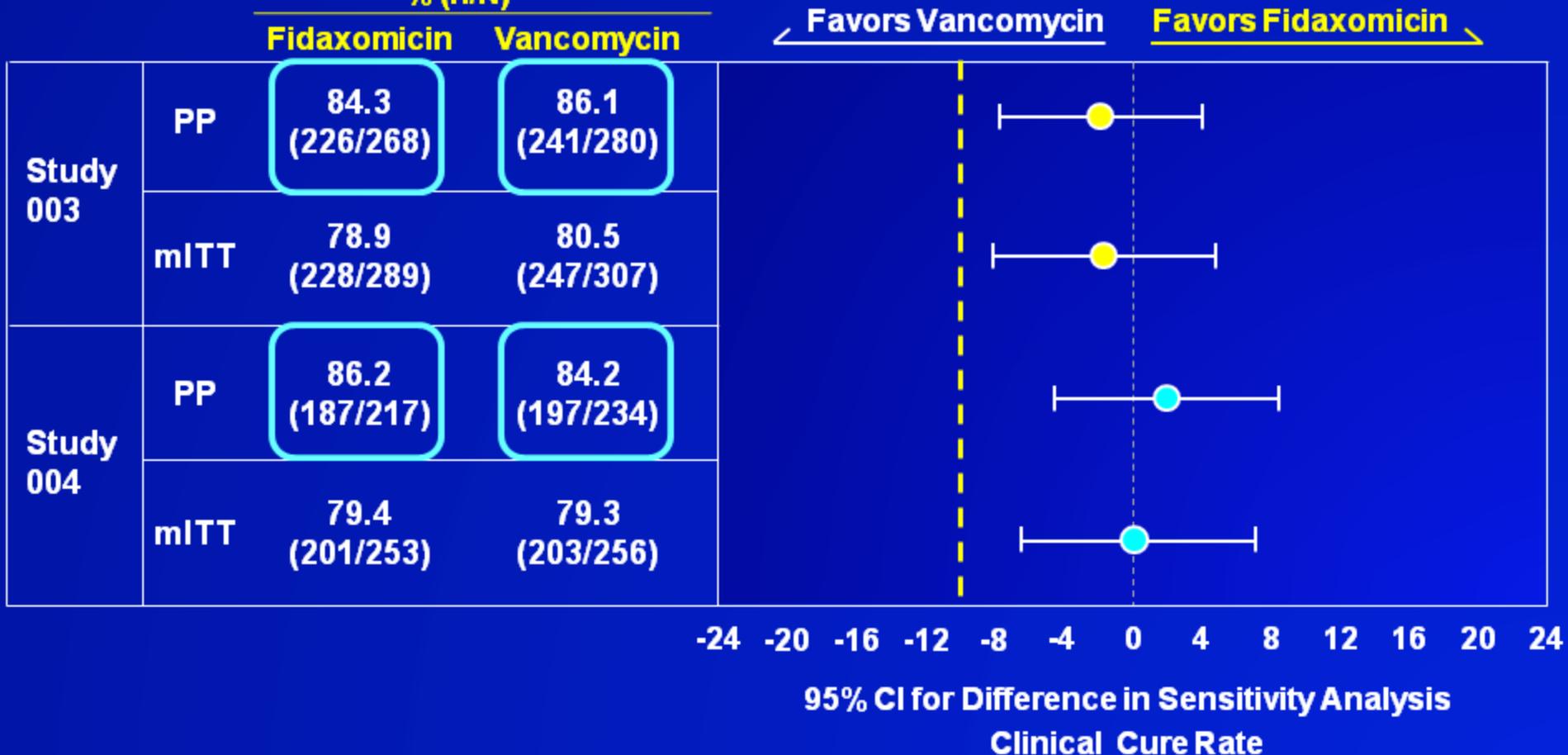
Primary Endpoint Clinical Cure

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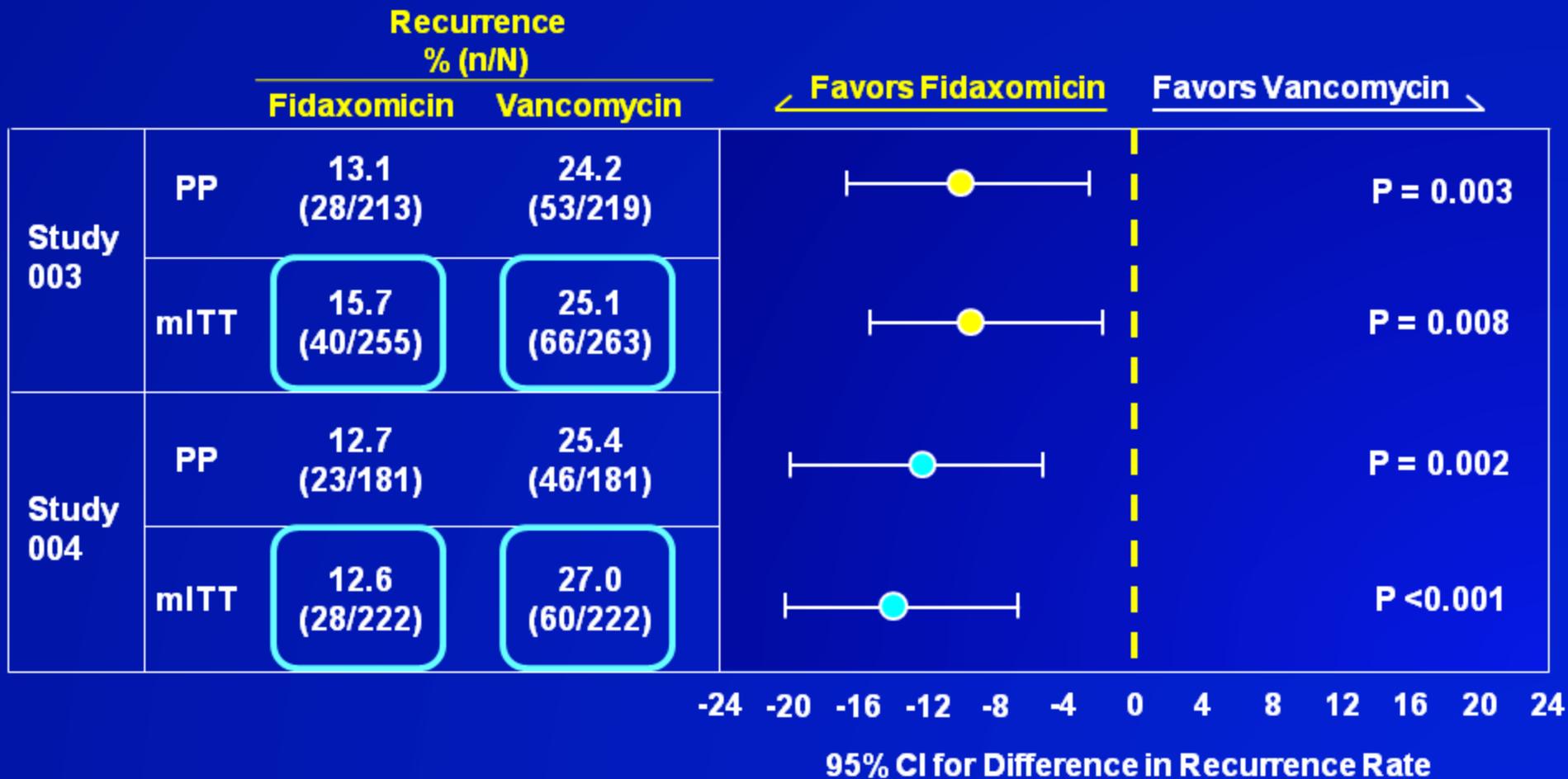
Sensitivity Analysis Clinical Cure Fidaxomicin Non-inferior to Vancomycin

