HHS Public Access
Author manuscript
Anaerobe. Author manuscript; available in PMC 2018 October 01.

Published in final edited form as:
Anaerobe. 2017 October ; 47: 115–119. doi:10.1016/j.anaerobe.2017.05.005.

Susceptibility of bacterial vaginosis (BV)-associated bacteria to secnidazole compared to metronidazole, tinidazole and clindamycin

Melinda A.B. Petrina[a], **Lisa A. Cosentino**[a], **Lorna K. Rabe**[a], and **Sharon L. Hillier**[a,b]

[a]Magee-Womens Research Institute, 204 Craft Avenue, Pittsburgh, PA 15213, USA

[b]University of Pittsburgh, Department of Obstetrics, Gynecology, and Reproductive Sciences, Magee-Womens Hospital, 300 Halket Street, Pittsburgh, PA 15213, USA

Abstract

Secnidazole, a 5-nitroimidazole with a longer half-life, is structurally related to metronidazole and tinidazole. For treatment of bacterial vaginosis (BV), secnidazole is a suitable single-dose oral drug having a longer serum half-life than metronidazole. The objective of this study was to evaluate the antimicrobial susceptibility of vaginal isolates of facultative and anaerobic bacteria to secnidazole, metronidazole, tinidazole and clindamycin.

A total of 605 unique BV-related bacteria and 108 isolates of lactobacilli recovered from the human vagina of US women during the years 2009–2015 were tested for antimicrobial susceptibility by the agar dilution CLSI reference method to determine the minimal inhibitory concentration (MIC).

The MIC_{90} (μg/mL) for secnidazole was similar to metronidazole and tinidazole for *Anaerococcus tetradius* (secnidazole: MIC_{90} 2; metronidazole: MIC_{90} 2; tinidazole: MIC_{90} 4), *Atopobium vaginae* (32; >128; 128), *Bacteroides* species (2; 2; 2), *Finegoldia magna* (2; 2; 4), *Gardnerella vaginalis* (128; 64; 32), *Mageeibacillus indolicus* (2; 2; 2), *Megasphaera*-like bacteria (0.5; 0.25; 0.5), *Mobiluncus curtisii* (128; >128; >128) and *Mobiluncus mulieris* (>128; >128; >128), *Peptoniphilus lacrimalis* (4; 4; 4) and *Peptoniphilus harei* (2; 2; 4), *Porphyromonas* species (0.25; 0.5; 0.25), *Prevotella bivia* (8; 8; 8), *Prevotella amnii* (2; 1; 2) and *Prevotella timonensis* (2; 2; 2). In this evaluation, 14 (40%) of 35 *P. bivia*, 5 (14%) of 35 *P. amnii* and 21 (58%) of 36 *P. timonensis* isolates were resistant to clindamycin with MIC values of >128 μg/mL. Secnidazole, like metronidazole, was superior to clindamycin for *Prevotella* spp., *Bacteroides* spp., *Peptoniphilus* spp., *Anaerococcus tetradius* and *Finegoldia magna*. Clindamycin had greater activity against *Atopobium vaginae, Gardnerella vaginalis* and *Mobiluncus* spp. compared to the nitroimidazoles. All 27 *Lactobacillus crispatus*, 26 (96%) of 27 *L. jensenii*, 5 (19%) of 27 *L.*

Corresponding author: Melinda A.B. Petrina, Magee-Womens Research Institute, 204 Craft Avenue, Pittsburgh, PA 15213, USA. Phone (412) 641-4015. Fax (412) 641-6170. mpetrina@mwri.magee.edu.

gasseri and 18 (67%) of 27 *L. iners* isolates were susceptible to clindamycin (MIC ≤2) while the MIC_{90} for all lactobacilli tested was >128 ug/mL for secnidazole, metronidazole and tinidazole.

Secnidazole has similar in vitro activity against the range of microorganisms associated with BV compared to metronidazole or tinidazole. Further, secnidazole spares lactobacilli, a characteristic which is desirable in drugs used to treat bacterial vaginosis.

