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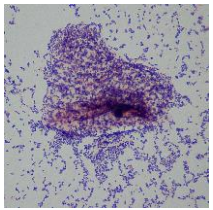
Updates in Bacterial Vaginosis and Trichomoniasis 2021



Christina A. Muzny, MD, MSPH
Associate Professor of Medicine & Epidemiology
Division of Infectious Diseases
University of Alabama at Birmingham

Cepheid WedEx – California Bay Laboratories

August 30, 2021

SOUTHEAST STD/HIV PREVENTION TRAINING CENTER

CONNECTING · PROVIDERS · PRACTICE · & PATIENTS

Disclosures (Research Support, Consulting Fees, and Honoraria)

Research Grants to My Institution:

- R01AI146065-01A1 (NIAID)
- Lupin Pharmaceuticals

Salary/Consulting Fees:

- Centers for Disease Control (CDC) – Consultant for 2021 STI Treatment Guidelines
- Lupin Pharmaceuticals - Consultant
- BioFire Diagnostics - Consultant
- Roche Molecular Diagnostics, PhagoMed, & Abbott - Scientific Advisory Board Member

Speaker and Reviewer Honoraria:

- Lupin Pharmaceuticals
- Cepheid
- Roche Molecular Diagnostics
- Becton Dickinson
- Abbott
- DynaMed

Learning Objectives

- Provide updates on the epidemiology and diagnosis of bacterial vaginosis (BV) and trichomoniasis, common vaginal infections
- Review updates in treatment in the BV and trichomonas sections of the 2021 CDC STI Treatment Guidelines

Sexually Transmitted Infections Treatment Guidelines, 2021

Kimberly A. Workowski, MD[1,2]; Laura H. Bachmann, MD[1]; Philip A. Chan, MD[1,3]; Christine M. Johnston, MD[1,4]; Christina A. Muzny, MD[1,5]; Ina Park, MD[1,6]; Hilary Reno, MD[1,7]; Jonathan M. Zenilman, MD[1,8]; Gail A. Bolan, MD[1]

[1]Division of STD Prevention, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, CDC, Atlanta, Georgia; [2]Emory University, Atlanta, Georgia; [3]Brown University, Providence, Rhode Island; [4]University of Washington, Seattle, Washington; [5]University of Alabama at Birmingham, Birmingham, Alabama; [6]University of California San Francisco, San Francisco, California; [7]Washington University, St. Louis, Missouri; [8]Johns Hopkins University, Baltimore, Maryland

