Battle of the Bugs: An Antibiotic Update

WHITNEY JONES NESBITT, PHARMD, BCPS
ANTIMICROBIAL STEWARDSHIP PHARMACIST
VANDERBILT UNIVERSITY MEDICAL CENTER
SEPTEMBER 15, 2017

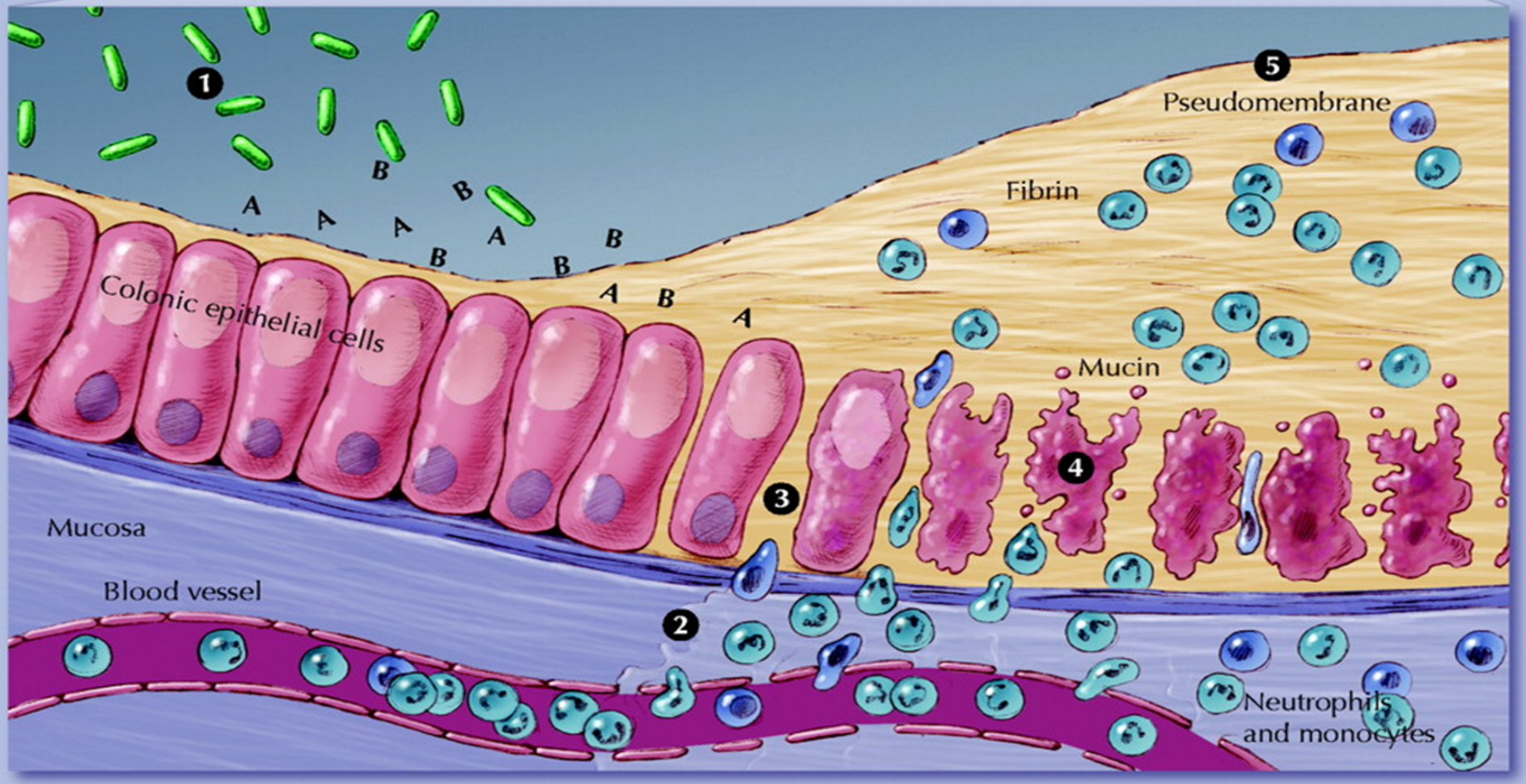
Disclosures

- No disclosures related to the material of this presentation

Objectives

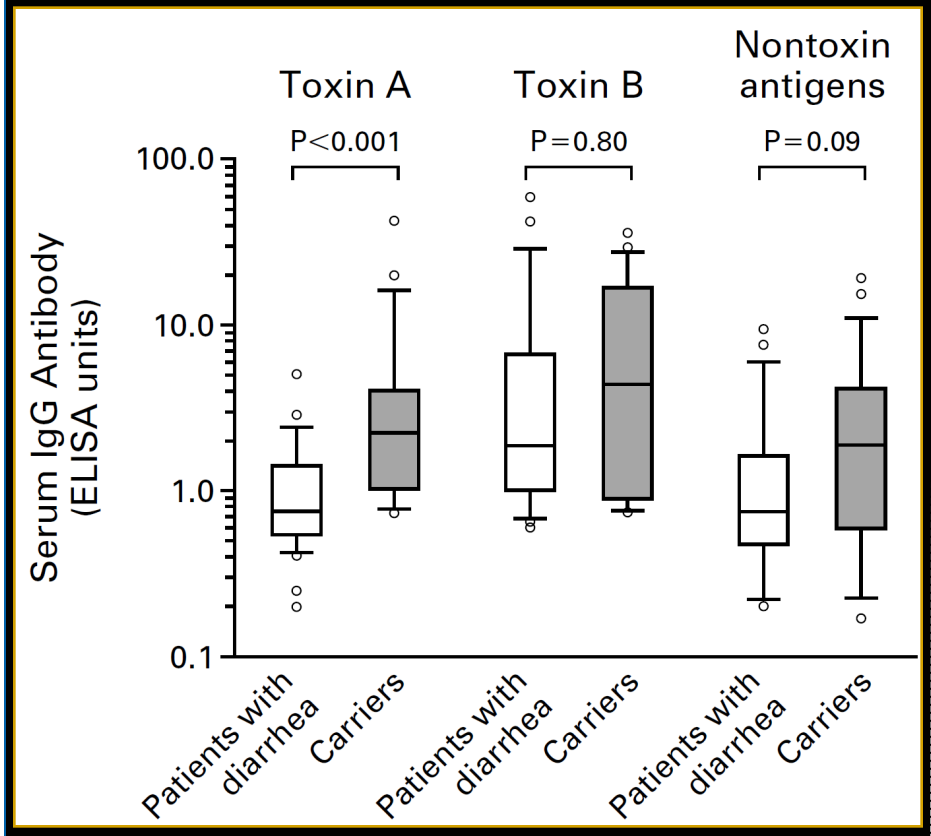
- Review new infectious diseases treatment options
- Describe the mechanisms of action and clinical efficacy of the new agents
- Identify potential places in therapy for which these agents may be used