Keywords

Secnidazole; Bacterial Vaginosis; Minimal Inhibitory Concentration

Introduction

Bacterial vaginosis (BV) is a common vaginal syndrome affecting 29% of reproductive age women in the United States [1]. BV is characterized by a shift in vaginal microbiota from *Lactobacillus* dominance to a high diversity microbiome with increased *Gardnerella vaginalis*, *Atopobium vaginae* and other anaerobic microorganisms, such as *Megasphaera*, *Sneathia*, and *Leptotrichia* species [2,3]. BV has been found to be associated with an increased risk of sexually transmitted infections, including *Chlamydia trachomatis* [4], *Neisseria gonorrhoeae* [4], herpes simplex virus 1 and 2 [5,6], human immunodeficiency virus (HIV) [7,8], and *Trichomonas vaginalis* [4]. In addition, BV is a risk factor for reproductive health sequelae including pelvic inflammatory disease (PID) [9] and preterm birth [10].

The 2015 Centers for Disease Control and Prevention (CDC) recommended treatments for BV include oral metronidazole taken twice a day for seven days, five days of an intravaginal metronidazole gel, or seven days of an intravaginal clindamycin cream [11]. Other FDA approved treatments for BV include tinidazole taken orally for multiple days [12], a single dose metronidazole gel [13] and a single dose clindamycin cream treatment [14]. Even with a variety of antimicrobial agents available for the treatment of BV, recurrence occurs after 12 months for almost 60% of women [15]. Therefore, new therapeutic strategies are needed to more effectively treat this common condition.

Secnidazole, a second-generation 5-nitroimidazole, has a longer half-life than both metronidazole and tinidazole (~20 vs ~8 vs ~14 hours) [16] and therefore has the potential of becoming a suitable single oral dose to treat women with BV. Outside of the United States, secnidazole is used not only to treat BV but also a variety of other infections including trichomoniasis, giardiasis and amoebiasis [17, 18]. A single dose of secnidazole was shown in a European study to provide a therapeutic response similar to that of oral metronidazole twice-a-day for 7 days for treatment of BV [19]. Secnidazole, like other nitroimidazoles, also has limited activity against beneficial microbes such as *Lactobacillus* species, a preferred characteristic for an antibiotic used to treat vaginal infections. The objective of this study was to evaluate the antimicrobial susceptibility of vaginal isolates of facultative and anaerobic bacteria to secnidazole compared to metronidazole, clindamycin and tinidazole.

Materials and Methods

Bacterial Isolates

A total of 605 BV-associated bacteria isolates and 108 isolates of lactobacilli were recovered from the human vagina of US women during the years 2009–2015 in human subject protocols approved by the University of Pittsburgh IRB. Vaginal cultures were performed as previously described [20]. The *G. vaginalis* isolates were identified by their characteristic colony morphology, beta hemolysis on human bilayer agar with Tween (Becton Dickinson, Rockville, MD), Gram stain showing gram-variable pleomorphic rods, and negative catalase reaction. DNA from the anaerobic bacteria was extracted using PrepMan™ Ultra Sample Preparation Reagent (Applied Biosystems, Foster City, CA). 16S rDNA for restriction fragment length polymorphism (RFLP) analysis was completed using HaeIII (Promega, Madison, WI) restriction enzyme for identification of *A. vaginae*, *Bacteroides* species, *Mageeibacillus indolicus, Mobiluncus* species, and *Prevotella* species. Hinf1 (Promega, Madison, WI) restriction enzyme was used to identify *A. tetradius, F. magna* and *Peptoniphilus* species. Both HaeIII and Hinf1 restriction enzymes were used to identify *Megasphaera*-like bacteria, novel bacteria which have not yet been placed into a taxonomic group. *Porphyromonas* species were identified using both HaeIII and TaqI (Promega, Madison, WI) restriction enzymes. *Lactobacillus* species were identified using repetitive sequence polymerase chain reaction fingerprinting [21] and if needed, 16S rDNA for RFLP analysis using HpyCH4V (New England Biolab, Ipswich, MA) restriction enzymes. The RFLP patterns for each species were confirmed by 16S rDNA sequences compared to the GenBank data library using the nucleotide BLAST program.