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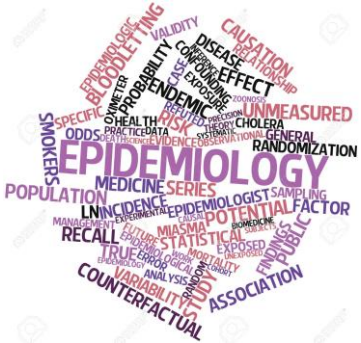
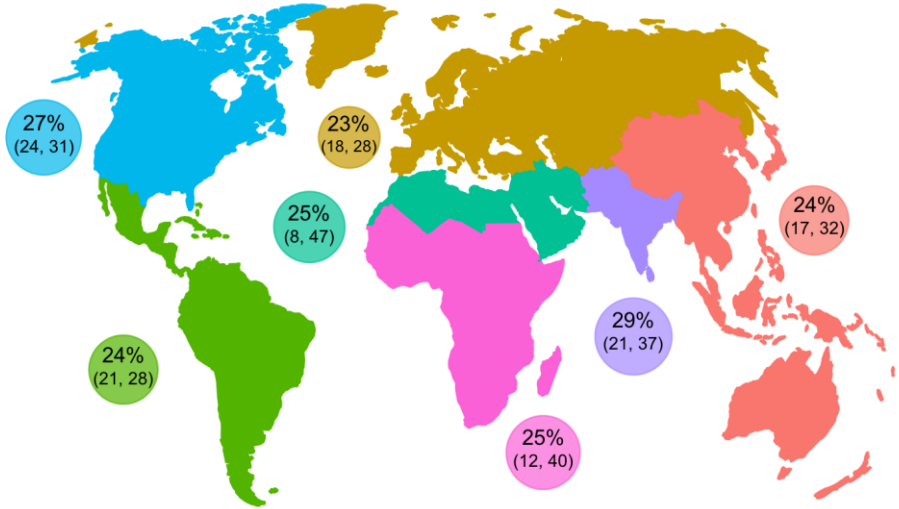
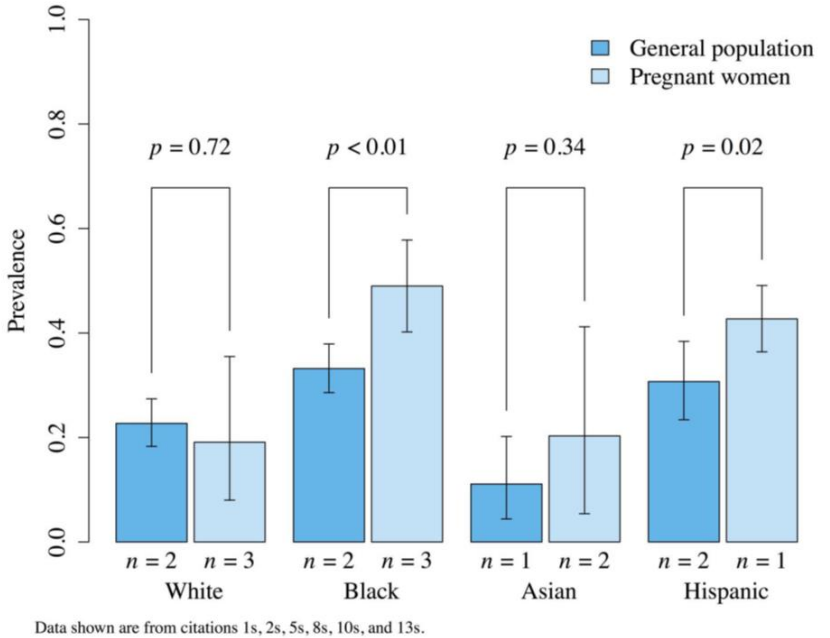
Updates in the Epidemiology of BV and *T. vaginalis* in the U.S.



Global Burden of BV





Annual global economic burden of treating symptomatic BV is US $4.8 (95% CI, $3.7-$6.1) billion

Sex Transm Dis 2019;46(5):304-311

Epidemiology of BV Strongly Supports Sexual Transmission of BV-Associated Bacteria[1] (1)

- BV associated with inconsistent condom use and increased numbers of recent and lifetime sexual partners[2]
- Women with BV have an earlier median age of sexual debut than women without[2]
- Most significant risk factor for incident BV is a new sexual partner while that for recurrent BV is a regular sexual partner[2]
- High level of BV concordance in women and their female sexual partners[3]

[1]*Curr Infect Dis Rep* 2013;15:130-135; [2]*J Infect Dis* 2016:214 (Suppl 1); [3]*J Infect Dis* 2002;185:1307-13

BV Epidemiology (2)

- Men with community state types (CSTs) 4-7 in their penile microbiota are significantly more likely to have a female partner with a high Nugent score[1]
- Penile microbiota of male partners significantly more similar to the vaginal microbiota of their female partners, compared to other non-partner women, regardless of circumcision status[2]
- Detection of PSA among women positively associated with BV recurrence[3]

[1]*MBio* 2015; 6(3):e00589; [2]*Microbiome* 2016; 4:16; [3]*Sex Transm Dis* 2016;43(3):172-6