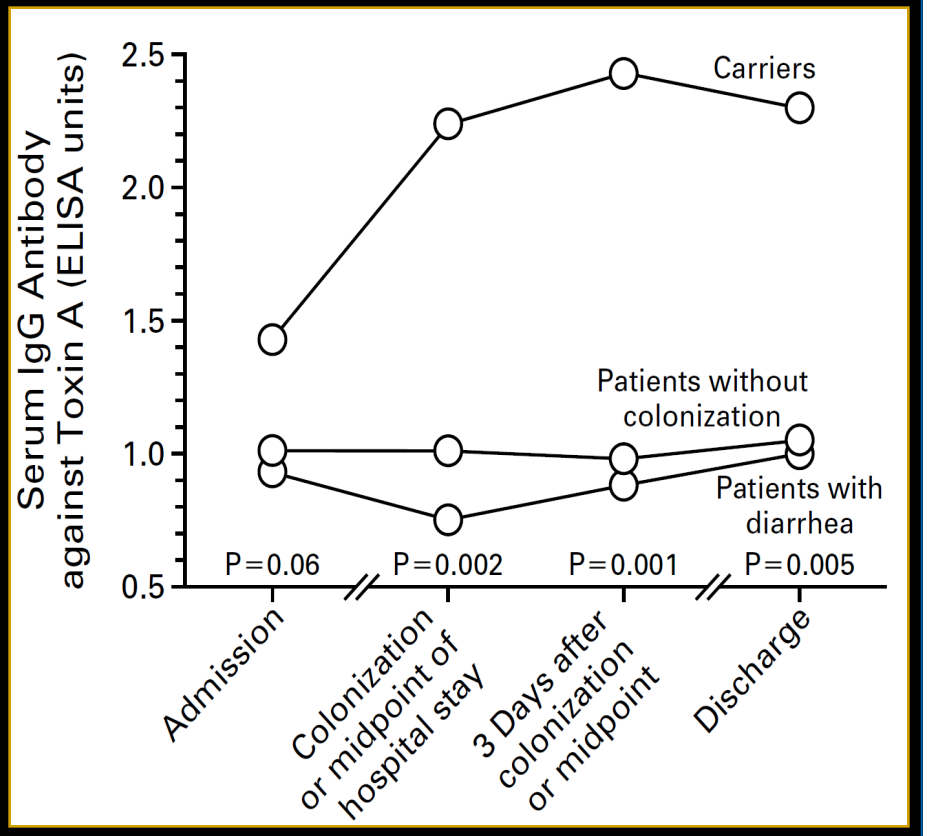
Clostridium difficile Infection



C. difficile vegetative cells produce toxins A and B and hydrolytic enzymes (**1**). Local production of toxins A and B leads to production of tumour necrosis factor-alpha and proinflammatory interleukins, increased vascular permeability, neutrophil and monocyte recruitment (**2**), opening of epithelial cell junctions (**3**) and epithelial cell apoptosis (**4**). Local production of hydrolytic enzymes leads to connective tissue degradation, leading to colitis, pseudomembrane formation (**5**) and watery diarrhea.

Asymptomatic Carriage of *C. difficile* and Serum IgG levels



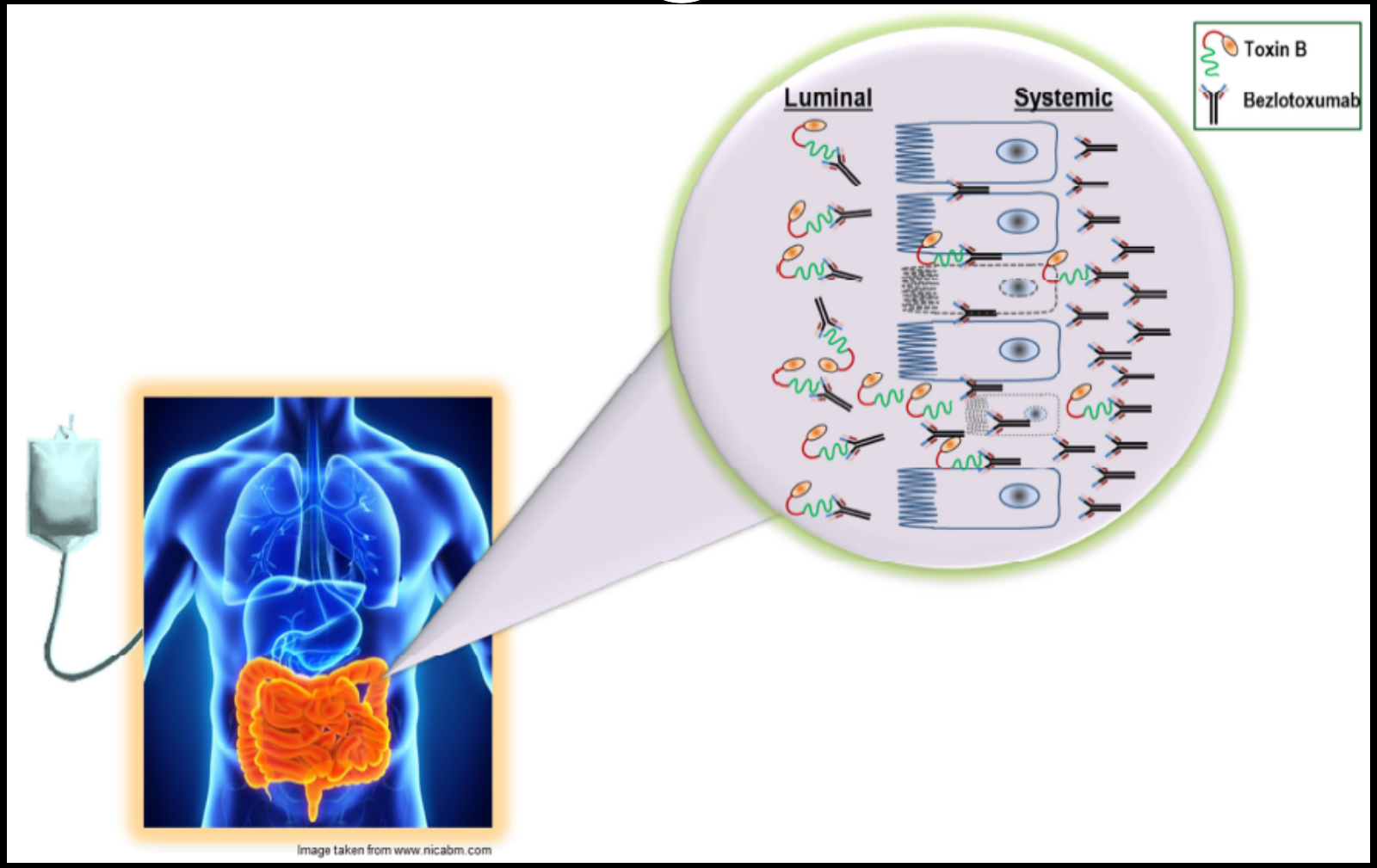


N Engl J Med 2000;342:390-7.

Bezlotoxumab Injection (Zinplava™)

- Fully human monoclonal IgG1/kappa antibody
- Inhibits binding of *C. difficile* toxin B to mammalian cells
  - Binds to an epitope conserved across strains
    - Amino acid sequence variation within epitope
      - Impact on binding affinity of bezlotoxumab
  - Prevents intracellular entry of toxin B
    - Includes enzymatic components responsible for pathogenicity
- Does NOT bind toxin A
- Does NOT have antibacterial activity
  - Must be used in combination

In Vivo Activity of Bezlotoxumab



Clinical Development and Regulatory History

- IND submission on November 25, 2005
- Early hypotheses for effective prevention of recurrence
  - Anti-toxin A antibody (actoxumab) or combination of anti-toxin A and B antibodies
- Phase 2 trial (2006-2008)
  - Combination of toxin A and B antibodies (n=101) versus placebo (n=99)
    - Patient received concomitant antibacterial therapy for CDI
  - Rate of recurrence
    - Combination of antibodies (7%) versus placebo (25%) ($p<0.001$)

Toxin B Antibody Prevents GI and Systemic CDI

Treatment (number of animals)	Gastrointestinal Disease,[a]	Systemic Disease,[b] %	Fatal Disease[c] %	TcdA/TcdB in Body Fluids, %	TcdA/TcdB in Feces, %
Anti-TcdA only					
Polyclonal (6)	mod-sev	100	83	0/50	100/100
HuMab (6)	mod-sev	100	67	67/67	100/100
Anti-TcdB only					
Polyclonal (6)	mild	0	0	0/0	100/100
HuMab (5)	mild	0	0*	0/0	100/100
Anti-TcdA and TcdB					
Polyclonal (6)	mild	0	0	0/0	100/100
HuMab (6)	mild-mod	0	0*	0/0	100/100
Control					
Polyclonal (5)	mod-sev	60	20	20/20	100/100
HuMab (4)	mod-sev	75	50	75/75	100/100

J Infect Dis 2013; 207:323-30.