Sensitivity Analysis Clinical Cure
% (n/N)



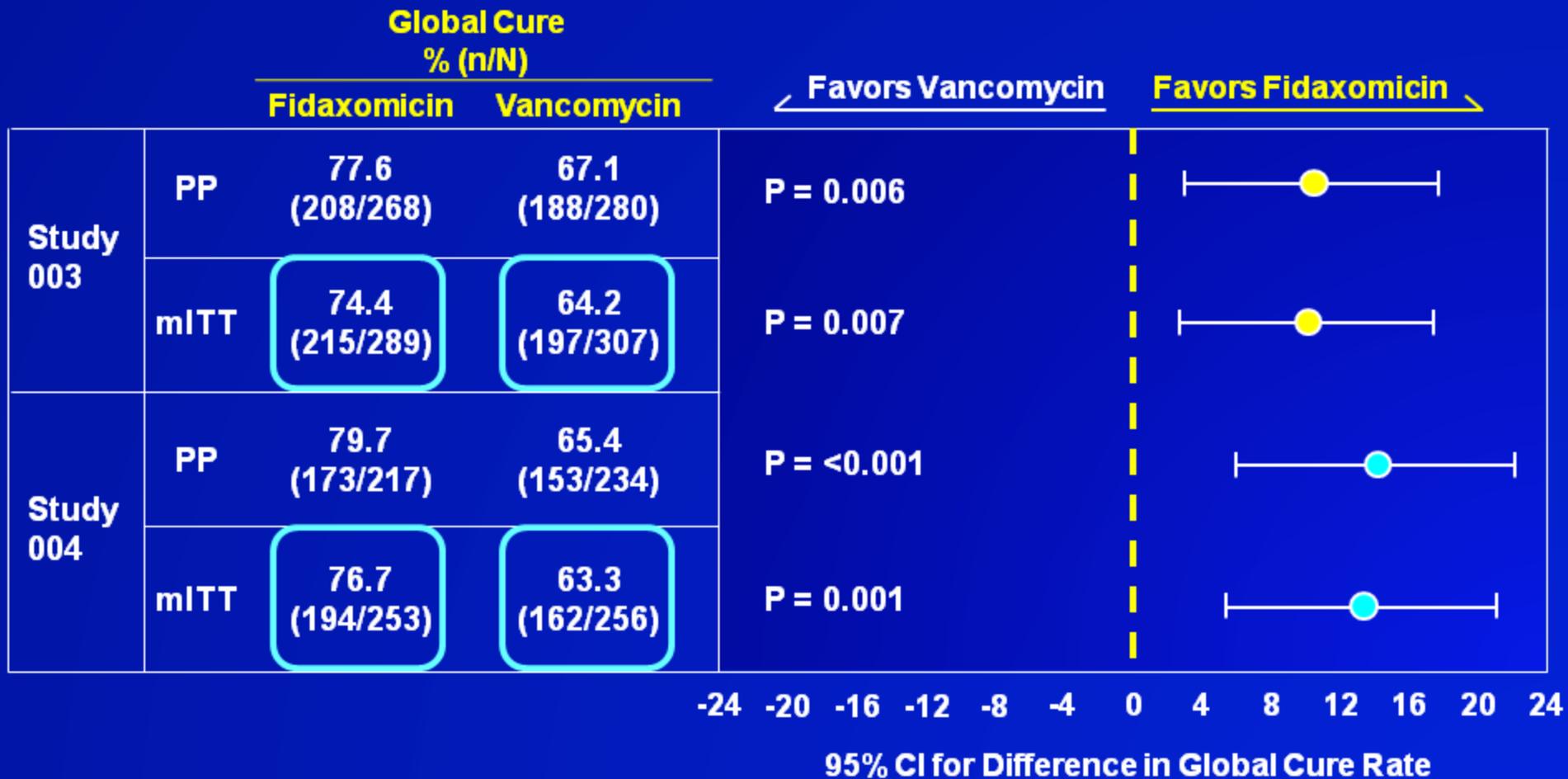
Secondary Endpoint – Recurrence

Fidaxomicin Superior to Vancomycin



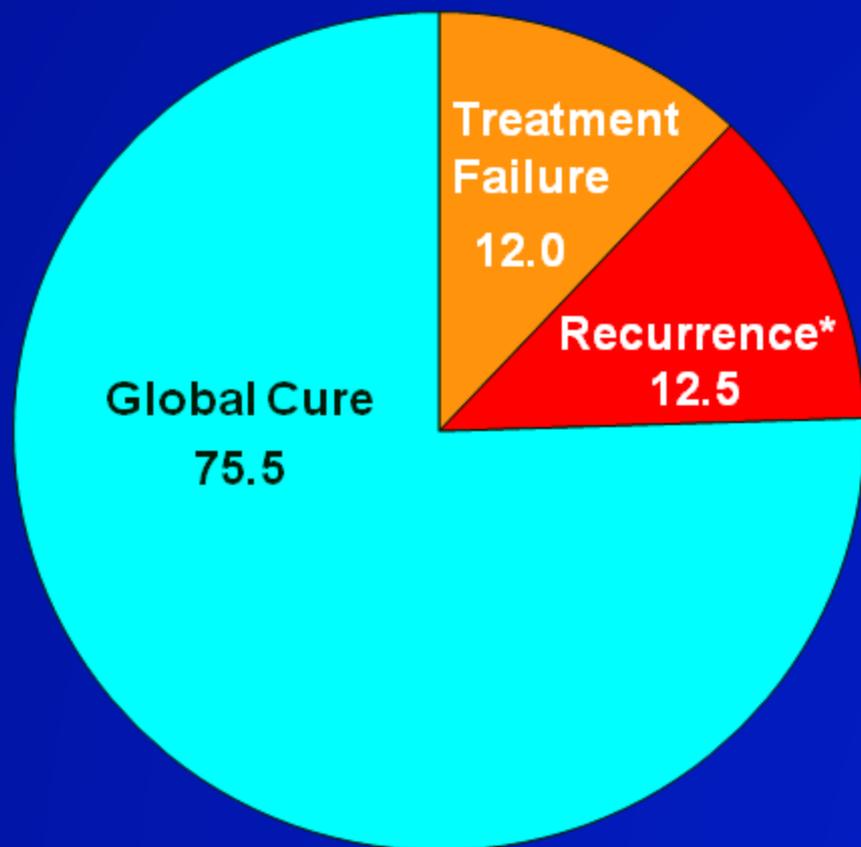