The following organisms were included in this susceptibility study: *Anaerococcus tetradius* (n=30); *Atopobium vaginae* (n=25); *Bacteroides* species (n=27); *Finegoldia magna* (n=30); *Gardnerella vaginalis* (n=110); *Mageeibacillus indolicus* (n=11); *Megasphaera*-like type 1 (n=76) and type 2 (n=47); *Mobiluncus curtisii* (n= 51) and *M. mulieris* (n=12); *Peptoniphilus harei* (n=30) and *P. lacrimalis* (n=30); *Porphyromonas* species (n=20); *Prevotella amnii* (n=35)*, P. bivia* (n=35) and *P. timonensis* (n=36); and *Lactobacillus crispatus* (n=27), *L. gasseri* (n=27), *L. iners* (n=27) and *L. jensenii* (n=27).

Agar Dilution Susceptibility Testing

The vaginal isolates were evaluated for susceptibility to secnidazole (Symbiomix, Newark, NJ), metronidazole, tinidazole and clindamycin (all from Sigma-Aldridge, St. Louis, MO) using the anaerobic agar dilution method described by the Clinical and Laboratory Standards Institute [22,23].

The concentrations of antimicrobial agents used ranged from 0.03 to 128 μg/mL. Prior to testing, *Lactobacillus* species were cultivated on Columbia agar with 5% sheep blood (Becton Dickinson, Rockville, MD) and incubated in anaerobic jars, *G. vaginalis* isolates were cultivated anaerobically on human bilayer agar with Tween (Becton Dickinson, Rockville, MD), and all other isolates were grown anaerobically on Brucella agar (Hardy Diagnostics, Santa Maria, CA). The isolates were isolated to purity and suspended in Brucella broth (Becton Dickinson, Rockville, MD) at a 0.5 McFarland suspension. Using a

Steer's replicator, Brucella agar (Remel, Lenexa, KS) plates with 5% Laked Sheep Blood (Hardy Diagnostic, Santa Maria, CA) and varying concentrations of test agent alongside a no drug growth control were inoculated and incubated in anaerobic jars for 48 hours at 37°C. The lowest antibiotic concentration yielding marked reduction to no growth was read as the Minimum Inhibitory Concentration (MIC). Three control strains, *Bacteroides fragilis* ATCC 25285, *Bacteroides thetaiotaomicron* ATCC 29741, and *Clostridium difficile* ATCC 700057 (American Type Culture Collection, Rockville, MD) were used to ensure quality of testing. *G. vaginalis* ATCC 14018 was also used as a supplemental control only when testing *G. vaginalis* isolates. The microbiological susceptibility and resistant breakpoints for clindamycin (≤2μg/mL and ≥8μg/mL) and metronidazole (≤8μg/mL and ≥32μg/mL) as defined by CLSI [22, 23] were used for interpretation of MIC results. CLSI does not have a defined susceptibility or resistant breakpoint for either secnidazole or tinidazole.

Results

The 713 female genital tract isolates were evaluated for susceptibility to secnidazole, clindamycin, metronidazole and tinidazole. As summarized in Tables 1–4, MIC_{50} and MIC_{90} values were similar for secnidazole, metronidazole and tinidazole for *Anaerococcus tetradius, A. vaginae, Bacteroides* species, *Finegoldia magna, G. vaginalis, Mageeibacillus indolicus, Megasphaera*-like bacteria, *Mobiluncus curtisii* and *M. mulieris, Peptoniphilus harei* and *P. lacrimalis, Porphyromonas species, Prevotella bivia, P. amnii* and *P. timonensis*, and all four *Lactobacillus* species.