Pharmacokinetics

- Absorption: 100%
- Distribution
  - Limited extravascular
  - Detection in stool of subjects with CDI
- Elimination
  - Half-life: 19 days
    - Measurable concentrations during first 12 weeks after treatment
  - Protein catabolism
    - Not dependent on a single organ
  - Clearance increases with increased body weight

MODIFY I and MODIFY II

- Two Phase 3 trials
  - Two double-blind, randomized, placebo-controlled
  - 322 sites in 30 countries
  - November 1, 2011 through May 22, 2015
- Participants and procedures
  - Adults ≥ 18 years with primary or recurrent CDI
  - Receiving standard-of-care antibiotics (metronidazole, oral vancomycin, fidaxomicin) x 10-14 days

N Engl J Med 2017;376:305-17.

Patients and Procedures

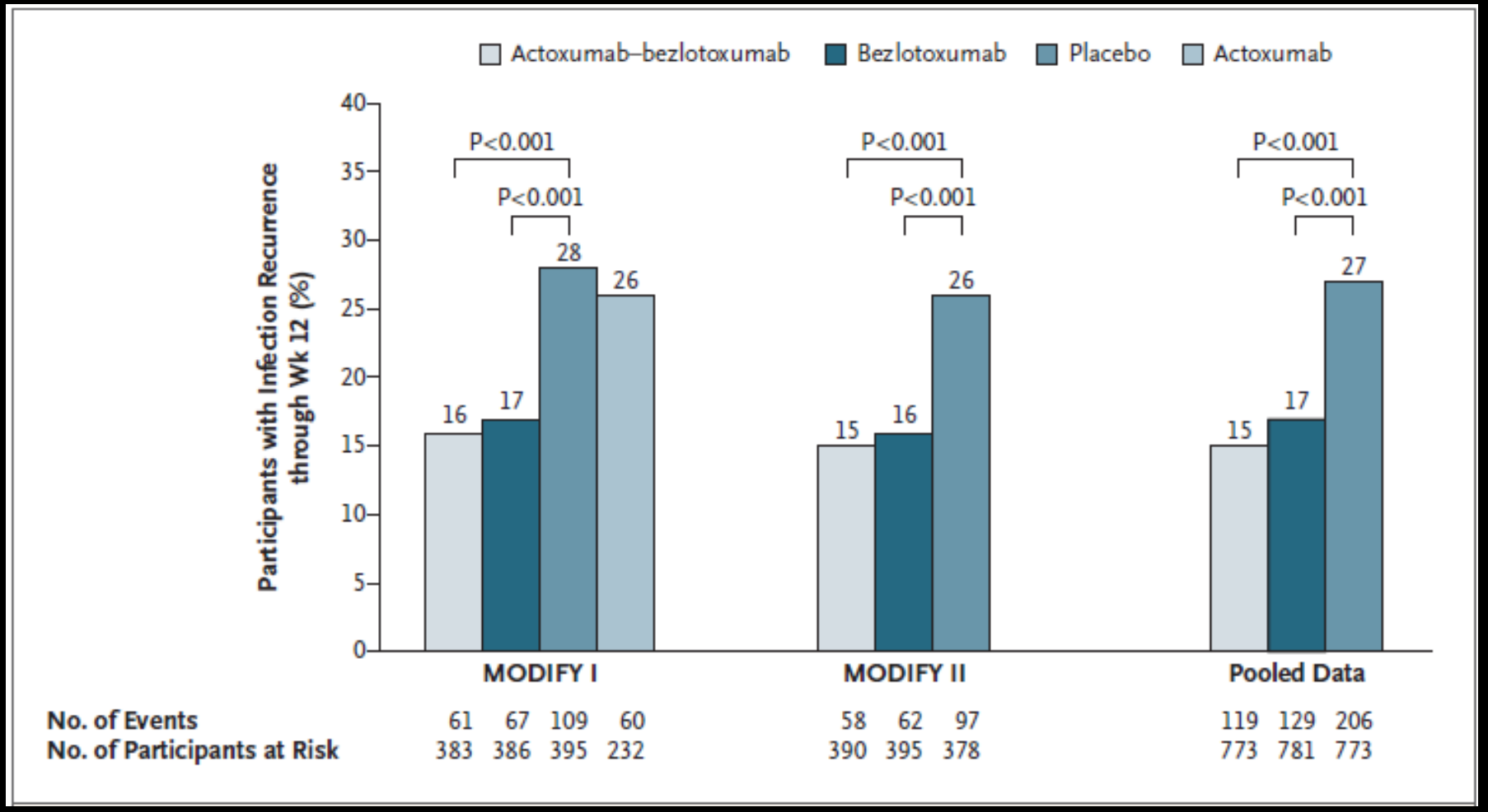
- 4 Groups:
  - Bezlotoxumab 10mg/kg alone
  - Actoxumab plus bezlotoxumab 10mg/kg each
  - Actoxumab 10mg/kg alone (MODIFY I only)
  - Placebo
- 60 minute infusion of study drug(s) or placebo Day 1
- Participants recorded unformed stools daily until day 80-90 after infusion

N Engl J Med 2017;376:305-17.

Characteristic	Actoxumab plus Bezlotoxumab (N=773)	Bezlotoxumab (N=781)	Actoxumab (N=232)	Placebo (N=773)	All Participants (N=2559)
	number of participants (percent)				
Standard-of-care antibiotic					
Metronidazole	366 (47.3)	365 (46.7)	112 (48.3)	353 (45.7)	1196 (46.7)
Vancomycin	366 (47.3)	370 (47.4)	113 (48.7)	372 (48.1)	1221 (47.7)
Fidaxomicin	25 (3.2)	30 (3.8)	7 (3.0)	30 (3.9)	92 (3.6)
Inpatient	523 (67.7)	530 (67.9)	158 (68.1)	520 (67.3)	1731 (67.6)
Female sex	423 (54.7)	442 (56.6)	130 (56.0)	449 (58.1)	1444 (56.4)
Age ≥65 years	441 (57.1)	390 (49.9)	122 (52.6)	405 (52.4)	1358 (53.1)
≥1 Episodes of *C. difficile* infection in previous 6 mo	200 (25.9)	216 (27.7)	69 (29.7)	219 (28.3)	704 (27.5)
≥2 Previous *C. difficile* infection episodes ever	103 (13.3)	100 (12.8)	34 (14.7)	126 (16.3)	363 (14.2)
Severe *C. difficile* infection*	142 (18.4)	122 (15.6)	31 (13.4)	125 (16.2)	420 (16.4)
Immunocompromised†	163 (21.1)	178 (22.8)	55 (23.7)	153 (19.8)	549 (21.5)
Other antibiotic use during standard-of-care therapy‡	333 (43.1)	292 (37.4)	86 (37.1)	317 (41.0)	1028 (40.2)
Other antibiotic use after standard-of-care therapy‡	274 (35.4)	273 (35.0)	83 (35.8)	275 (35.6)	908 (35.5)
Renal impairment§	96 (12.4)	123 (15.7)	37 (15.9)	110 (14.2)	366 (14.3)
Hepatic impairment¶	56 (7.2)	49 (6.3)	14 (6.0)	44 (5.7)	163 (6.4)
Region of enrollment‖					
Africa	2 (0.3)	5 (0.6)	1 (0.4)	2 (0.3)	10 (0.4)
Asia–Pacific	80 (10.3)	79 (10.1)	10 (4.3)	77 (10.0)	246 (9.6)
Latin America	37 (4.8)	30 (3.8)	9 (3.9)	35 (4.5)	111 (4.3)
Europe	292 (37.8)	313 (40.1)	80 (34.5)	293 (37.9)	978 (38.2)
North America	362 (46.8)	354 (45.3)	132 (56.9)	366 (47.3)	1214 (47.4)
PCR ribotype					
Participants with positive culture	477 (61.7)	490 (62.7)	144 (62.1)	486 (62.9)	1597 (62.4)
Most common strains**††	222 (46.5)	210 (42.9)	57 (39.6)	233 (47.9)	722 (45.2)
027, 078, or 244 strain††	90 (18.9)	102 (20.8)	30 (20.8)	115 (23.7)	337 (21.1)
027 strain††	76 (15.9)	89 (18.2)	24 (16.7)	100 (20.6)	289 (18.1)