Secondary Endpoint – Global Cure

Fidaxomicin Superior to Vancomycin

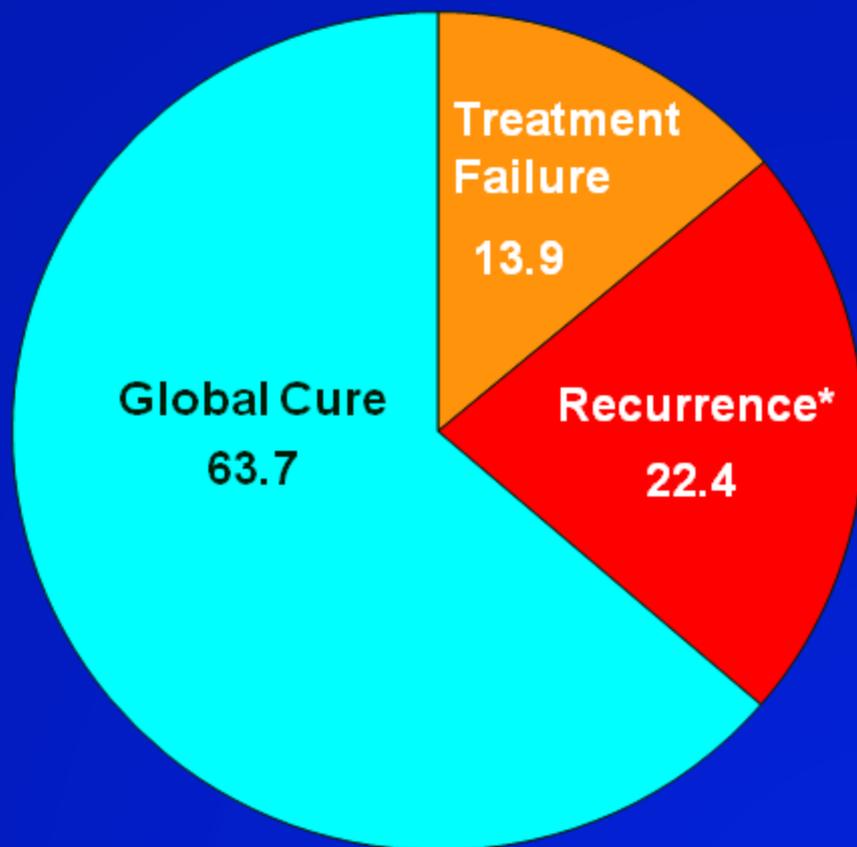


Global Cure Rate is Mainly Driven by Recurrence Rate

Fidaxomicin



Vancomycin