BV-associated bacteria had susceptibility patterns for clindamycin and the three nitroimidazoles that distributed into three distinct groups. The first group of BV-associated bacteria (Table 1) consisted of anaerobic gram-negative rods and anaerobic gram-positive cocci which were susceptible to metronidazole based on a CLSI susceptibility breakpoint of ≤8 μg/mL. For secnidazole, only two *P. bivia* isolates had a MIC value of 16 μg/mL. One *F. magna* isolate also had a MIC of 16 μg/mL for tinidazole. All of the other isolates had MIC values ≤8 μg/mL for secnidazole and tinidazole. Clindamycin resistance, on the other hand, was observed in 38% of *Prevotella* species, 30% of *Bacteroides* species, 38% of *Peptoniphilus* species, 20% of *Anaerococcus tetradius* isolates, and 33% of *Finegoldia magna* isolates tested. All of the *Prevotella* and *Bacteroides* species resistant to clindamycin had MIC values of >128 μg/mL.

A second group of BV-associated bacteria (Table 2) consisted of anaerobic gram-positive and facultative gram-variable rods that were susceptible to clindamycin but had varying degrees of resistance to metronidazole. These included 9 *M. curtisii* isolates resistant to clindamycin (MIC values ≥8 μg/mL) and half of the *A. vaginalis*, *G. vaginalis* and *Mobiluncus* isolates having metronidazole resistance (MIC values ≥32 μg/mL). Secnidazole had a very similar range of activity against these BV-associated bacteria compared to metronidazole. Overall, 64% *A. vaginae*, 30% *G. vaginalis*, 69% *M. curtisii* and 42% *M. mulieris* isolates had secnidazole MIC values ≥32 μg/mL. Likewise, tinidazole had MIC values of ≥32 μg/mL for 72% *A. vaginae*, 22% *G. vaginalis*, 82% *M. curtisii* and 42% *M. mulieris* isolates. Similar rates of resistance were observed for metronidazole among these species.

A third group of BV-associated bacteria (Table 3) were susceptible to both clindamycin and metronidazole including the novel bacteria *Mageeibacillus indolicus* and *Megasphaera*-like type I and II bacteria. For secnidazole and tinidazole, the highest MIC concentration among *Megasphaera*-like bacteria isolates was 1 μg/mL with the exception of one *Megasphaera*-like type I isolate which had an MIC value of 16 μg/mL. All of the *Mageeibacillus indolicus* and *Porphyromonas* species isolates had MIC values of ≤2 μg/mL for secnidazole and tinidazole. Only one *Porphyromonas asaccharolytica* isolate was resistant to clindamycin.

As summarized in Table 4, metronidazole and tinidazole had no activity against any of the lactobacilli tested. Secnidazole had no activity (MICs >128μg/mL) against *L. crispatus* (excluding one isolate with an MIC of 1 μg/mL, 2 with an MIC of 8 μg/mL, and one with an MIC of 64 μg/mL), *L. gasseri*, *L. iners* or *L. jensenii*. All 27 *L. crispatus*, 96% *L. jensenii*, 19% *L. gasseri* and 67% *L. iners* were susceptible to clindamycin (MIC ≤2).

Discussion

The present study evaluated the susceptibility of a broad range of vaginal isolates to four antibiotics used to treat bacterial vaginosis. The taxonomic status of many of the microorganisms associated with bacterial vaginosis has changed in the past several years making it difficult to compare the present results to those from previously published studies for individual microorganisms. Clindamycin resistance among anaerobic isolates recovered from women with bacterial vaginosis has been reported previously [24]. The data generated in this study suggests that greater than a third of *Prevotella* species colonizing the vagina may be resistant to clindamycin.

Metronidazole remains the most commonly used antimicrobial agent for the treatment of BV despite limited in vitro activity against *G. vaginalis* and *A. vaginae*, both of which are uniformly present among women with BV. Secnidazole had a very similar range of activity in vitro against these microorganisms compared to metronidazole. *Megasphaera*-like bacteria have been described as being strongly associated with BV using culture independent methods and were until recently considered to be noncultivable. The data generated from this study suggests that this novel Gram-negative microorganism is susceptible to both nitroimidazoles and clindamycin. Consistent with previously published data [25], the nitroimidazoles provide excellent coverage against most of the anaerobic microbiota associated with bacterial vaginosis. Nitroimidazoles have no in vitro activity against lactobacilli recovered from the vagina [26] while clindamycin has activity against these beneficial microorganisms as shown in the present study.