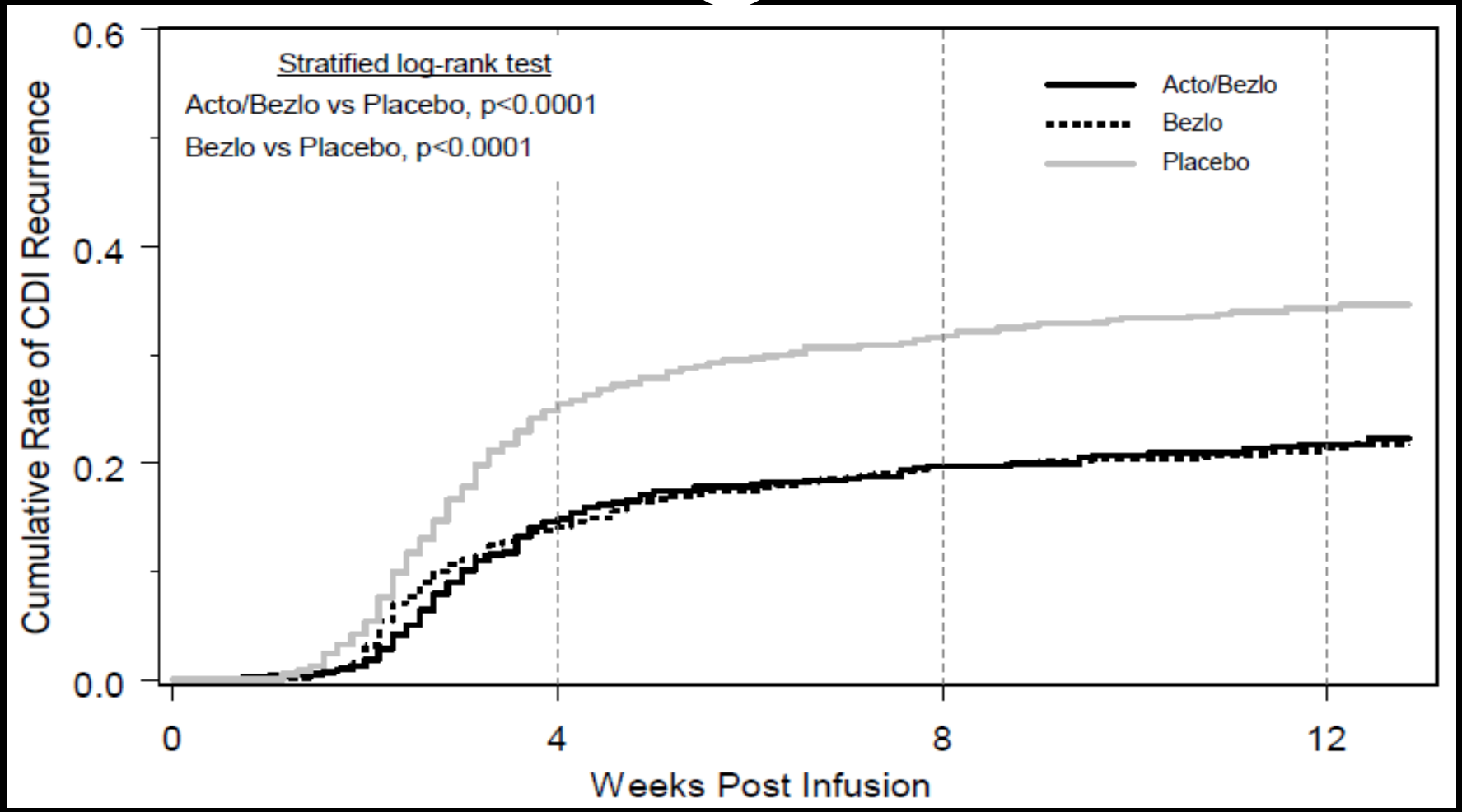
N Engl J Med 2017;376:305-17.

Recurrent CDI During 12-Week Follow-Up

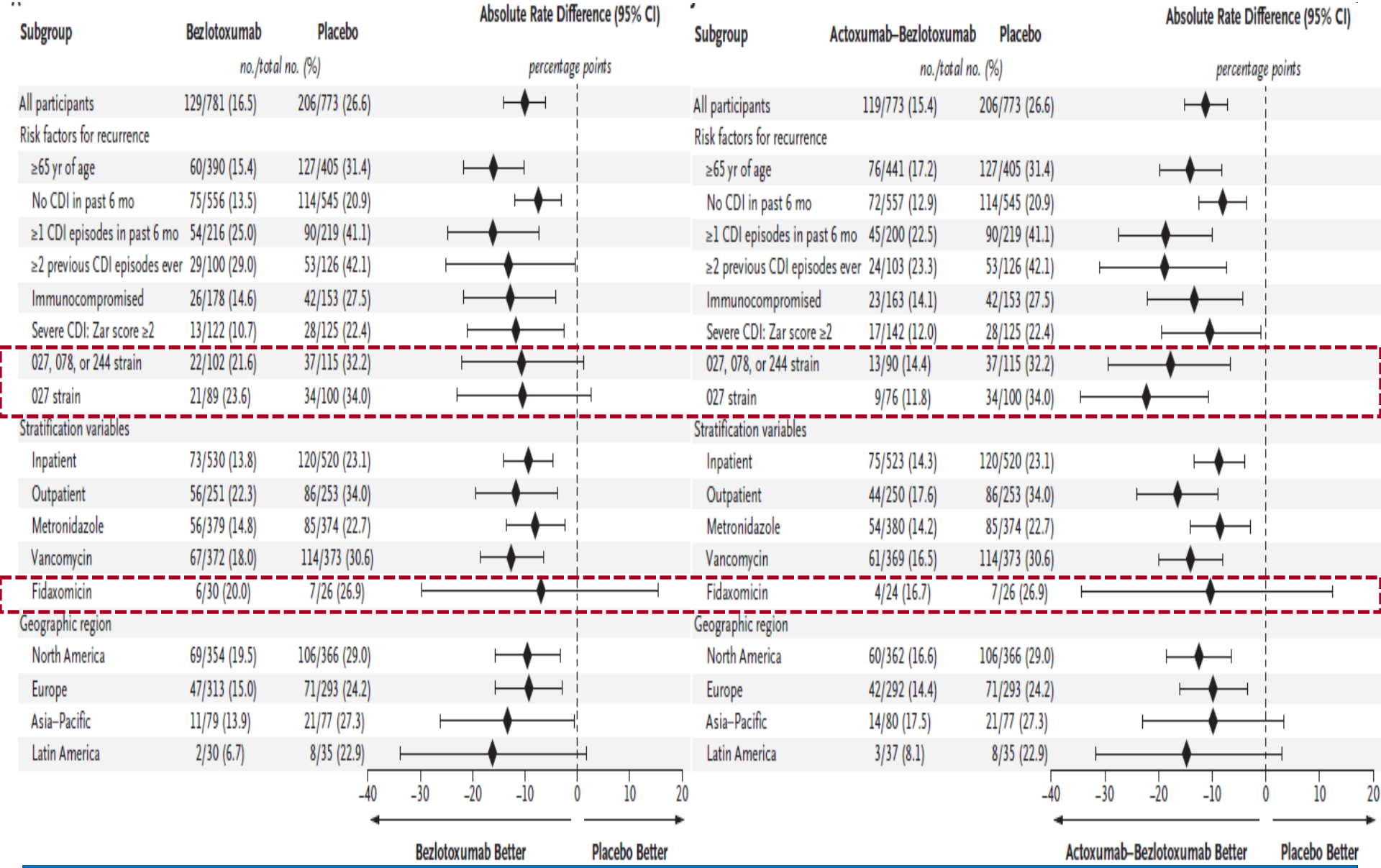


N Engl J Med 2017;376:305-17.

Time to CDI Recurrence



N Engl J Med 2017;376:305-17.



N Engl J Med 2017;376:305-17.