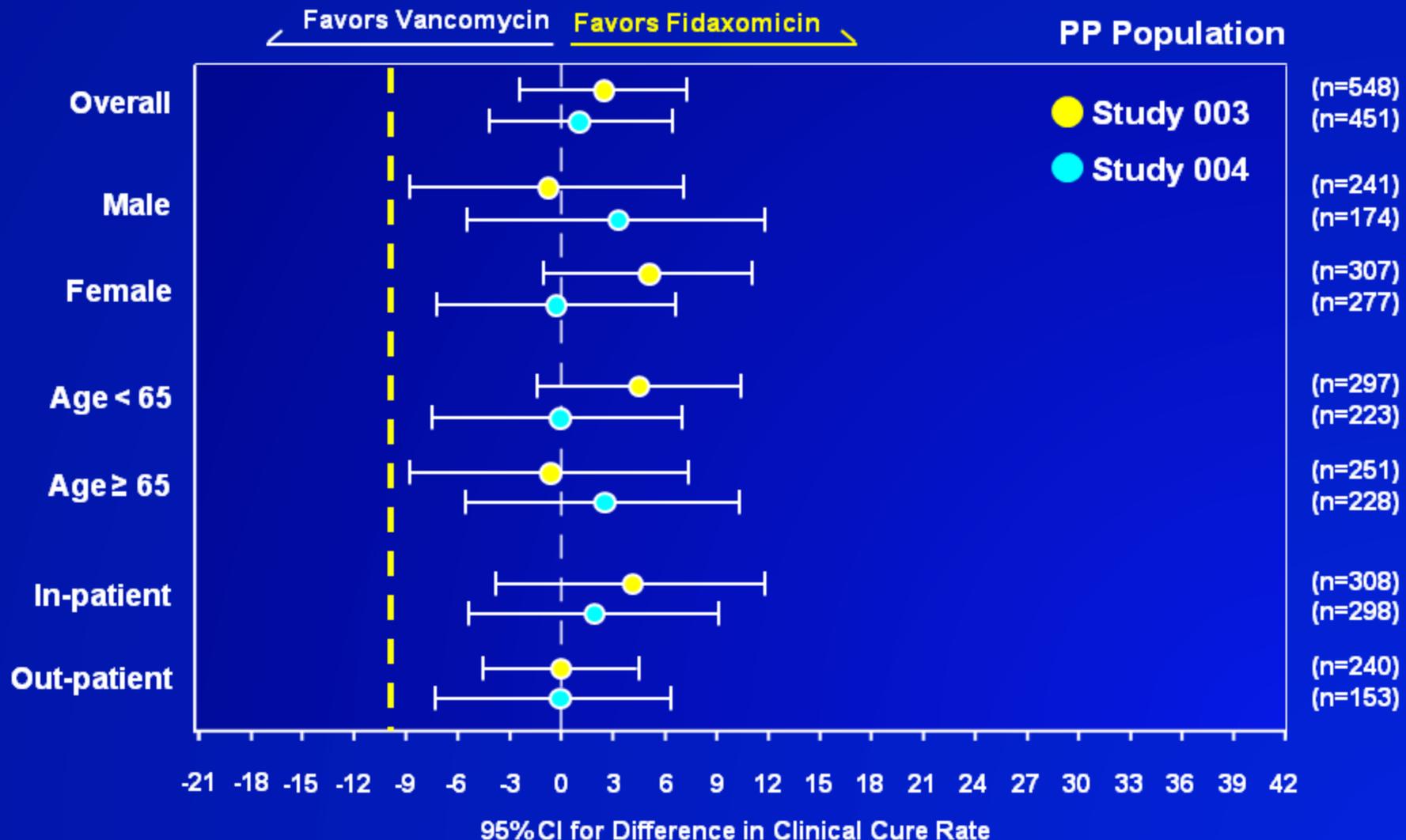


* Presented as percent of total population

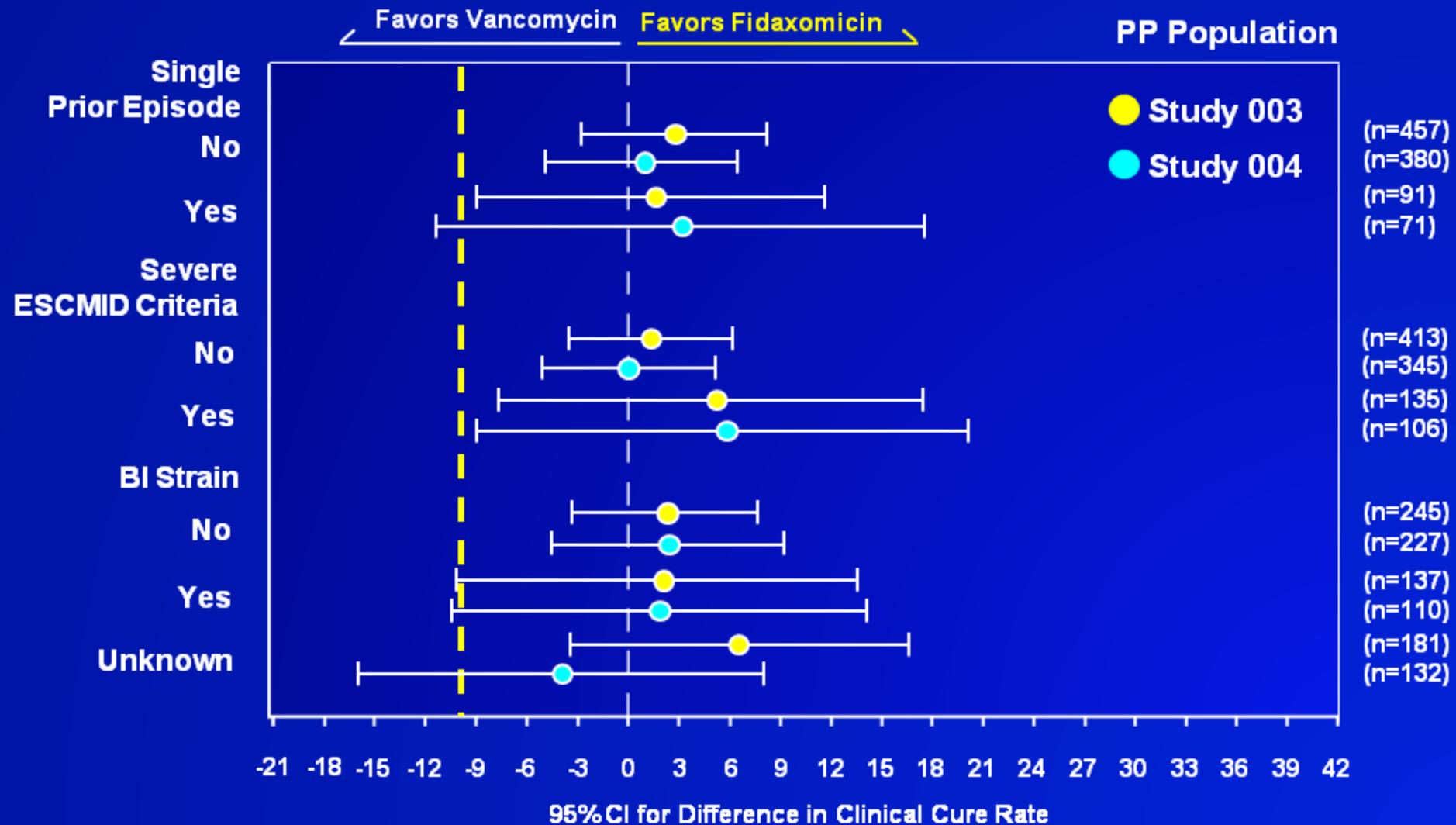
Pooled data, mITT

Subgroup Analyses

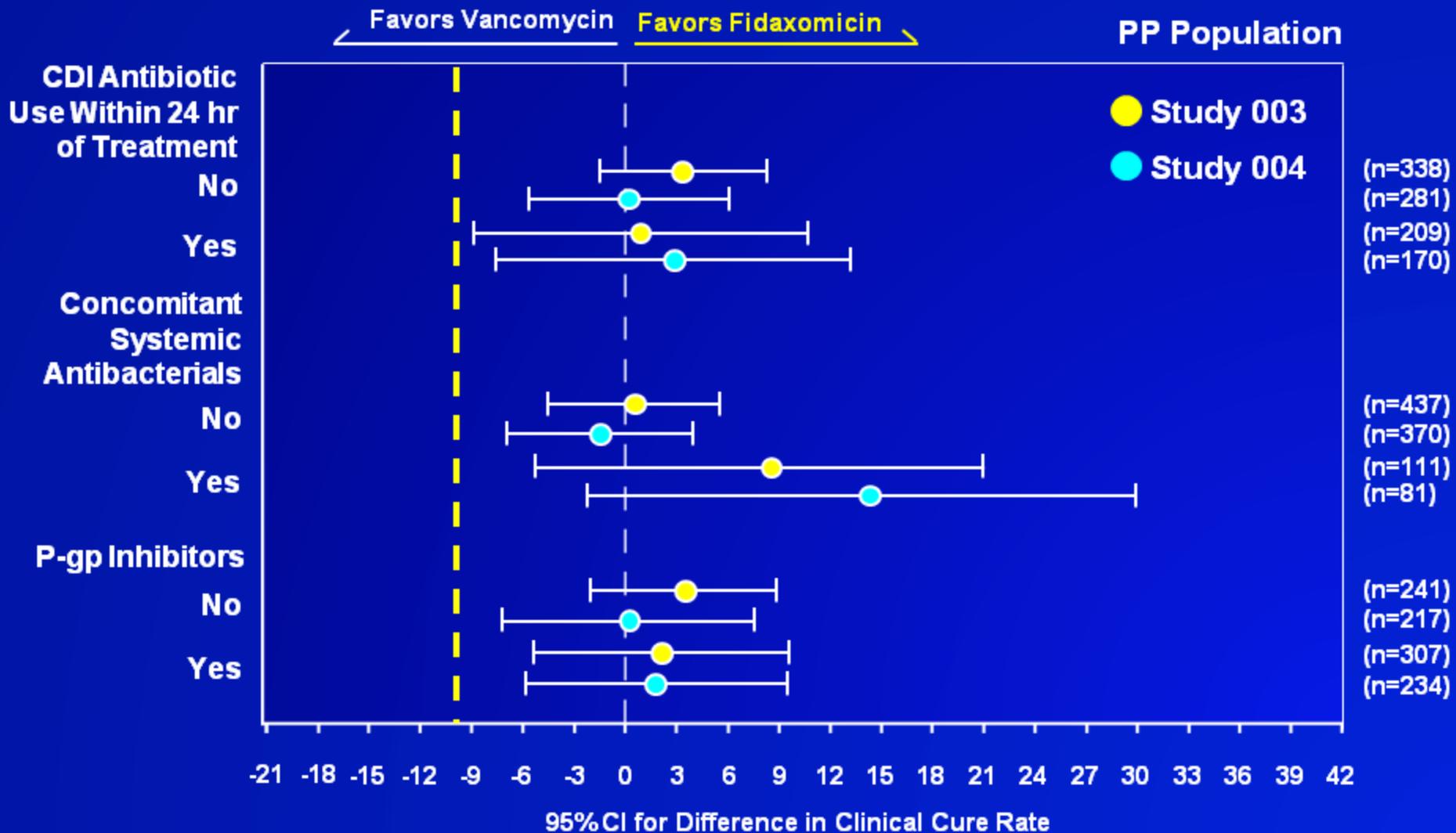
