

Revised Abstract

Background: The Tigecycline European Surveillance Trial has surveyed a large number of isolates to determine the variability, if any, of tigecycline's *in vitro* activity against clinical pathogens taken from various infectious sources. This report evaluates differences in susceptibility of anaerobic isolates from different body sites collected in Europe between 2009-2010. **Methods:** 2,292 clinically significant anaerobes from 32 cumulative sites in 7 European countries were analyzed. Isolates were identified to the species level at the participating sites and confirmed by the central laboratory. MICs were determined using agar dilution and interpreted according to EUCAST breakpoints where available. MIC₉₀ values and % susceptible were analyzed to identify any significant differences in antibiograms from different sources. **Results:** Summary data of tigecycline activity against selected pathogens and body sources are shown in the table below:

Organism	Tigecycline - MIC ₉₀ /%Susceptible (n)					
	Blood	Gastro-intestinal	Genito-urinary	Skin / Skin Structures	Body fluids	Other
<i>Bacteroides</i> spp.	2/100 (45)	4/100 (48)	2/100 (14)	2/98 (298)	2/99 (489)	4/96 (134)
<i>Clostridium</i> spp.*	2/100 (26)	1/100 (17)	na/100 (2)	1/99 (81)	0.5/100 (153)	0.5/100 (79)
<i>Peptoniphilus</i> spp.	na/100 (5)	na/100 (2)	--/ (0)	0.06/100 (32)	≤0.06/100 (17)	0.12/100 (21)
<i>Peptostrept.</i> spp.	≤ 0.06/100 (11)	na/100 (10)	na/100 (2)	0.12/100 (147)	0.12/100 (135)	0.12/100 (68)
<i>Prevotella</i> spp.	na/100 (9)	1/94 (18)	0.5/100 (12)	0.5/99 (113)	0.5/100 (184)	1/99 (120)

na, MIC₉₀ not calculated for n≤10. *Does not include *C. difficile*.

Conclusions: Tigecycline showed excellent inhibitory activity against all groups of anaerobic pathogens regardless of isolation site. Bacteria isolated from different body sites had similar antibiograms, with no isolates from any single source showing significantly different sensitivity patterns (p>0.05, Fisher's exact test). Tigecycline's MIC₉₀ of ≤4 mcg/ml against all anaerobic isolates validates the potent activity of this antimicrobial against a variety of anaerobic pathogens.

Introduction

Increasing antibacterial resistance in anaerobes over the past two decades has increased the necessity for periodic monitoring of local and regional resistance patterns of clinically important isolates. Emergence of highly virulent or multidrug-resistant strains adversely affects clinical outcome, resulting in increased probability of treatment failure and mortality. Management of anaerobic infections encompasses surgical procedures, antibacterial therapy and adjuncts. Since many clinical laboratories do not perform susceptibility testing on anaerobes, most therapy is empirical, with clinicians relying on published studies to guide therapy. At present, metronidazole, carbapenems, and β-lactam/β-lactamase inhibitor combinations exhibit the most promising activity, though reports of increasing resistance to these agents are emerging [1]. Recent data from the Tigecycline European Surveillance Trial (TEST) has shown that in addition to the above agents, tigecycline also exhibits promising activity with high susceptibilities against a wide range of anaerobes [2]. Tigecycline has also demonstrated promising activity against recent clinical isolates of *Bacteroides fragilis* with reduced carbapenem susceptibility [3]. The current study describes data from TEST, 2009 to 2010, based on the activity of tigecycline and comparators against 2,292 anaerobic isolates from various body sites.

Materials & Methods

Clinical isolates: A total of 2,292 clinical isolates of gram-negative and gram-positive anaerobes were studied. These included 1,028 isolates of *Bacteroides* spp., 358 *Clostridium* spp. (not including *C. difficile*), 77 *Peptoniphilus* spp., 373 *Peptostreptococcus* spp. and 456 *Prevotella* spp. Isolates were identified to the species level and tested at each participating laboratory. All organisms were deemed clinically significant by local participant criteria. Isolate inclusion was independent of medical history, antimicrobial use, age or gender. Sites identified each study isolate utilizing local laboratory criteria. All isolates were from the period 2009 – 2010 and originated from various countries in Europe and from multiple clinical sources and locations.