Sustained Cure

Sustained cure	Bezlotoxumab No. (%), n=386	Actoxumab-Bezlotoxumab No. (%), n=383	Placebo No. (%), n=395
MODIFY I	232 (60)	225 (59)	218 (55)
MODIFY II	264 (67)*	224 (57)	197 (52)
Pooled results	496 (64%)	449 (58)	415 (54)

N Engl J Med 2017;376:305-17.

Adverse Events

Time Period and Event	Actoxumab plus Bezlotoxumab (N=777)	Bezlotoxumab (N=786)	Actoxumab (N=235)	Placebo (N=781)
		number of participants (percent)		
During the 24 hours after infusion				
Infusion-specific reaction*	62 (8.0)	81 (10.3)	26 (11.1)	59 (7.6)
Treatment stopped because of an adverse event	0	1 (0.1)	1 (0.4)	0
During the 4 weeks after infusion				
One or more adverse events	455 (58.6)	485 (61.7)	158 (67.2)	478 (61.2)
Serious adverse event	123 (15.8)	156 (19.8)	65 (27.7)	167 (21.4)
Death	28 (3.6)	32 (4.1)	14 (6.0)	32 (4.1)
Drug-related adverse event†	50 (6.4)	59 (7.5)	17 (7.2)	46 (5.9)
Serious drug-related adverse event‡	5 (0.6)	4 (0.5)	3 (1.3)	2 (0.3)
Most common adverse events§				
Abdominal pain	32 (4.1)	34 (4.3)	15 (6.4)	34 (4.4)
Diarrhea	46 (5.9)	47 (6.0)	13 (5.5)	45 (5.8)
Nausea	47 (6.0)	52 (6.6)	28 (11.9)	39 (5.0)
Vomiting	24 (3.1)	31 (3.9)	10 (4.3)	21 (2.7)
Fatigue	21 (2.7)	18 (2.3)	11 (4.7)	12 (1.5)
Pyrexia	31 (4.0)	36 (4.6)	11 (4.7)	27 (3.5)
C. difficile infection¶	27 (3.5)	23 (2.9)	20 (8.5)	48 (6.1)
Urinary tract infection	24 (3.1)	32 (4.1)	13 (5.5)	35 (4.5)
Headache	33 (4.2)	35 (4.5)	14 (6.0)	24 (3.1)
During the 12 weeks after infusion				
Serious adverse event‖	212 (27.3)	231 (29.4)	104 (44.3)	255 (32.7)
Death	51 (6.6)	56 (7.1)	27 (11.5)	59 (7.6)

N Engl J Med 2017;376:305-17.

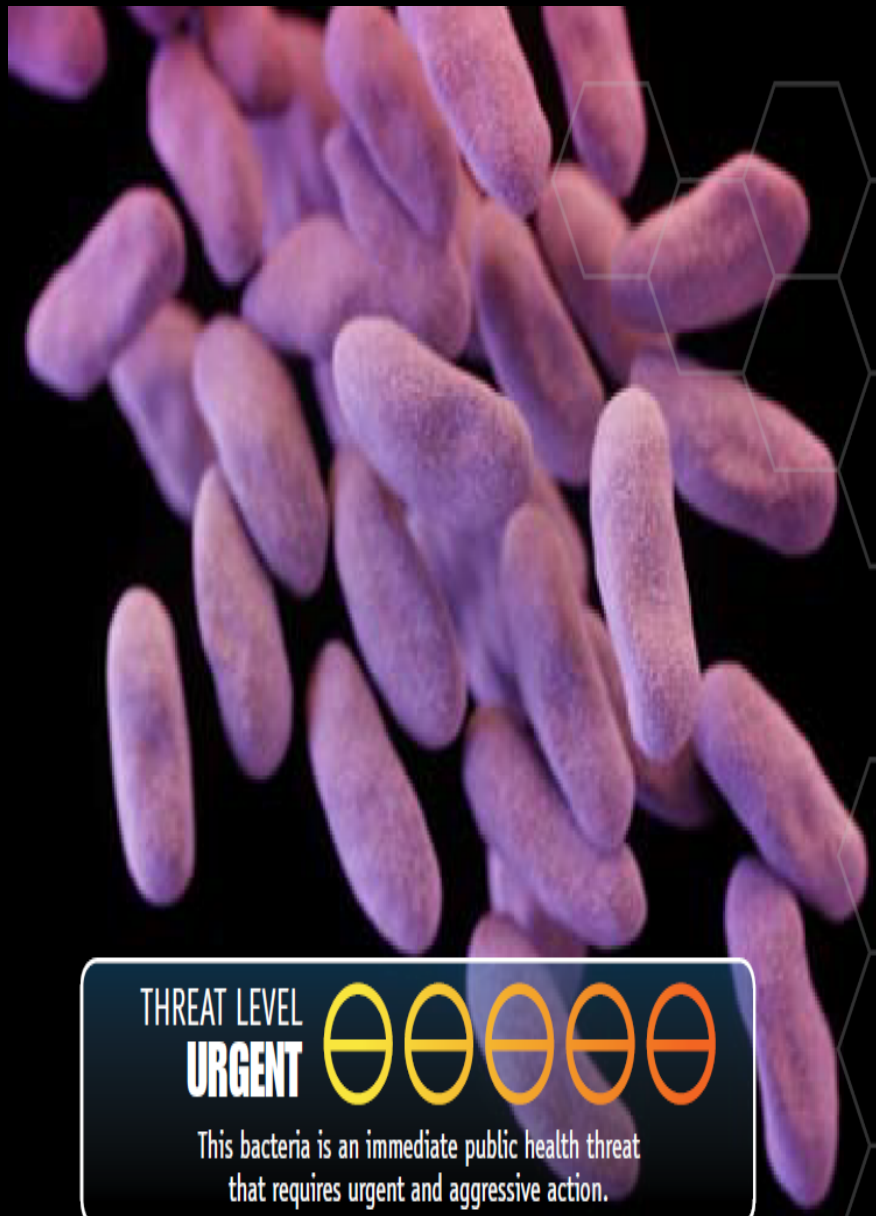
Bezlotoxumab Benefit

- Trials included substantial number of patient with ≥ 1 risk factor
  - ≥ 65 years: 53%
  - ≥ CDI episode within 6 mo.: 28% (incl. 14% with multiple)
  - Severe CDI: 16%
  - Immunocompromised: 20%
  - 027 ribotype: 18%
  - 027, 078, or 244 ribotype: 21%

- Reduction in CDI recurrence
  - MODIFY I and II
    - -10.0 difference → NNT = 10 patients
    - 40% relative risk
      - 83,000 episodes of CDI recurrence/year → prevent 33,000/year

FDA Approval and Availability

- Approval October 2016
- McKesson Plasma and Biologics
  - $3,800/1000mg vial
- CMS New Technology Add-On Payment in 2018
  - Maximum of $1,900



CARBAPENEM-RESISTANT ENTEROBACTERIACEAE

9,000 DRUG-RESISTANT INFECTIONS PER YEAR

600 DEATHS

CARBAPENEM-RESISTANT *KLEBSIELLA* SPP. **7,900**

1,400 CARBAPENEM-RESISTANT *E. COLI*

CRE HAVE BECOME RESISTANT TO ALL OR NEARLY ALL AVAILABLE ANTIBIOTICS

THREAT LEVEL
URGENT

This bacteria is an immediate public health threat that requires urgent and aggressive action.

Meropenem-Vaborbactam (Vabormere™)

- FDA-approved August 2017
  - Complicated urinary tract infections (cUTI), including pyelonephritis
- Meropenem
  - Carbapenem antibiotic
  - Mechanism of action:
    - Inhibition of cell wall synthesis
- Vaborbactam
  - New class of β -lactamase inhibitor
  - Activity against β -lactamases which hydrolyze extended spectrum β -lactam antibiotics and carbapenems:
    - Class A β -lactamases: ESBLs and *Klebsiella pneumoniae* carbapenemases (KPC)
    - Class C β-lactamases: AmpC
  - Not active against metallo-β-lactamases or oxacillinases with carbapenemase activity

Antimicrob Agents Chemother 2017; [Ahead of publication].