In summary, the data generated from these studies suggests that secnidazole has similar activity against the range of microorganisms associated with BV compared to metronidazole or tinidazole. Further, secnidazole spares lactobacilli, a characteristic which is desirable in drugs used to treat bacterial vaginosis. Taken together, these results illustrate the potential of secnidazole for the treatment of bacterial vaginosis.

Acknowledgments

This work was supported by Symbiomix Therapeutics, LLC, Baltimore, MD and the following grants from the National Institutes of Health: AI082639, AI102835 and AI084024.

References

1. Koumans EH, Sternberg M, Bruce C, McQuillan G, Kendrick J, Sutton M, Markowitz LE. The prevalence of bacterial vaginosis in the United States, 2001–2004 associations with symptoms, sexual behaviors, and reproductive health. Sex Transm Dis. 2007; 34(11):864–9. [PubMed: 17621244]
2. Shipitsyna E, Roos A, Datcu R, et al. Composition of the vaginal microbiota in women of reproductive age--sensitive and specific molecular diagnosis of bacterial vaginosis is possible? PLoS One. 2013; 8(4):e60670. [PubMed: 23585843]
3. Fredricks DN, Fiedler TL, Marrazzo JM. Molecular identification of bacteria associated with bacterial vaginosis. N Engl J Med. 2005; 353:1899–911. [PubMed: 16267321]
4. Brotman RM, Klebanoff MA, Nansel TR, et al. Bacterial vaginosis assessed by gram stain and diminished colonization resistance to incident gonococcal, chlamydial, and trichomonal genital infection. J Infect Dis. 2010; 202(12):1907–15. [PubMed: 21067371]
5. Allsworth JE, Lewis VA, Peipert JF. Viral sexually transmitted infections and bacterial vaginosis: 2001–2004 National Health and Nutrition Examination Survey data. Sex Transm Dis. 2008; 35(9): 791–796. [PubMed: 18607314]
6. Cherpes TL, Meyn LA, Krohn MA, Lurie JG, Hillier SL. Association between acquisition of herpes simplex virus type 2 in women and bacterial vaginosis. Clin Infect Dis. 2003; 37:319–325. [PubMed: 12884154]
7. Cohen CR, Lingappa JR, Baeten JM, et al. Bacterial vaginosis associated with increased risk of female-to-male HIV-1 transmission: a prospective cohort analysis among African couples. PLoS Med. 2012; 9(6):e1001251. [PubMed: 22745608]
8. Moodley P, Connolly C, Sturm AW. Interrelationships among human immunodeficiency virus type 1 infection, bacterial vaginosis, trichomoniasis, and the presence of yeast. J Infect Dis. 2002; 185:69–73. [PubMed: 11756983]
9. Ness RB, Kip KE, Hillier SL, et al. A cluster analysis of bacterial vaginosis-associated microflora and pelvic inflammatory disease. Am J Epidemiol. 2005; 162(6):585–90. [PubMed: 16093289]
10. Lamont RF, Nhan-Chang CL, Sobel JD, Workowski K, Conde-Agudelo A, Romero R. Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous preterm birth: a systematic review and metaanalysis. Am J Obstet Gynecol. 2011; 205(3):177–190. [PubMed: 22071048]
11. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines. MMWR. 2015; 64(3):69–72.
12. Livengood CH III, Ferris DG, Wiesenfeld HC, et al. Effectiveness of two tinidazole regimens in treatment of bacterial vaginosis: a randomized controlled trial. Obstet Gynecol. 2007; 110(2 Pt 1): 302–309. [PubMed: 17666604]
13. Schwebke JR, Marrazzo J, Beelen AP, Sobel JD. A phase 3, multicenter, randomized, double-blind, vehicle-controlled study evaluating the safety and efficacy of metronidazole vaginal gel 1.3% in the treatment of bacterial vaginosis. Sex Transm Dis. 2015; 42(7):376–381. [PubMed: 26222750]
14. Faro S, Skokos CK. The efficacy and safety of a single dose of Clindesse vaginal cream versus a seven-dose regimen of Cleocin vaginal cream in patients with bacterial vaginosis. Infect Dis Obstet Gynecol. 2005; 13(3):155–160. [PubMed: 16240515]
15. Bradshaw CS, Morton AN, Hocking, et al. High recurrence rates of bacterial vaginosis over the course of 12 months after oral metronidazole therapy and factors associated with recurrence. J Infect Dis. 2006; 193:1478–86. [PubMed: 16652274]
16. Thulkar J, Kriplani A, Agarwal N. A comparative study of oral single dose of metronidazole, tinidazole, secniazole and ornidazole in bacterial vaginosis. Indian J Pharmacol. 2012; 44(2):243–245. [PubMed: 22529484]