Susceptibility testing: All isolates were sent to a single reference laboratory for final evaluation. Minimum inhibitory concentrations (MICs) were determined by agar dilution as specified by the Clinical and Laboratory Standards Institute (CLSI) [4]. Susceptibilities were determined using EUCAST clinical breakpoints [5] for all agents except tigecycline, where FDA clinical breakpoints [6] were used and cefoxitin, where CLSI breakpoints were used [7].

References

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Results

Table 1. Activity of tigecycline and comparators against 1,028 *Bacteroides* spp. from different body sites, 2009 – 2010.

Drug	MIC ₅₀ / MIC ₉₀ (mcg/ml)					
	Blood (45)	GI (48)	GU (14)	SSS (298)	Body Fluids (489)	Other (134)
Cefoxitin	8/32	8/32	8/32	4/32	4/32	4/32
Clindamycin	2/>8	0.5/>8	1/>8	1/>8	1/>8	1/>8
Meropenem	0.12/4	≤0.06/0.5	0.12/1	0.12/0.5	0.12/0.5	≤0.06/0.5
Metronidazole	0.5/1	0.5/2	1/1	1/2	0.5/2	0.5/2
Pip-Tazo	0.5/8	0.5/8	0.5/16	0.5/8	0.25/8	0.25/16
Tigecycline	0.5/2	0.25/4	0.25/2	0.5/2	0.5/2	0.25/4

GI = Gastrointestinal; GU = Genital/urinary; SSS = Skin and skin structures.

Table 2. Activity of tigecycline and comparators against 358 *Clostridium* spp.* from different body sites, 2009 – 2010.

Drug	MIC ₅₀ / MIC ₉₀ (mcg/ml)					
	Blood (26)	GI (17)	GU (2)	SSS (81)	Body Fluids (153)	Other (79)
Clindamycin	1/>8	≤0.25/>8	na	0.5/>8	1/>8	0.5/>8
Meropenem	≤0.06/0.5	≤0.06/2	na	≤0.06/1	≤0.06/1	≤0.06/1
Metronidazole	0.5/2	0.5/2	na	0.5/4	1/2	1/2
Penicillin	≤0.25/1	0.5/32	na	≤0.25/1	≤0.25/2	≤0.25/1
Pip-Tazo	0.12/2	1/32	na	0.12/4	0.25/4	≤0.06/1
Tigecycline	0.25/2	≤0.06/1	na	≤0.06/1	≤0.06/0.5	≤0.06/0.5

GI = Gastrointestinal; GU = Genital/urinary; SSS = Skin and skin structures; na = MIC₅₀/MIC₉₀ not calculated for n ≤10. *Does not include *C. difficile*.

Table 3. Activity of tigecycline and comparators against 77 *Peptoniphilus* spp. from different body sites, 2009 – 2010.

Drug	MIC ₅₀ / MIC ₉₀ (mcg/ml)				
	Blood (5)	GI (2)	SSS (32)	Body Fluids (17)	Other (21)
Clindamycin	na	na	≤0.25/>8	≤0.25/1	1/>8
Meropenem	na	na	≤0.06/≤0.06	≤0.06/≤0.06	≤0.06/≤0.06
Metronidazole	na	na	0.25/1	0.25/0.5	0.5/1
Penicillin	na	na	≤0.25/≤0.25	≤0.25/≤0.25	≤0.25/≤0.25
Pip-Tazo	na	na	≤0.06/≤0.06	≤0.06/≤0.06	≤0.06/0.5
Tigecycline	na	na	≤0.06/0.06	≤0.06/≤0.06	≤0.06/0.12

GI = Gastrointestinal; GU = Genital/urinary; SSS = Skin and skin structures; na = MIC₅₀/MIC₉₀ not calculated for n ≤10.

Table 4. Activity of tigecycline and comparators against 373 *Peptostreptococcus* spp. from different body sites, 2009 – 2010.

