

Revised Abstract

Background: The TEST program 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 2007-2008. **Methods:** 1,882 clinically significant anaerobes from 32 sites in 7 European countries were analyzed. Isolates were identified to the species level at the participating sites and confirmed by the central laboratory. Tigecycline MICs were determined using agar dilution and interpreted according to FDA breakpoints. 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 / %Sus (n)				
	Blood	Gastro-intestinal	Genito-urinary	Skin / Skin Structures	Other
<i>Bacteroides</i> spp. (790)	2/95.4 (65)	4/94.1 (136)	4/97 (33)	1/99.2 (133)	2/98.3 (423)
<i>Clostridium</i> spp. (541)	0.5/100 (32)	0.5/98.9 (179)	≤0.06/100 (2)	1/98.5 (66)	0.5/100 (262)
<i>Peptoniphilus</i> spp. (51)	≤0.06/100 (3)	≤0.06/100 (2)	0.12/100 (3)	0.12/100 (19)	0.25/100 (24)
<i>Peptostreptococcus</i> spp. (183)	0.12/100 (10)	≤0.06/100 (8)	≤0.06/100 (7)	0.12/100 (75)	0.12/100 (83)
<i>Prevotella</i> spp. (317)	1/100 (6)	0.5/100 (21)	1/97 (33)	1/99 (105)	1/99.3 (152)

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). Tigecycline's MIC₉₀ of ≤2 mcg/ml against all anaerobic isolates validate 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 beta-lactam/beta-lactamase inhibitor combinations exhibit the most promising activity though reports of increasing resistance to these agents are emerging (1). Recent data from the Tigecycline Evaluation and Surveillance Trial (T.E.S.T.) 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 T.E.S.T. Europe, from 2007 to 2008, based on the activity of tigecycline and comparators against 2,333 anaerobic isolates from various body sites.

Materials & Methods

Clinical isolates: A total of 2,333 clinical isolates of gram-negative and gram-positive anaerobes were studied. These included 952 isolates of *Bacteroides* spp., 787 *Clostridium* spp., 60 *Peptoniphilus* spp., 197 *Peptostreptococcus* spp. and 337 *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 2007 – 2008 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 evaluation. Minimum inhibitory concentrations (MICs) were determined by agar dilution as specified by the Clinical and Laboratory Standards Institute (CLSI) (4). Tigecycline susceptibility was determined using FDA clinical breakpoints (5); susceptibility to all other agents was determined using CLSI breakpoints (6).

References

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Results

Table 1. Activity of tigecycline and comparators against 952 *Bacteroides* spp. from different body sites, 2007 – 2008.

Drug	Blood (118)	GI (49)	GU (41)	SSS (161)	Body Fluids (409)	Other (174)
Cefoxitin	8/32	8/32	8/32	8/32	8/32	4/16
Clindamycin	1/>8	1/>8	1/>8	1/>8	1/>8	1/>8
Meropenem	0.12/0.5	0.12/1	0.12/0.5	0.12/0.5	0.12/0.5	0.12/0.5
Metronidazole	0.5/1	0.5/2	0.5/2	0.5/1	0.5/1	0.5/1
Pip/Tazo	0.5/8	1/8	0.5/16	0.5/8	0.5/8	0.5/8
Tigecycline	0.5/2	0.5/1	0.5/4	0.5/2	0.5/2	0.5/2

GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and skin structures

Table 2. Activity of tigecycline and comparators against 787 *Clostridium* spp. from different body sites, 2007 – 2008.

Drug	Blood (49)	GI (185)	GU (5)	SSS (67)	Body Fluids (322)	Other (159)
Clindamycin	1/8	4/8	na	1/8	2/8	4/8
Meropenem	≤0.06/1	1/2	na	≤0.06/1	0.5/2	0.5/1
Metronidazole	1/2	0.5/2	na	0.5/2	0.5/2	0.5/2
Penicillin	≤0.25/1	1/4	na	≤0.25/1	1/4	1/4
Pip/Tazo	0.12/8	4/8	na	0.12/4	2/8	4/8
Tigecycline	≤0.06/1	≤0.06/0.25	na	0.12/1	≤0.06/0.5	≤0.06/0.5

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

Table 3. Activity of tigecycline and comparators against 60 *Peptoniphilus* spp. from different body sites, 2007 – 2008.

Drug	Blood (6)	GI (2)	GU (7)	SSS (15)	Body Fluids (16)	Other (14)
Clindamycin	na	na	na	≤0.25/8	≤0.25/8	≤0.25/0.5
Meropenem	na	na	na	≤0.06/0.12	≤0.06/0.06	≤0.06/0.12
Metronidazole	na	na	na	0.5/1	0.5/1	0.5/1
Penicillin	na	na	na	≤0.25/0.5	≤0.25/0.25	≤0.25/0.5
Pip/Tazo	na	na	na	≤0.06/0.5	≤0.06/0.12	≤0.06/0.5
Tigecycline	na	na	na	≤0.06/0.12	≤0.06/0.25	≤0.06/0.12

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

Table 4. Activity of tigecycline and comparators against 197 *Peptostreptococcus* spp. from different body sites, 2007 – 2008.