Similar Results in Clinical Cure Rate Across Demographic Subgroups



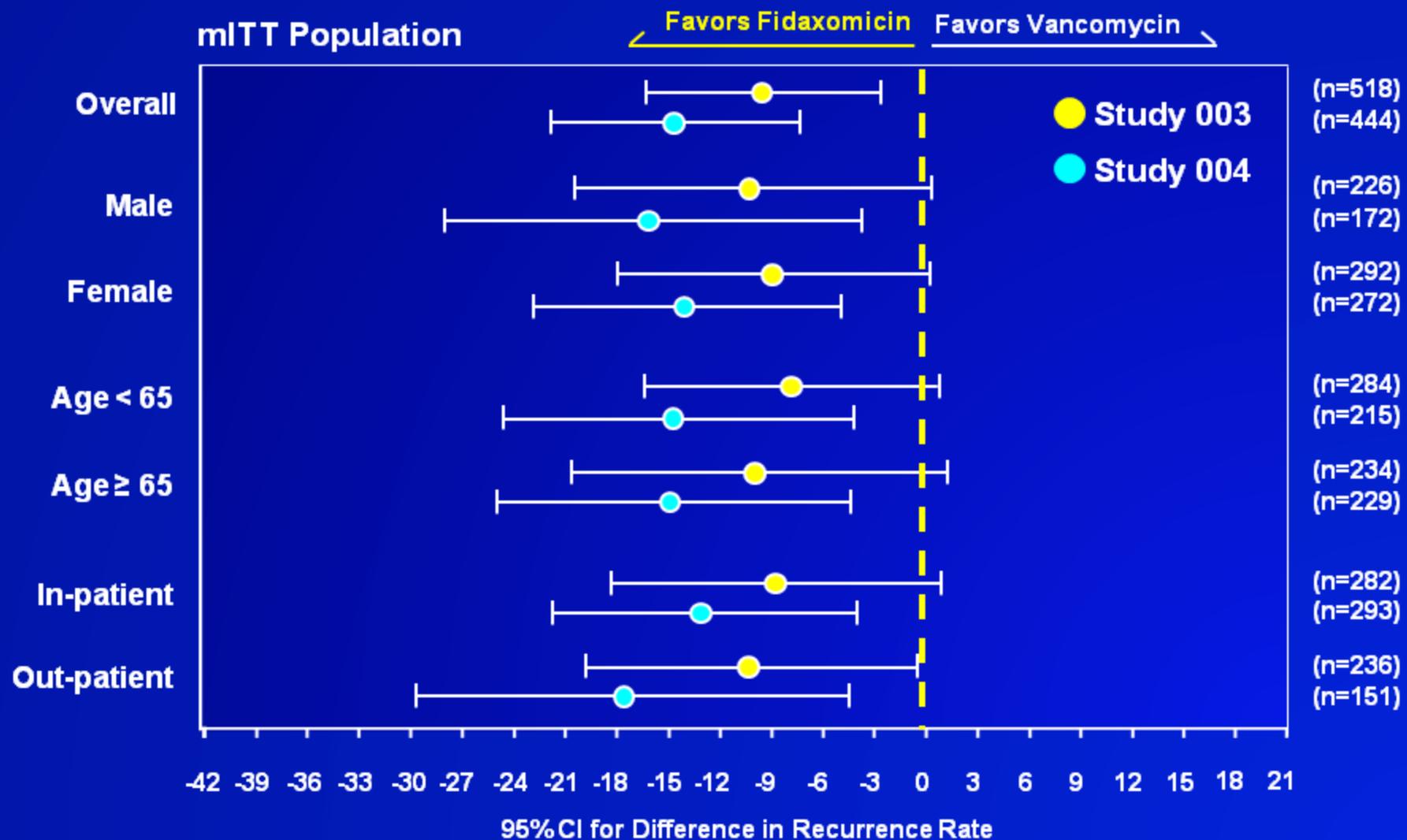
Similar Results in Clinical Cure Rate Across Disease State Subgroups