Drug	MIC ₅₀ / MIC ₉₀ (mcg/ml)					
	Blood (11)	GI (10)	GU (2)	SSS (147)	Body Fluids (135)	Other (68)
Clindamycin	≤0.25/≤0.25	na	na	≤0.25/4	≤0.25/2	≤0.25/1
Meropenem	≤0.06/≤0.06	na	na	≤0.06/0.25	≤0.06/0.25	≤0.06/0.12
Metronidazole	0.25/0.5	na	na	0.25/0.5	0.12/0.5	0.25/0.5
Penicillin	≤0.25/≤0.25	na	na	≤0.25/≤0.25	≤0.25/≤0.25	≤0.25/0.5
Pip-Tazo	≤0.06/≤0.06	na	na	≤0.06/0.25	≤0.06/0.25	≤0.06/0.25
Tigecycline	≤0.06/≤0.06	na	na	≤0.06/0.12	≤0.06/0.12	≤0.06/0.12

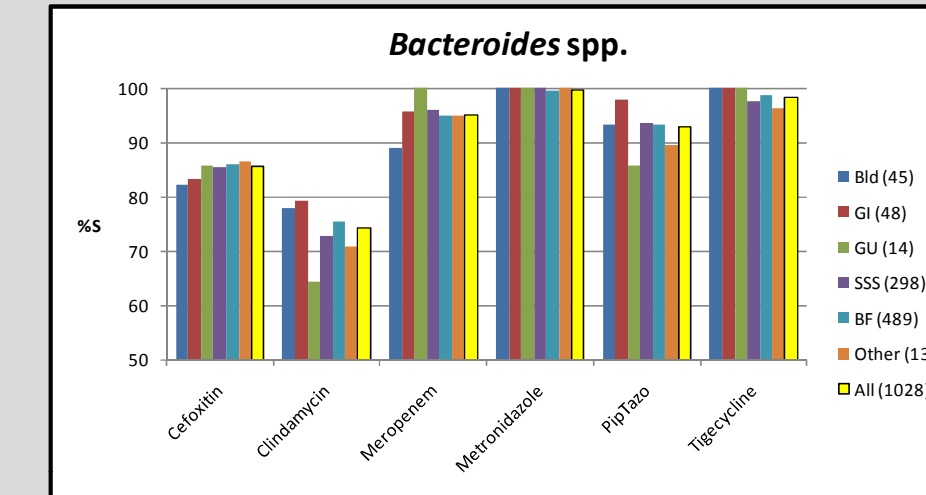
GI = Gastrointestinal; GU = Genital/urinary; SSS = Skin and skin structures; na = MIC₅₀/MIC₉₀ not calculated for n ≤10.

Table 5. Activity of tigecycline and comparators against 456 *Prevotella* spp. from different body sites, 2009 – 2010.

Drug	MIC ₅₀ / MIC ₉₀ (mcg/ml)					
	Blood (9)	GI (18)	GU (12)	SSS (113)	Body Fluids (184)	Other (120)
Cefoxitin	na	≤2/8	≤2/≤2	≤2/8	≤2/8	≤2/4
Clindamycin	na	0.5/>8	≤0.25/0.5	≤0.25/>8	≤0.25/>8	≤0.25/>8
Meropenem	na	≤0.06/0.12	≤0.06/≤0.06	≤0.06/0.12	≤0.06/0.25	≤0.06/0.12
Metronidazole	na	0.5/2	1/1	0.5/2	0.5/1	0.5/2
Pip-Tazo	na	≤0.06/1	≤0.06/≤0.06	≤0.06/1	≤0.06/1	≤0.06/1
Tigecycline	na	0.25/1	≤0.06/0.5	0.12/0.5	0.12/0.5	0.12/1