17. Gillis JC, Wiseman LR. Secnidazole. A review of its antimicrobial activity, pharmacokinetic properties and therapeutic use in the management of protozoal infections and bacterial vaginosis. Drugs. 1996; 51(4):621–638. [PubMed: 8706597]
18. Moraes ME, Cunha GH, Bezerra MM, et al. Efficacy of the Mentha crispa in the treatment of women with Trichomonas vaginalis infection. Arch Gynecol Obstet. 2012; 286(1):125–130. [PubMed: 22350328]
19. Bohbot JM, Vicaut E, Fagnen D, Brauman M. Treatment of bacterial vaginosis: A multicenter, double-blind, double-dummy, randomised phase III study comparing secnidazole and metronidazole. Inf Dis in Ob and Gynecol. 2010; E2010:705692.
20. Hillier SL, Krohn MA, Rabe LK, Klebanoff SJ, Eschenbach DA. The normal vaginal flora, H_20_2 –producing lactobacilli, and bacterial vaginosis in pregnant women. Clin Infect Dis. 1993; 16(Suppl 4):S273–81. [PubMed: 8324131]
21. Antonio MA, Hillier SL. DNA fingerprinting of Lactobacillus crispatus strain CTV-05 by repetitive element sequence-based PCR analysis in a pilot study of vaginal colonization. J Clin Microbiol. 2003; 41(5):1881–7. [PubMed: 12734221]
22. Clinical and Laboratory Standards Institute (CLSI). Methods for antimicrobial susceptibility testing of anaerobic bacteria. eighth. Wayne, PA: Clinical and Laboratory Standards Institute; 2012. CLSI document M11-A-8Approved Standard
23. Clinical and Laboratory Standards Institute (CLSI). Standards for antimicrobial susceptibility testing. 26. Wayne, PA: Clinical and Laboratory Standards Institute; 2016. CLSI supplement M100-S26
24. Austin MN, Beigi RH, Meyn LA, Hillier SL. Microbiologic response to treatment of bacterial vaginosis with topical clindamycin and metronidazole. J Clin Microbiol. 2005; 43(9):4492–4497. [PubMed: 16145097]
25. Beigi RH, Austin MN, Meyn LA, Krohn MA, Hillier SL. Antimicrobial resistance associated with the treatment of bacterial vaginosis. Am J Obstet Gynecol. 2004; 191(4):1124–9. [PubMed: 15507930]
26. Austin MN, Meyn LA, Hillier SL. Susceptibility of vaginal bacteria to metronidazole and tinidazole. Anaerobe. 2006; 12:227–30. [PubMed: 16893662]

Author Manuscript

Author Manuscript

Author Manuscript

Highlights

- Secnidazole, an azole drug with a longer half-life than metronidazole, has activity against the bacteria associated with bacterial vaginosis.
- Like metronidazole, secnidazole has limited activity against vaginal *Lactobacillus* species.
- Secnidazole has the potential to be used for treatment of bacterial vaginosis.