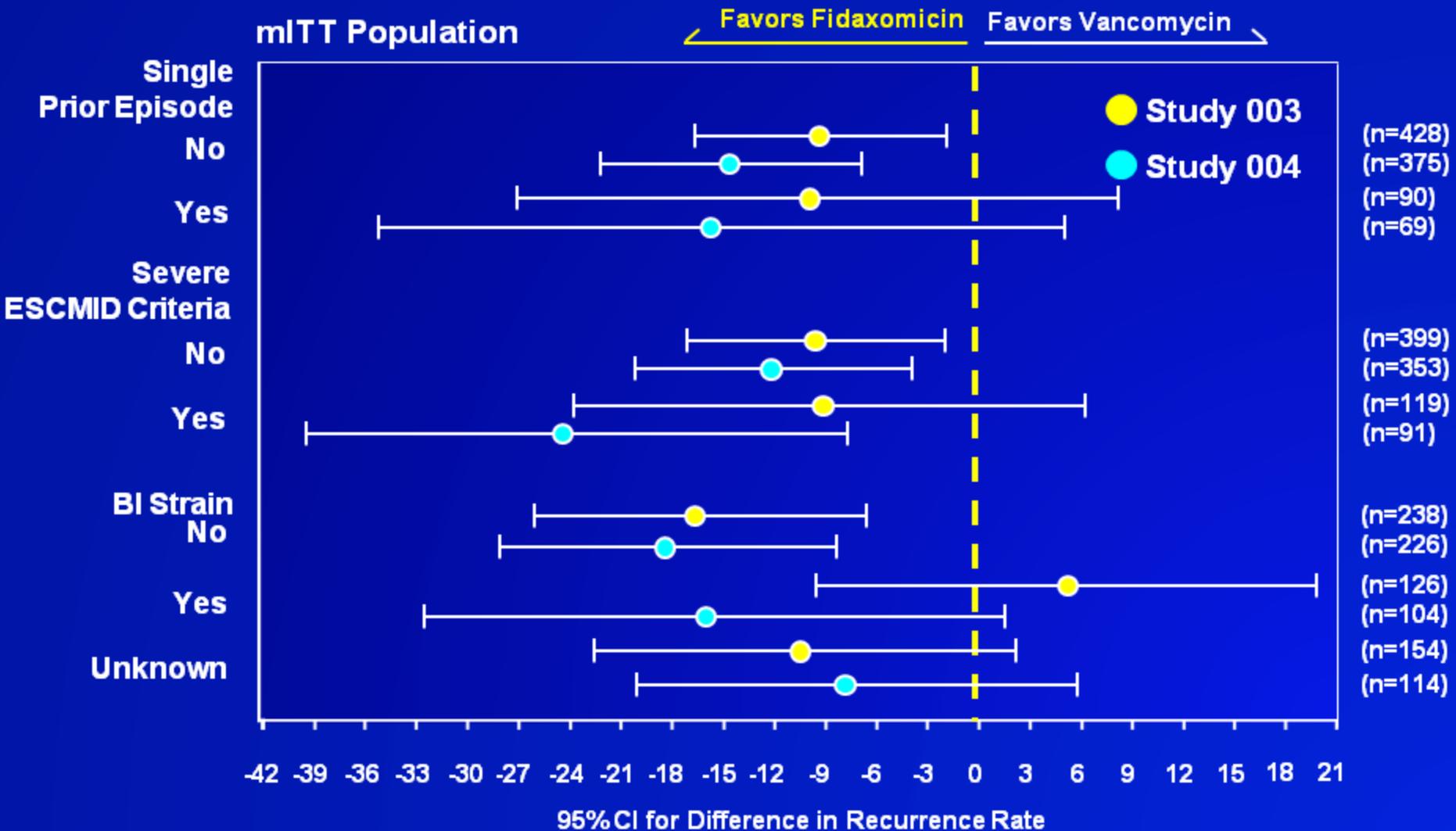
Similar Results in Clinical Cure Rate Antibiotics and P-gp Inhibitors



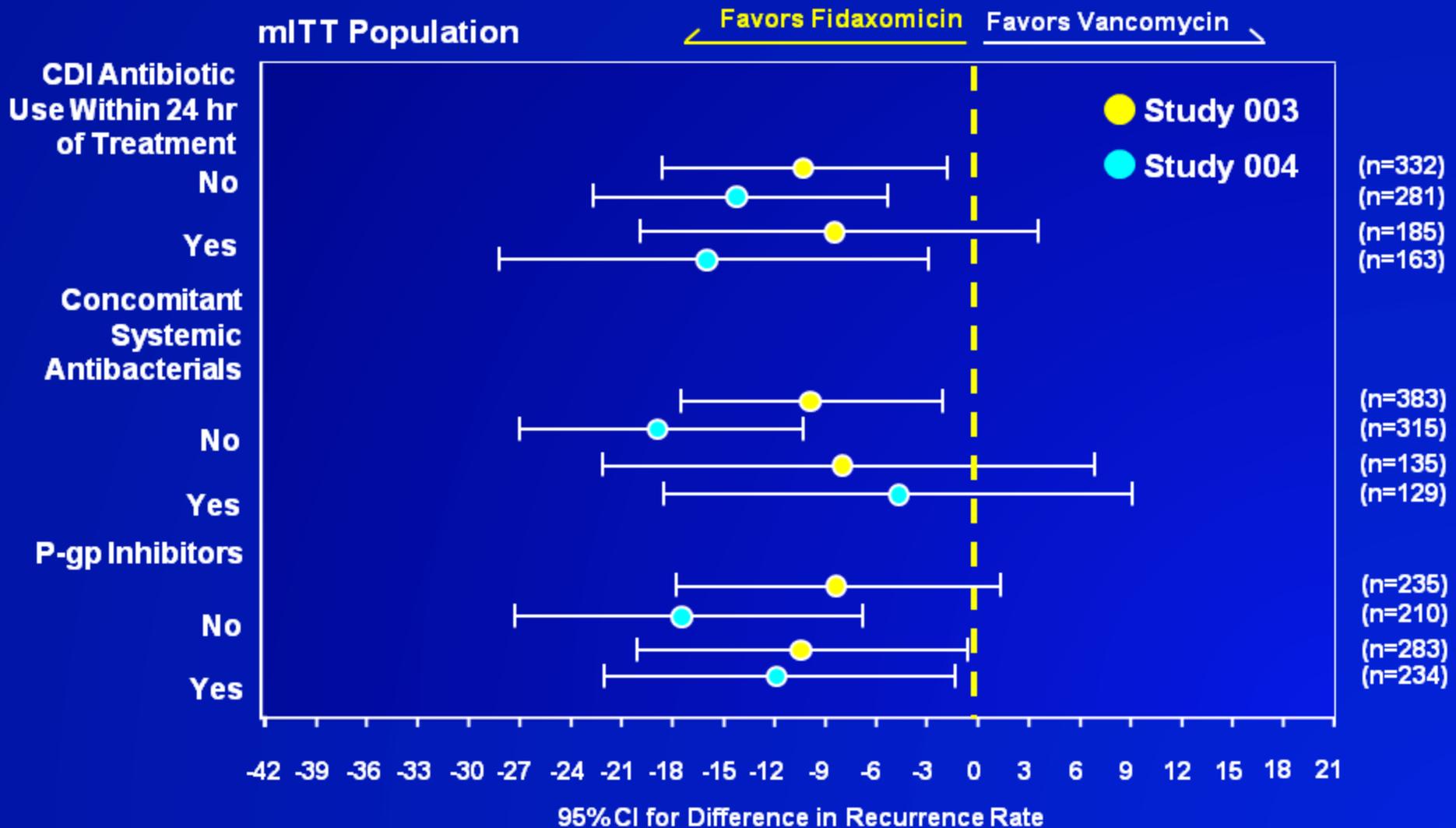
Recurrence Rates Favoring Fidaxomicin Across Demographic Subgroups