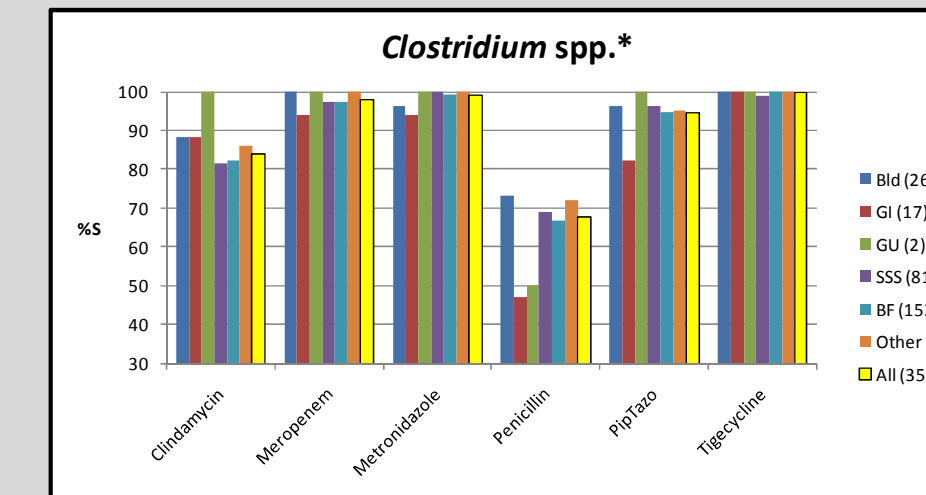
GI = Gastrointestinal; GU = Genital/urinary; SSS = Skin and skin structures; na = MIC₅₀/MIC₉₀ not calculated for n ≤10.

Figure 1. Susceptibility of 1,028 *Bacteroides* spp. to tigecycline and comparators by body site.



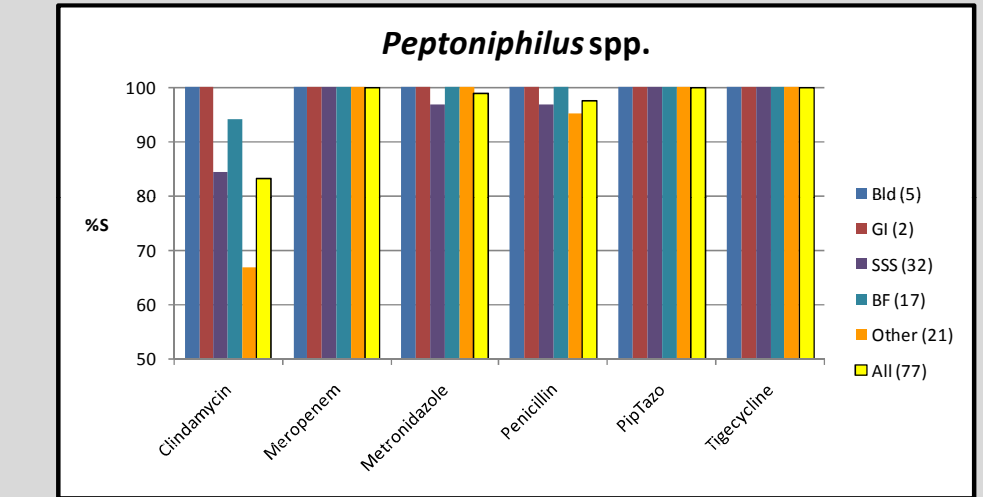
Bld = Blood; GI = Gastrointestinal; GU = Genital/Urinary; SSS = Skin and Skin Structures; BF = Body Fluid.

Figure 2. Susceptibility of 358 *Clostridium* spp. to tigecycline and comparators by body site.