Table 1

The comparative in vitro activity of secnidazole, metronidazole, tinidazole and clindamycin against 253 bacterial vaginosis (BV) related organisms susceptible to metronidazole

			MIC (ug/mL)			
Species	N[a]	Antimicrobial Agent	Range	50%	90%	n[b] (%)[c]
Anaerococcus tetradius	30	Clindamycin	0.5 – >128	1	>128	6 (20)
		Metronidazole	1 – 4	2	2	0
		Secnidazole	0.5 – 4	2	2	ND[d]
		Tinidazole	0.5 – 4	2	4	ND
Bacteroides species[e]	27	Clindamycin	0.03 – >128	1	>128	8 (30)
		Metronidazole	0.25 – 2	1	2	0
		Secnidazole	0.5 – 4	1	2	ND
		Tinidazole	0.25 – 2	1	2	ND
Finegoldia magna	30	Clindamycin	0.5 – >128	2	>128	10 (33)
		Metronidazole	0.5 – 8	1	2	0
		Secnidazole	0.5 – 8	2	2	ND
		Tinidazole	0.5 – 16	2	4	ND
Peptoniphilus harei	30	Clindamycin	3.125 – >128	0.5	8	4 (13)
		Metronidazole	1 – 4	2	2	0
		Secnidazole	1 – 4	2	2	ND
		Tinidazole	2 – 4	2	4	ND
Peptoniphilus lacrimalis	30	Clindamycin	3.125 – >128	64	>128	19 (63)
		Metronidazole	0.125 – 4	1	4	0
		Secnidazole	0.25 – 4	2	4	ND
		Tinidazole	0.125 – 4	2	4	ND
Prevotella amnii	35	Clindamycin	0.03 – >128	0.03	>128	5 (14)
		Metronidazole	0.25 – 4	0.5	1	0
		Secnidazole	0.25 – 4	1	2	ND
		Tinidazole	0.5 – 2	1	2	ND

				MIC (ug/mL)		
Species	**N**[a]	**Antimicrobial Agent**	**Range**	**50%**	**90%**	**n**[b] **(%)**[c]
Prevotella bivia	35	Clindamycin	0.03 – >128	0.06	>128	14 (40)
		Metronidazole	1 – 8	4	8	0
		Secnidazole	0.5 – 16	4	8	ND
		Tinidazole	2 – 8	4	8	ND
Prevotella timonensis	36	Clindamycin	0.03 – >128	>128	>128	21 (58)
		Metronidazole	0.25 – 8	2	2	0
		Secnidazole	0.5 – 4	2	2	ND
		Tinidazole	0.125 – 2	1	2	ND

[a]Number of isolates tested

[b]Number of resistant isolates

[c]Percent resistant (n/N)

[d]Resistance is not defined (ND) for secnidazole and tinidazole by CLSI

[e]*Bacteroides* species includes 2 *B. caccae*, 1 *B. clarus*, 1 *B. fragilis*, 4 *B. ovatus*, 2 *B. salyersiae*, 1 *B. species*, 2 *B. stercoris*, 1 *B. thetaaitaomicron*, 3 *B. uniformis*, 6 *B. vulgatus*, 2 *B. vulgatus/dorei* and 2 *B. xylanisolvens*

Table 2

The comparative in vitro activity of secnidazole, metronidazole, tinidazole and clindamycin against 198 bacterial vaginosis (BV) related organisms susceptible to clindamycin

			MIC (ug/mL)			
Species	**N[a]**	**Antimicrobial Agent**	**Range**	**50%**	**90%**	**n[b] (%)[c]**
Atopobium vaginae	25	Clindamycin	0.03 – 0.125	0.125	0.125	0
		Metronidazole	8 – >128	64	>128	18 (72)
		Secnidazole	8 – 64	32	32	ND[d]
		Tinidazole	0.25 – >128	32	128	ND
Gardnerella vaginalis	110	Clindamycin	0.03 – 0.5	0.125	0.5	0
		Metronidazole	1 – >128	8	64	30 (27)
		Secnidazole	1 – >128	8	128	ND
		Tinidazole	0.25 – >128	4	32	ND
Mobiluncus curtisii	51	Clindamycin	0.06 – >128	0.125	>128	9 (18)
		Metronidazole	2 – >128	128	>128	46 (90)
		Secnidazole	1 – >128	128	128	ND
		Tinidazole	2 – >128	>128	>128	ND
Mobiluncus mulieris	12	Clindamycin	0.03 – 0.25	0.06	0.125	0
		Metronidazole	2 – >128	8	>128	5 (42)
		Secnidazole	4 – >128	8	>128	ND
		Tinidazole	2 – >128	8	>128	ND