Spectrum of Activity Against Carbapenem-Resistant Gram-Negatives

Drug(s)	MIC_{50} (μg/ml)	MIC_{90} (μg/ml)
K. pneumoniae (KPC^+) ($n = 121$)		
Piperacillin-tazobactam	>128/4	>128/4
Ceftazidime	>16	>16
Gentamicin	>8	>8
Amikacin	32	64
Ciprofloxacin	>4	>4
Trimethoprim-sulfamethoxazole	>4	>4
Meropenem	8	64
Meropenem-RPX7009 (4 μg/ml)	0.06/4	2/4
Meropenem-RPX7009 (8 μg/ml)	0.03/8	0.5/8
A. baumannii ($n = 84$)		
Ampicillin-sulbactam	32/16	>32/16
Piperacillin-tazobactam	>128/4	>128/4
Ceftazidime	>16	>16
Gentamicin	>8	>8
Amikacin	4	>64
Ciprofloxacin	>4	>4
Trimethoprim-sulfamethoxazole	>4	>4
Meropenem	32	64
Meropenem-RPX7009 (4 μg/ml)	32/4	64/4
Meropenem-RPX7009 (8 μg/ml)	32/8	64/8
P. aeruginosa ($n = 98$)		
Piperacillin-tazobactam	16/4	>128/4
Ceftazidime	8	>16
Amikacin	4	16
Ciprofloxacin	>4	>4
Meropenem	8	32
Meropenem-RPX7009 (4 μg/ml)	8/4	32/4
Meropenem-RPX7009 (8 μg/ml)	8/8	32/8

Antimicrob Agents Chemother 2015; 59: 4856.

Restoration of Activity for KPCs

	Antibiotics MIC (µg/ml) in the presence of varied concentrations of vaborbactam (µg/ml)								
	0	***0.015***	***0.03***	***0.06***	***0.125***	***0.25***	***0.5***	***1***	**MPC_{16}**
Meropenem	**16**	2	1	0.5	0.25	0.25	0.125	≤0.06	**0.03**
Biapenem	**16**	4	4	1	1	0.5	0.25	0.25	**0.06**
Ertapenem	**32**	8	2	1	0.5	0.25	0.25	≤0.06	**0.03**
Tebipenem	**32**	8	2	1	0.5	0.25	0.125	0.125	**0.03**
Imipenem	**8**	8	4	2	1	0.5	0.5	0.5	**0.25**
Aztreonam	**32**	32	32	32	2	1	0.25	0.125	**0.125**
Ceftazidime	**64**	64	64	32	8	4	1	1	**0.25**
Cefepime	**4**	4	2	0.5	0.125	0.06	0.03	0.03	**0.125**

Antimicrob Agents Chemother 2017; [Ahead of publication].

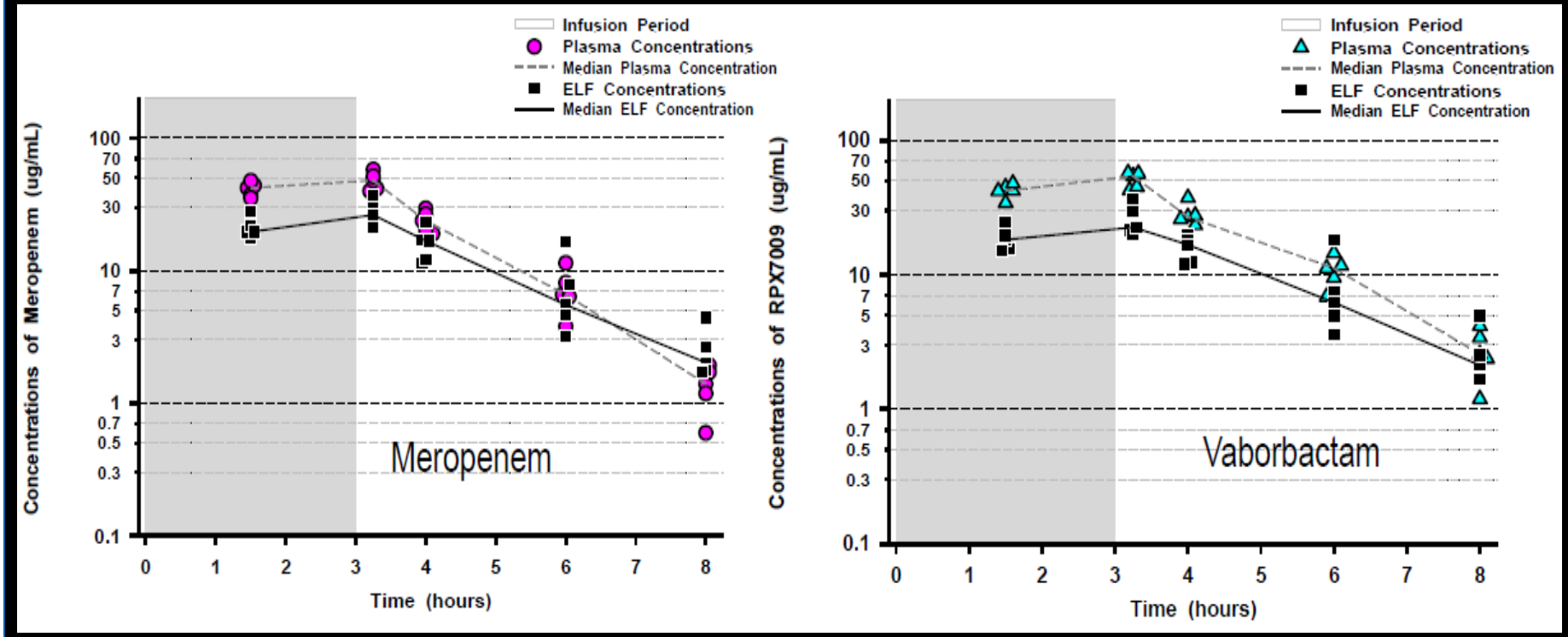
In Vitro Comparison of Activity

MDR strains of Enterobacteriaceae (N=235)

Antibiotic	MIC_{50}	MIC_{90}
Meropenem	0.125	32
Meropenem-vaborbactam	$\leq$ 0.06	1
Ceftazidime	64	>64
Ceftazidime-avibactam	0.5	4
Ceftolozane	8	>32
Ceftolozane-tazobactam	2	>32

Pharmacokinetics

Distribution



Antimicrob Agents Chemother 2015; 59: 7232.

Pharmacokinetics

- Metabolism
  - Hydrolysis of meropenem
  - Vaborbactam does not undergo metabolism
- Excretion
  - Half-life: ~1.5hr
  - Urine
    - 40-60% of meropenem
    - 75-95% vaborbactam
  - 38% meropenem and 53% vaborbactam removed by HD