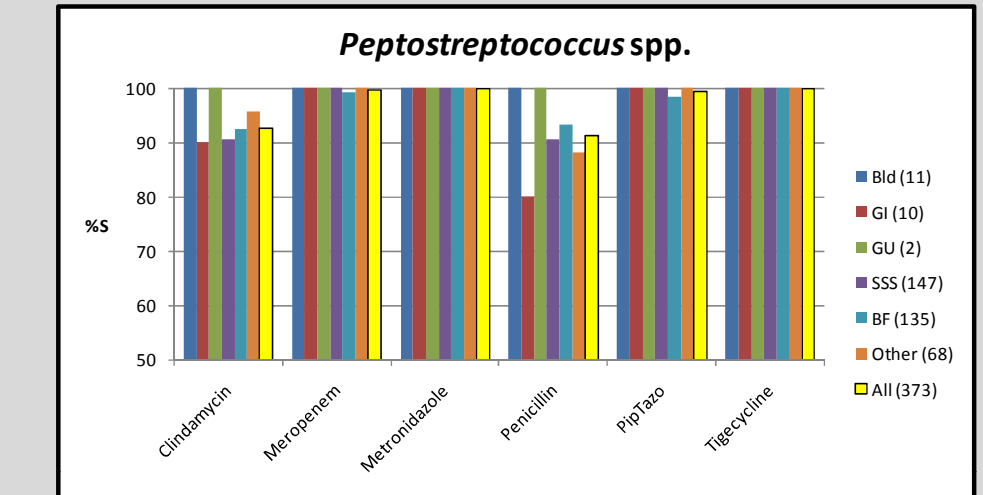
Bld = Blood; GI = Gastrointestinal; GU = Genital/Urinary; SSS = Skin and Skin Structures; BF = Body Fluid; OT = Other *Does not include *C. difficile*

Figure 3. Susceptibility of 77 *Peptoniphilus* spp. to tigecycline and comparators by body site.



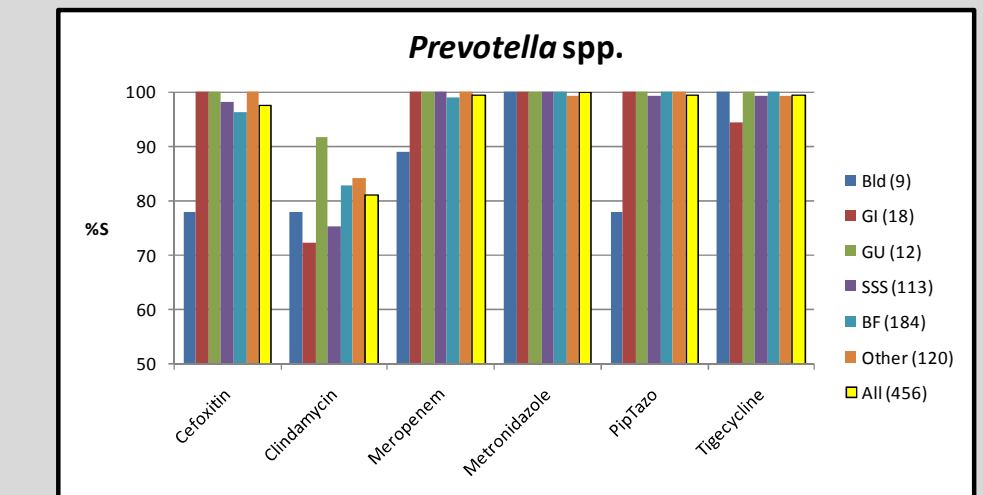
Bld = Blood; GI = Gastrointestinal; SSS = Skin and Skin Structures; BF = Body Fluid.

Figure 4. Susceptibility of 373 *Peptostreptococcus* spp. to tigecycline and comparators by body site.



Bld = Blood; GI = Gastrointestinal; GU = Genital/Urinary; SSS = Skin and Skin Structures; BF = Body Fluid.

Figure 5. Susceptibility of 456 *Prevotella* spp. to tigecycline and comparators by body site.



Bld = Blood; GI = Gastrointestinal; GU = Genital/Urinary; SSS = Skin and Skin Structures; BF = Body Fluid.

Conclusions

- Bacteria isolated from different body sites had similar antibiograms, with no isolates from any single source showing significantly different sensitivity patterns when each body site was compared to other body sites for each antibiotic (p>0.05, Fisher's exact test).
- Percent susceptibilities for *Bacteroides* spp. were >90% for metronidazole and tigecycline for all isolates.
- Tigecycline exhibited excellent *in vitro* activity against all groups of anaerobic bacteria isolated from hospitals in Europe throughout 2009- 2010 with an MIC₉₀ of ≤4 mcg/ml against all isolates and susceptibility ≥98% for all studied species.