[a]Number of isolates tested

[b]Number of resistant isolates

[c]Percent resistant (n/N)

[d]Resistance is not defined (ND) for secnidazole and tinidazole by CLSI

Table 3

The comparative in vitro activity of secnidazole, metronidazole, tinidazole and clindamycin against 154 bacterial vaginosis (BV) related organisms susceptible to clindamycin and metronidazole

			MIC (ug/mL)			
Species	**N[a]**	**Antimicrobial Agent**	**Range**	**50%**	**90%**	**n[b] (%)[c]**
Mageeibacillus indolicus (BVAB3)	11	Clindamycin	0.06 – 1	0.06	1	0
		Metronidazole	1 – 2	2	2	0
		Secnidazole	1 – 2	1	2	ND[d]
		Tinidazole	0.5 – 2	0.5	2	ND
Megasphaera-like type I	76	Clindamycin	0.03–2	0.03	0.06	0
		Metronidazole	0.03–8	0.25	0.25	0
		Secnidazole	0.03–16	0.5	1	ND
		Tinidazole	0.03–16	0.5	0.5	ND
Megasphaera-like type II	47	Clindamycin	0.03–2	0.03	0.125	0
		Metronidazole	0.03–0.5	0.125	0.25	0
		Secnidazole	0.03–1	0.25	0.5	ND
		Tinidazole	0.03–1	0.25	0.5	ND
Porphyromonas species[e]	20	Clindamycin	0.03 – 64	0.03	0.125	1 (5)
		Metronidazole	0.06 – 1	0.25	0.5	0
		Secnidazole	0.03 – 2	0.125	0.25	ND
		Tinidazole	0.03 – 2	0.125	0.25	ND

[a] Number of isolates tested

[b] Number of resistant isolates

[c] Percent resistant (n/N)

[d] Resistance is not defined (ND) for secnidazole and tinidazole by CLSI

[e] *Porphyromonas* species includes 10 *P. asaccharolytica* and 10 *P. uenonis*

Table 4

The comparative in vitro activity of secnidazole, metronidazole, tinidazole and clindamycin against 108 *Lactobacillus* species

Species	N[a]	Antimicrobial Agent	MIC (ug/mL) Range	50%	90%	n[b] (%)[c]
Lactobacillus crispatus	27	Clindamycin	0.03 – 0.5	0.125	0.125	0
		Metronidazole	>128	>128	>128	27 (100)
		Secnidazole	1 – >128	>128	>128	ND[d]
		Tinidazole	0.06 – >128	16	>128	ND
Lactobacillus gasseri	27	Clindamycin	0.25 – 8	4	8	12 (44)
		Metronidazole	>128	>128	>128	27 (100)
		Secnidazole	>128	>128	>128	ND
		Tinidazole	>128	>128	>128	ND
Lactobacillus iners	27	Clindamycin	0.125 – >128	0.5	>128	9 (33)
		Metronidazole	>128	>128	>128	27 (100)
		Secnidazole	>128	>128	>128	ND
		Tinidazole	>128	>128	>128	ND
Lactobacillus jensenii	27	Clindamycin	0.25 – 8	0.5	1	1 (4)
		Metronidazole	>128	>128	>128	27 (100)
		Secnidazole	>128	>128	>128	ND
		Tinidazole	>128	>128	>128	ND

[a] Number of isolates tested

[b] Number of resistant isolates

[c] Percent resistant (n/N)

[d] Resistance is not defined (ND) for secnidazole and tinidazole by CLSI