Recurrence Rates Favoring Fidaxomicin Across Most Disease State Subgroups



Recurrence Rates Favoring Fidaxomicin Antibiotics and P-gp Inhibitors



Fidaxomicin is Effective

- Non-inferior Clinical Cure rate
- Significantly superior in reducing Recurrence rate
- Significantly superior Global Cure rate
- Consistent results across subgroups and two studies

Safety of Fidaxomicin in Phase 3 Studies

Michael Corrado, MD, FIDSA

Chief Scientific Officer

INC Research

Overview of Safety

- Pooled AE data from the two Phase 3 studies
 - Allows comparison to vancomycin
 - N=564 fidaxomicin
- Safety variables
 - Occurrence of AEs
 - Occurrence of SAEs
 - Changes in laboratory evaluations
 - Changes in vital signs and ECGs

Overall Incidence of Adverse Events was Similar between Treatment Groups

Subjects with	Fidaxomicin N=564		Vancomycin N=583	
	n	%	n	%
AEs	385	68.3	382	65.5
Severe AEs	108	19.1	98	16.8
Study drug relationship = related	60	10.6	65	11.1
AEs leading to discontinuation of study drug	33	5.9	40	6.9
AEs leading to dose modification or use of concomitant medication	2	0.4	8	1.4
Serious AEs	145	25.7	135	23.2
All-cause mortality	36	6.4	38	6.5

Similar Adverse Events between Fidaxomicin and Vancomycin Subjects

AEs Occurring in $\geq 5\%$ of Subjects in Either Treatment Arm

Preferred Term	Fidaxomicin N=564		Vancomycin N=583	
	n	%	n	%
AEs	385	68.3	382	65.5
Nausea	62	11.0	66	11.3
Vomiting	41	7.3	37	6.3
Hypokalemia	41	7.3	38	6.5
Headache	37	6.6	27	4.6
Abdominal pain	33	5.9	23	3.9
Diarrhea	28	5.0	39	6.7
Pyrexia	24	4.3	31	5.3

Few AEs Leading to Discontinuation (≥ 2 Subjects in Either Treatment Arm)

Preferred Term	Fidaxomicin N=564		Vancomycin N=583	
	N	%	n	%
AEs leading to discontinuation	33	5.9	40	6.9
Respiratory failure	-	-	4	0.7
Vomiting	3	0.5	3	0.5
Pneumonia	2	0.4	2	0.3
Megacolon	2	0.4	-	-
Colitis	2	0.4	-	-
Abdominal pain	2	0.4	-	-
<i>Clostridium difficile</i> colitis	2	0.4	-	-
Dehydration	1	0.2	2	0.3
Sepsis	1	0.2	2	0.3
Nausea	-	-	2	0.3
<i>Escherichia</i> sepsis	-	-	2	0.3
Wound dehiscence	-	-	2	0.3
Confusional state	-	-	2	0.3
Mental status changes	-	-	2	0.3

SAEs Occurring in $\geq 1\%$ of Subjects in Fidaxomicin Treatment Group

Preferred Term	Fidaxomicin N=564		Vancomycin N=583	
	n	%	n	%
SAEs	145	25.7	135	23.2
Pneumonia	8	1.4	10	1.7
<i>Clostridium difficile</i> colitis*	8	1.4	9	1.5
Sepsis	7	1.2	5	0.9
Hyponatremia	6	1.1	3	0.5

* Meets the definition of an SAE (e.g. requires/prolongs hospitalization)

Overall Death Rate Similar to Vancomycin

	Fidaxomicin N=564	Vancomycin N=583
	n	n
Total	36	38
Cardiac disorder	2	7
Gastrointestinal disorders	3	6
General disorders, admin. site conditions	1	4
Infections and infestations	11	11
Injury, poisoning, procedural complications	1	-
Metabolism and nutrition disorders	-	3
Neoplasms	5	3
Nervous system disorders	-	1
Renal and urinary disorders	3	-
Respiratory, thoracic, mediastinal disorders	9	3
Vascular disorders	1	-

GI Events Similar to Vancomycin

Subjects with gastrointestinal disorders	Fidaxomicin N=564		Vancomycin N=583	
	n	%	n	%
AEs	177	31.4	170	29.2
AEs leading to discontinuation	13	2.3	8	1.4
SAEs	26	4.6	24	4.1
Deaths	3	0.5	6	1.0

GI Bleeding According to Preferred Term

	Fidaxomicin		Vancomycin	
	n	%	n	%
Total AEs	20	3.5	10	1.7
Hematochezia	7	1.2	1	0.2
Diarrhoea haemorrhagic	5	0.9	-	-
Gastrointestinal haemorrhage	5	0.9	1	0.2
Rectal haemorrhage	2	0.4	3	0.5
Haemorrhoidal haemorrhage	1	0.2	1	0.2
Haematemesis	-	-	1	0.2
Oesophageal varices haemorrhage	-	-	1	0.2
Upper gastrointestinal haemorrhage	-	-	1	0.2
Occult blood positive	-	-	1	0.2