Drug	Blood (10)	GI (6)	GU (10)	SSS (54)	Body Fluids (80)	Other (37)
Clindamycin	≤0.25/0.5	na	≤0.25/0.5	≤0.25/1	≤0.25/1	≤0.25/1
Meropenem	≤0.06/≤0.06	na	≤0.06/0.12	≤0.06/0.25	≤0.06/0.25	≤0.06/0.12
Metronidazole	0.25/0.5	na	0.25/0.5	0.25/1	0.25/0.5	0.25/0.5
Penicillin	≤0.25/≤0.25	na	≤0.25/0.5	≤0.25/0.5	≤0.25/0.5	≤0.25/0.5
Pip/Tazo	≤0.06/≤0.06	na	≤0.06/0.25	≤0.06/0.25	≤0.06/0.25	≤0.06/0.25
Tigecycline	≤0.06/≤0.06	na	≤0.06/≤0.06	≤0.06/0.12	≤0.06/0.12	≤0.06/0.25

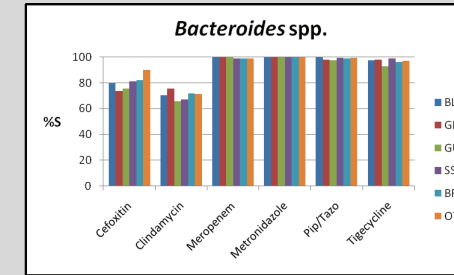
GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and skin structures; na = MIC₉₀/MIC₅₀ not calculated for n ≤10

Table 5. Activity of tigecycline and comparators against 337 *Prevotella* spp. from different body sites, 2007 – 2008.

Drug	Blood (7)	GI (25)	GU (62)	SSS (81)	Body Fluids (113)	Other (49)
Cefoxitin	na	≤2/8	≤2/8	≤2/8	4/16	≤2/8
Clindamycin	na	≤0.25/8	≤0.25/8	≤0.25/8	≤0.25/8	≤0.25/2
Meropenem	na	≤0.06/0.25	≤0.06/0.25	≤0.06/0.12	≤0.06/0.25	≤0.06/0.25
Metronidazole	na	1/1	1/2	1/2	1/2	0.5/1
Pip/Tazo	na	≥0.06/2	≤0.06/0.5	≤0.06/1	0.12/2	≤0.06/4
Tigecycline	na	0.25/1	0.5/2	0.25/1	0.25/1	0.12/0.5

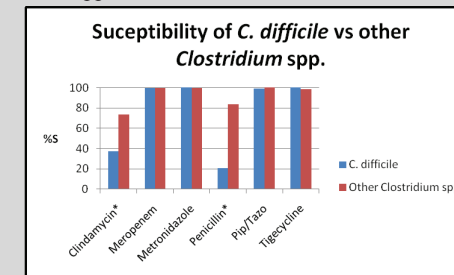
GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and skin structures; na = MIC₉₀/MIC₅₀ not calculated for n ≤10

Figure 1. % Susceptible of *Bacteroides* spp. from different body sites



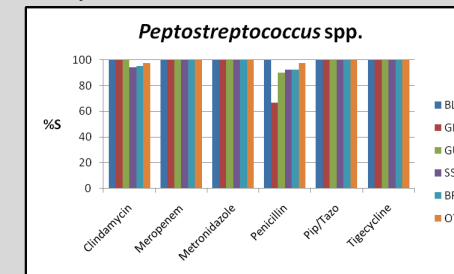
BLD = Blood; GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and Skin Structures; BF = Body Fluid; OT = Other

Figure 3. Susceptibility (%) of 285 *C. difficile* vs 341 other *Clostridium* spp.



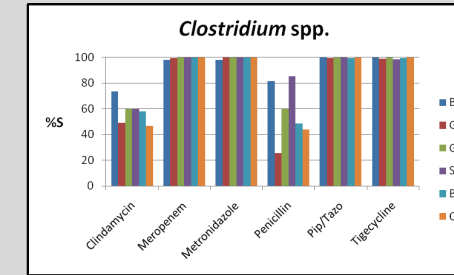
*p<0.0001

Figure 5. % Susceptible of *Peptostreptococcus* spp. from different body sites



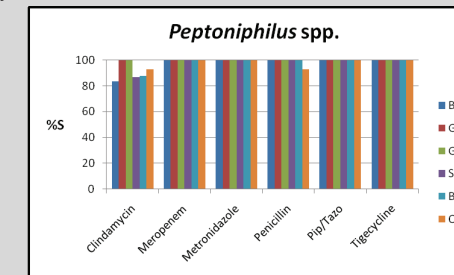
BLD = Blood; GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and Skin Structures; BF = Body Fluid; OT = Other

Figure 2. % Susceptible of *Clostridium* spp. from different body sites



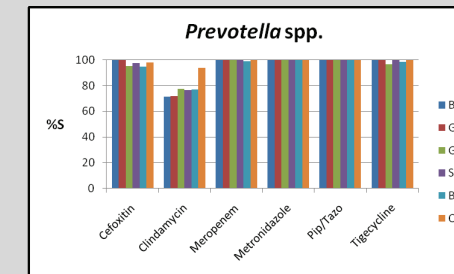
BLD = Blood; GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and Skin Structures; BF = Body Fluid; OT = Other

Figure 4. % Susceptible of *Peptoniphilus* spp. from different body sites



BLD = Blood; GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and Skin Structures; BF = Body Fluid; OT = Other

Figure 6. % Susceptible of *Prevotella* spp. from different body sites



BLD = Blood; GI = Gastrointestinal; GU = Genitourinary; SSS = Skin and Skin Structures; BF = Body Fluid; OT = Other

Conclusions

- Tigecycline exhibited excellent *in vitro* activity against anaerobic bacteria isolated from hospitals throughout 2007 to 2008 with an MIC₉₀ of ≤4 mcg/ml against all isolates.
- There were no marked differences in activity by body site for most drug/species combinations (p>0.05) where sufficient data exist.
- Percent susceptibilities for *Bacteroides* spp. were >90% for meropenem, metronidazole, piperacillin/tazobactam and tigecycline.
- While susceptibility of *Clostridium* spp. showed variability by body site (p<0.05), an uneven distribution of *C. difficile* among body sites accounts for the statistical differences.