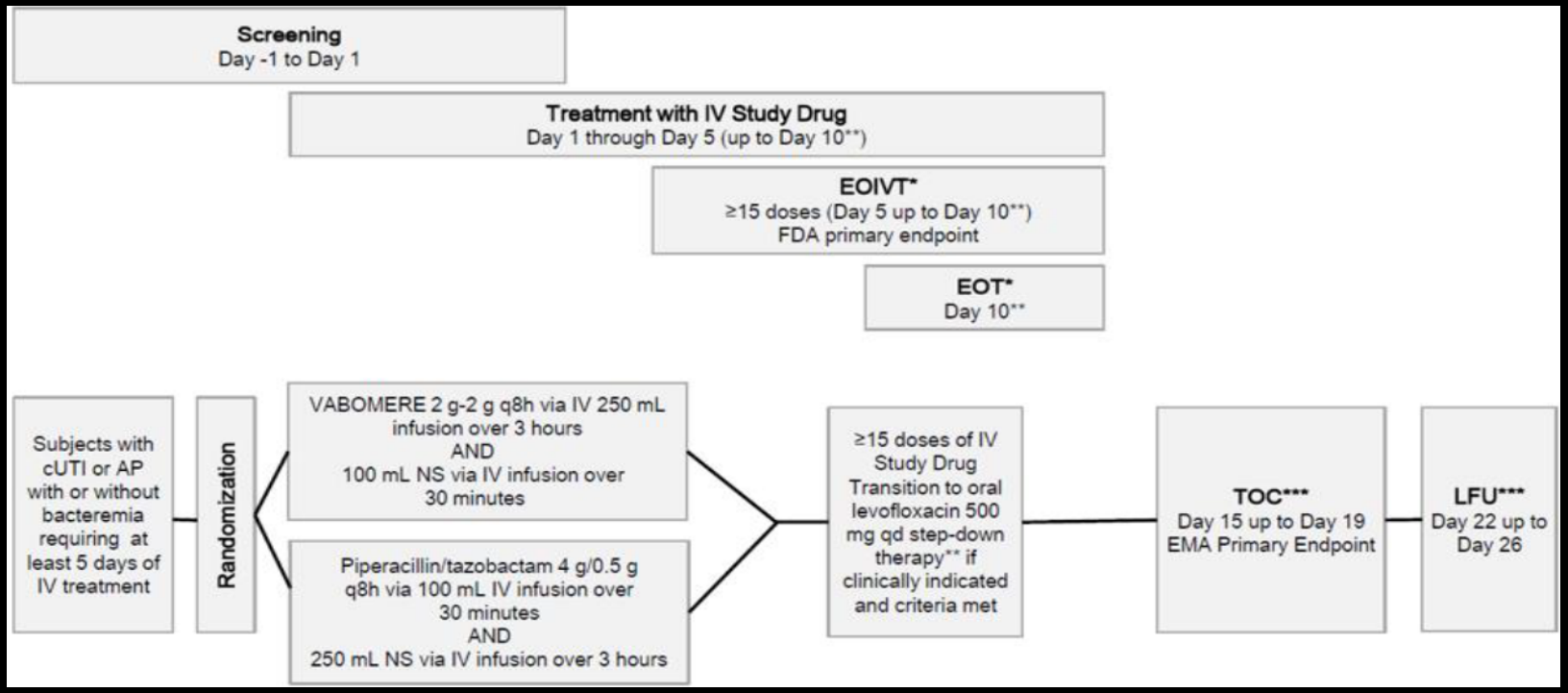
Dosing Recommendations

Creatinine Clearance (mL/min)	Dose	Dosing Interval
≥ 50	4 grams	Q8 hours
30 – 49	2 grams	Q8 hours
15 – 29	2 grams	Q12 hours
< 15 or IHD*	1 gram	Q12 hours

*Give after hemodialysis (IHD)
Administered as a 3 hour infusion

Targeting Antibiotic Non-susceptible Gram-negative Organisms (TANGO I)

- Multicenter, double-blind, double-dummy, randomized, parallel-group study
  - Treatment of cUTI, including acute pyelonephritis (AP)

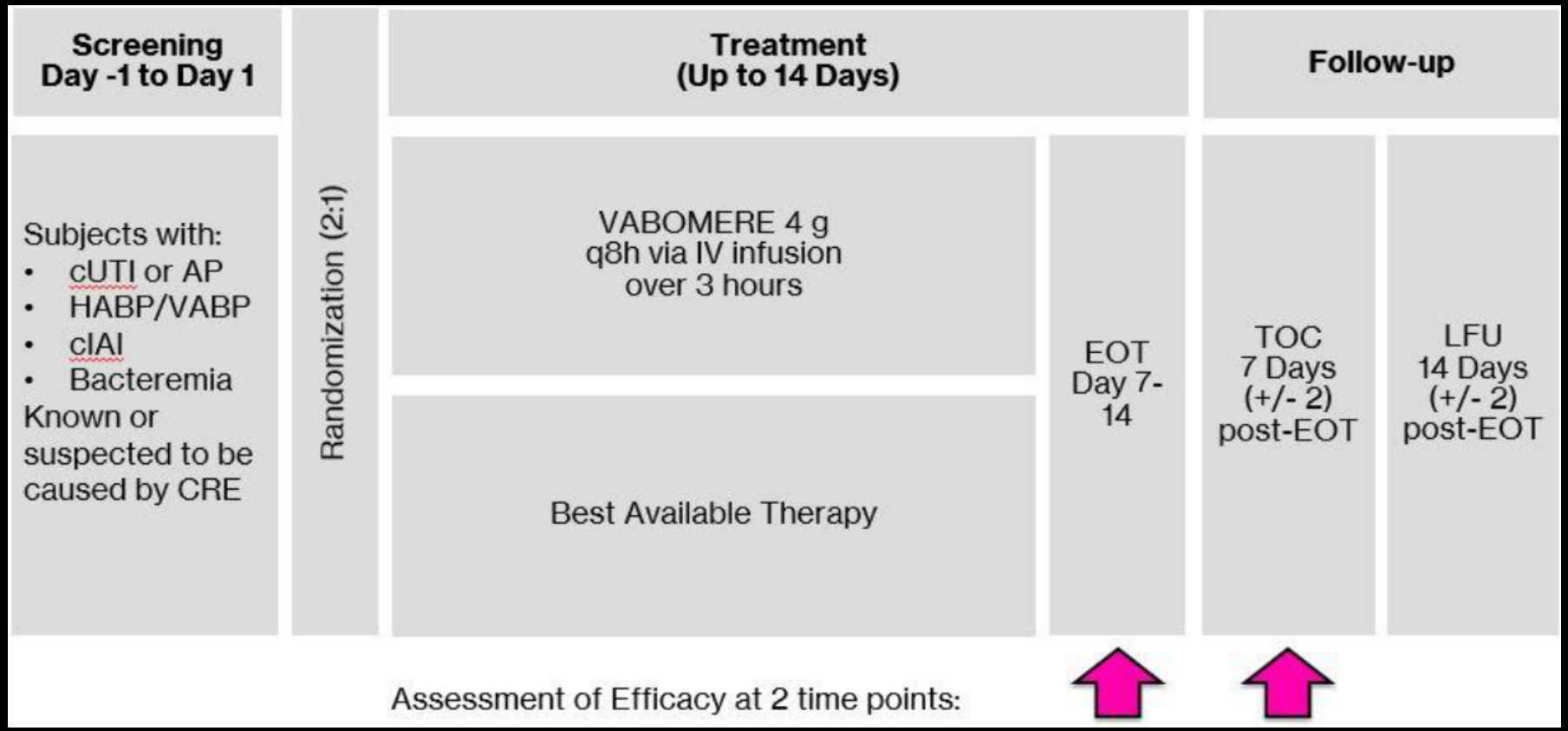


Results by Primary Endpoint

Primary Endpoint	VABOMERE (n=192) n (%)	piperacillin/ tazobactam (n=182) n (%)	Difference (95% CI)
FDA*			
Overall success rate at EOIVT			
m-MITT Population	182/192 (98.4)	171/182 (94.0)	4.5 (0.7, 9.1)
EMA**			
Overall eradication rate at TOC			
m-MITT population	128/192 (66.7)	105/182 (57.7)	9.0 (-0.9, 18.7)
ME population	118/178 (66.3)	102/169 (60.4)	5.9 (-4.2, 16.0)