GI Bleeding Events Similar Between Treatment Groups

	Fidaxomicin		Vancomycin	
	n	%	n	%
Total AEs & SAEs	23	4.1	18	3.1
AEs GI bleeding preferred term	20	3.5	10	1.7
AEs GI bleeding verbatim term				
Haemorrhoids (bloody)	1	0.2	-	-
SAEs with GI bleeding component				
Ischemic colitis (bloody stools)	-	-	1	0.2
Large intestine perforation (GI bleed)	-	-	2	0.3
CDI recurrence (bloody stools)	-	-	1	0.2
Toxic megacolon (bloody diarrhea)	2	0.4	-	-
Feculent vomiting (melena)	-	-	1	0.2
Urosepsis (occult blood positive)	-	-	1	0.2
Meningitis (bloody stools)	-	-	1	0.2
Septic shock (rectal bleeding)	-	-	1	0.2

Nonclinical Studies Showed No Suggestion for GI Bleeding

- Nonclinical studies
 - 3 months oral dosing in dogs
 - 1 g/kg/day
- Results
 - No evidence of GI bleeding
 - No microscopic findings indicative of GI toxicity

Conclusion GI Bleeding Events

- GI bleeding events similar between fidaxomicin and vancomycin group
- Nonclinical studies no signal for GI bleeding

Leukopenic or Neutropenic Adverse Events

	Fidaxomicin N=564		Vancomycin N=583	
	n	%	n	%
Total subjects n (%)	15	2.7	5	0.9
Leukopenia	8	1.4	4	0.7
Neutropenia	5	0.9	-	-
Neutrophil count decreased	5	0.9	-	-
Febrile neutropenia*	2	0.4	-	-
White Blood Cell count decreased	2	0.4	1	0.2
Pancytopenia	1	0.2	-	-
Neutropenic sepsis*	1	0.2	-	-
Granulocytopenia	-	-	1	0.2

* One case each of febrile neutropenia and neutropenic sepsis had neutropenia at study entry.

Predisposing Factors for Leukopenia

	Leukopenia	
	Fidaxomicin	Vancomycin
Total	15	5
Description of Predisposing Factor		
Chemotherapy initiated on study	5	1
Lupus	2	-
Prior SCT/BMT	3	-
No decrease in WBC	2*	-
Other/ Unexplained	5	4

* Two subjects on fidaxomicin had two predisposing factors each

Nonclinical Studies Showed No Signal for Leukopenia

- Nonclinical studies
 - 3 months in dogs (exposure 117 fold)
 - Approximately 2 weeks in rats and rabbits (exposure 134 and 33 fold, respectively)
 - 28 days in monkeys (exposure 4 fold)
- Results
 - No impact on hematology parameters or bone marrow

Leukopenia Summary

- Higher rate of fidaxomicin subjects
 - Treated with chemotherapy
 - Had lupus
 - Had bone marrow transplant
- Majority of leukopenias resolved without sequelae
- Nonclinical studies showed no signal for leukopenia

No Clinically Significant Changes in Laboratory Values and Vital Signs

- Changes in lab values generally reflect underlying medical conditions and concomitant therapies
 - ALT, AST and bilirubin not significantly changed
- No clinically significant changes in vital signs and ECGs

Safety Conclusions

Fidaxomicin is Well-tolerated

- Incidence of AEs, SAEs, deaths similar to vancomycin
- SAEs and fatalities consistent with underlying clinical condition
- GI bleeding events: generally similar between groups
- More fidaxomicin subjects with underlying medical condition that could lead to leukopenia
 - No signal in nonclinical studies
- No significant changes in vital signs and ECGs

Concluding Remarks

Sherwood Gorbach, MD, FIDSA

Chief Scientific Officer

Optimer Pharmaceuticals

Post Approval Plan

- Microbiologic and strain typing surveillance
 - 6 centers
 - 450 isolates per year
- Intervention study in subjects with multiple recurrences
- Sporulation, germination and inhibition of toxin production studies - *in vitro*

Planned Pediatric Program

- Orphan drug status
- Program under discussion with FDA
- Two studies
 - Study 1: safety + PK
 - Study 2: safety + efficacy
- Studies in children age 2-18 years
- Oral suspension under development

Additional Treatment Options are Needed

- CDI is a serious disease of increasing incidence
- Recurrences are common 20-30%
- Two current treatment options have limitations
- Unmet need for new treatments
 - Lower the Recurrence rate
 - Increase Global Cure rate

Fidaxomicin has an Excellent Profile for Treating *C. difficile* Infections

- Bactericidal against *C. difficile*
- Minimal perturbation of the normal gut microbiota
- High fecal concentration
- Acts locally within the GI tract with minimal systemic absorption
- Unique mechanism of action
- No cross resistance

Fidaxomicin is Effective

- Non-inferior Clinical Cure rate
- Significantly superior reduction in Recurrence rate
- Significantly superior Global Cure rate

Fidaxomicin is Well-tolerated

- Incidence of AEs, discontinuations due to AEs, SAEs and deaths similar to vancomycin-treated subjects
- GI bleeding events are similar between groups
- More fidaxomicin subjects with underlying medical conditions that could lead to leukopenia
 - No signal in nonclinical studies
- No clinically meaningful drug-drug interactions identified

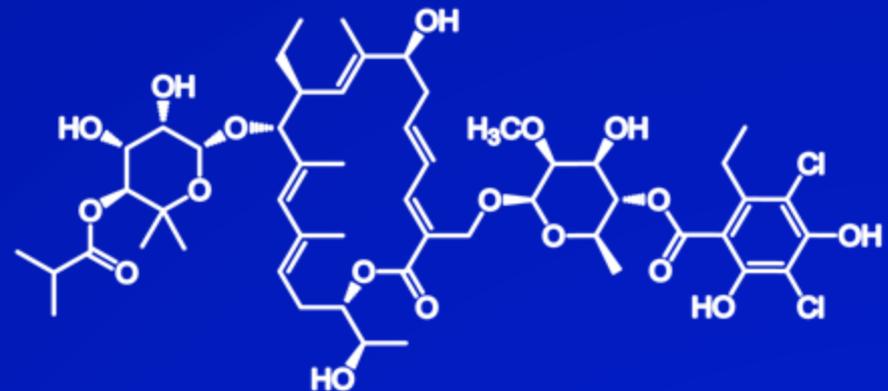
Benefit / Risk for Fidaxomicin Positive

■ Benefit

- High Clinical Cure rate similar to vancomycin
- Significantly superior reduction in Recurrences
- Significantly superior Global Cure rate
- Less potential for colonization with VRE

■ Risk

- Similar safety profile to vancomycin



Dificid™ (fidaxomicin) 200 mg Tablets

Optimer Pharmaceuticals

April 5, 2011

Anti-Infective Drugs Advisory Committee of the
Food and Drug Administration