TANGO II Trial

- Multicenter, randomized, open-label trial



Patient Baseline Characteristics	VABOMERE N = 28 n, (%)	BAT N = 15 n, (%)	Total N = 43 N, (%)
Age years: mean (± SD)	63.9 (± 14.0)	60.2 (±13.0)	62.6 (± 13.6)
>65 years	14 (50.0%)	6 (40.0%)	20 (46.5%)
>75 years	6 (21.4%)	3 (20.0%)	9 (20.9%)
CrCl ≥50 mL/min	22 (78.6%)	9 (60.0%)	31 (72.1%)
30-49 ml/min	3 (10.7%)	2 (13.3%)	5 (11.6%)
20-29 ml/min	1 (3.6%)	2 (13.3%)	3 (7.0%)
< 20 ml/min	1 (3.6%)	0 (0%)	1 (2.3%)
Infection type, n (%)			
Bacteremia	12 (43)	8 (53)	20 (47)
cUTI/AP	11 (39)	4 (27)	15 (35)
HABP/VABP	4 (14)	1 (7)	5 (12)
cIAI	1 (4)	2 (13)	3 (7)
Baseline pathogen, n (%)*			
Klebsiella pneumoniee	25/28 (89.3%)	12/15 (80%)	37/43 (86%)
Escherichia coli	2/28 (7.1%)	1/15 (6.7%)	3/43 (7%)
Enterobacter cloacae species complex	1/28 (3.6)	2/15 (13.3%)	3/43 (7%)
Proteus mirabilis	0/28 (0)	2/15 (13.3%)	2/43 (4.7%)
Serratia marcescens	1/28 (3.6%)	1/15 (6.7%)	2/32 (4.7%)
Enrolled as known CRE, n (%)	20 (71)	14 (93)	34 (79)
Enrolled as suspected CRE, n (%)	8 (29)	1 (7)	9 (21)
Diabetes mellitus	9 (32.1%)	7 (46.7%)	16 (37.2%)
SIRS**	12 (42.9%)	6 (40.0%)	18 (41.9%)
Charlson Comorbidity Index Score ≥ 5	21 (75.0%)	12 (80.0%)	33 (76.7%)
Immunocompromised†	10 (35.7%)	8 (53.3%)	18 (41.9%)

Clinical Outcomes Across All Indications (mCRE-MITT Population)

Time Point Clinical Response	VABOMERE (N=28) n, (%)	BAT (N=15) n, (%)	Absolute Percent Difference (VAB-BAT) 95% CI	Relative Percent Difference [(VAB-BAT)/BAT]
End of Therapy				
Cure	18 (64.3%)	5 (33.3%)	30.9% (1.2% to 60.7%) p = 0.04	+60.8%
Test of Cure				
Cure	16 (57.1%)	4 (26.7%)	30.4% (1.5% to 59.4%) p = 0.03	+113.9%
Day-28 Mortality	5 (17.9%)	5 (33.3%)	-15.5% (-43.23% to 12.28%)	-46.2%

Sensitivity Analysis & Safety

Time Point Clinical Response	VABOMERE (N=19) n, (%)	BAT (N=15) n, (%)	Absolute Percent Difference (VAB-BAT) 95% CI	Relative Percent Difference [(VAB-BAT)/BAT]
End of Therapy				
Cure	16 (84.2%)	5 (33.3%)	50.9% (21.9% to 79.8%)	+152.9%
Test of Cure				
Cure	13 (68.4%)	4 (26.7%)	41.8% (11.1% to 72.4%)	+156.2%
Day-28 Mortality	1 (5.3%)	5 (33.3%)	-28.1% (-57.2% to 6.3%)	-84.1%

- Common adverse reactions:
  - Headache (8%)
  - GI upset (5.2%)
  - Phlebitis (4.4%)
  - Hypersensitivity (1.8%)

Delafloxacin (Baxdela™)

- FDA-approved August 2017
  - Acute bacterial skin and skin structure infections (ABSSSIs)
- Fluoroquinolone
  - Mechanism of action: topoisomerase IV and DNA gyrase
- Enhancements
  - Increased activity in acidic environments (abscesses, urine, vagina, and stomach)
  - Higher affinity for targets → more resistance required for resistance
  - Biofilm activity

Spectrum of Activity

Gram-Positive	Gram-Negatives	Anaerobes	Atypicals
S. aureus (MRSA)	*E. coli*	*Bacteroides* sp.	*Mycoplasma* sp.
S. lugdunensis	*E. cloacae*	*Prevotella* sp.	*Ureaplasma* sp.
S. haemolyticus	*K. pneumoniae*	*C. difficile*	*Chlamydia* sp.
S. anginosus Group	*P. aeruginosa*	*C. perfringens*	
S. pneumoniae	*H. influenzae*		**Other**
S. agalactiae	*M. catarrhalis*		*M. tuberculosis*
S. pyogenes	*N. gonorrhoeae*		
E. faecalis	*N. meningitidis*		

Pharmacokinetics

- Absorption
  - Oral bioavailability 58.8%
- Distribution
  - Plasma protein binding 84%
- Metabolism via glucuronidation
- Elimination
  - Half life ~3.7h
  - 65% excreted in urine, 28% in feces

Dosing Recommendations

Creatinine Clearance (eGFR)	PO	IV (60 min infusion)
≥ 90	450mg q12h	300mg q12h
30-89	No adjustment	No adjustment
15-29	No adjustment	200mg q12h OR 200mg q12h, then 450mg PO q12h
< 15, including HD	Not recommended	

19% removed by hemodialysis

Delafloxacin versus Tigecycline for cSSTIs

	Delafloxacin 300mg IV	Delafloxacin 450 mg IV	Tigecycline 50 mg IV
Staphylococcus aureus	*n*=22	*n* =27	*n* = 20
Cure, *n* (%)	21 (95.5)	25 (92.6)	18 (90.0)
Failure, *n* (%)	1 (4.5)	2 (7.4)	2 (10.0)
MRSA	*n*=14	*n* =20	*n* = 14
Cure, *n* (%)	13 (92.9)[a,b]	19 (95.0)[c]	12 (85.7)
Failure, *n* (%)	1 (7.1)	1 (5.0)	2 (14.3)
MSSA	*n*=8	*n* =7	*n* = 6
Cure, *n* (%)	8 (100.0)	6 (85.7)	6 (100.0)
Failure, *n* (%)	-	1 (14.3)	-

Int J Infect Dis 2015;3:67-73.

Delafloxacin versus Vancomycin or Linezolid for ABSSSIs

	Delafloxacin	Linezolid	Vancomycin
Outcome/measurement technique			
erythema/digital measurement			
cessation of spread,[a] *n/N* (%)	61/78 (78.2)	56/75 (74.7)	69/95 (72.6)
20% reduction, *n/N* (%)	58/78 (74.4)	55/75 (73.3)	65/95 (68.4)
percentage change in area at follow-up, mean (SD)	−96.4 (13.96)	−87.7 (39.22)	−84.5 (35.73)[b]
Induration/digital measurement			
cessation of spread,[a] *n/N* (%)	54/78 (69.2)	47/75 (62.7)	72/95 (75.8)
20% reduction, *n/N* (%)	44/78 (56.4)	40/75 (53.3)	66/95 (69.5)
percentage change in area at follow-up, mean (SD)	−73.5 (48.56)	−77.1 (47.02)	−84.8 (30.05)
Body temperature (°C)[c]			
change from baseline to follow-up, mean (SD)	−0.2 (0.53)	−0.2 (0.59)	−0.2 (0.76)
Serum CRP (mg/L)[d]			
change from baseline to follow-up, mean (SD)	−37.4 (64.90)	−38.1 (54.51)	−43.2 (64.90)
Serum IL-6 (ng/L)[e]			
change from baseline to follow-up, mean (SD)	−7.9 (15.84)	−8.7 (19.11)	−9.7 (19.33)[b]

J Antimicrob Chemother 2016;71:821-29.

Still to Come…

- Safety and efficacy in acute bacterial exacerbation of chronic bronchitis
  - Phase 2
- Phase 3 studies
  - Delafloxacin versus vancomycin + aztreonam → ABSSSIs
  - Delafloxacin for community-acquired pneumonia
- Oral delafloxacin versus IM ceftriaxone for uncomplicated gonorrhea

Adverse Effects and Warnings

- Fluoroquinolone class effects
  - Tendonitis and tendon rupture
  - Peripheral neuropathy
  - CNS reactions
  - Exacerbation of Myasthenia Gravis

Adverse Reactions	BAXDELA N = 741 (%)
Nausea	8%
Diarrhea	8%
Headache[#]	3%
Transaminase Elevations*	3%
Vomiting	2%

Baxdela [Package Insert] 2017

Battle of the Bugs: An Antibiotic Update

WHITNEY JONES NESBITT, PHARMD, BCPS
ANTIMICROBIAL STEWARDSHIP PHARMACIST
VANDERBILT UNIVERSITY MEDICAL CENTER
SEPTEMBER 15, 2017