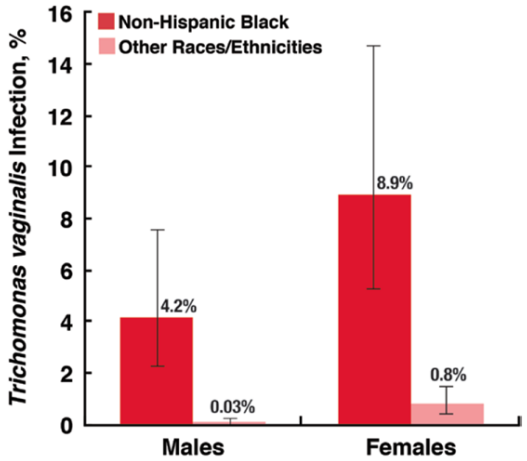
BV Epidemiology (3)

- Partner concurrency significantly associated with prevalent BV[1]
- Among WSW with incident BV versus those without, the relative rate of any sexual activity prior to incident BV was 40% higher (p=0.010), digital-vaginal sex 57% higher (p=0.005), and digital-anal sex 5.6 times higher (p<0.001)[2]
- In a systematic review of male circumcision and STIs & BV, male circumcision was found to result in lower BV prevalence in women[3]

[1]*Sex Transm Inf* 2018; 94(1):75-77; [2]*Sex Transm Infect* 2019; 95(7):511-515; [3]*Front Public Health* 2019; 7:4

Epidemiology of *T. vaginalis* in U.S. Women and Men, NHANES 2013-2014[1]

- Prevalence among U.S. women (1.8%) and men (0.5%) ages 18-59 (urine specimens tested with the Hologic Gen-Probe Aptima *T. vaginalis* NAAT)



- *T. vaginalis* significantly associated with female sex, black race, older age, <high school education, being below the poverty level, and having ≥2 sexual partners in the past year
  - **Racial disparity for *T. vaginalis* in the black population exceeds that for chlamydia, HSV-2, and HPV**
- Prevalence estimates exceed estimates of *T. vaginalis* burden in other high-income countries (i.e. UK)[2]

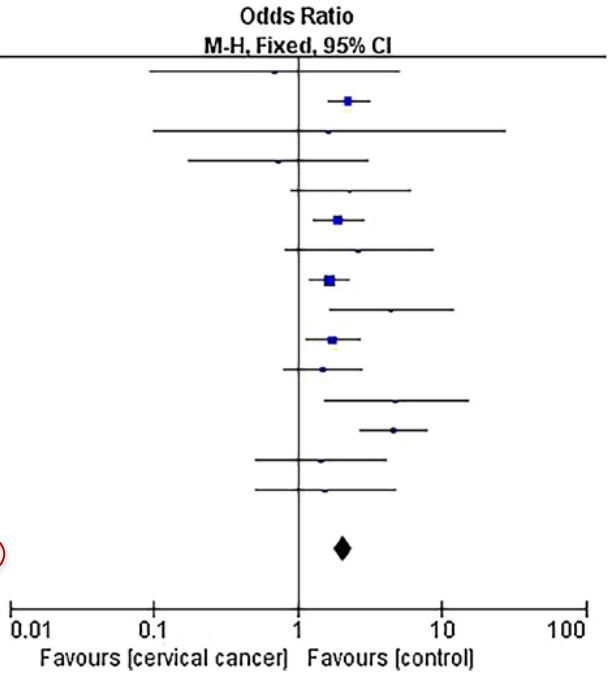
[1]*Clin Infect Dis* 2018; 67(2):211-217, [2]*Sex Transm Infect* 2018; 94(3):226-229

T. vaginalis and Risk of Cervical Cancer

Study or Subgroup	Cervical cancer Events	Total	Control Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Barcelos 2011	2	100	2	70	1.1%	0.69 [0.10, 5.05]
Donders 2013	42	5567	194	57684	16.0%	2.25 [1.61, 3.15]
Fernando B. Guijon 1985	1	32	1	52	0.3%	1.65 [0.10, 27.26]
Guijon F 1992	4	106	4	79	2.1%	0.74 [0.18, 3.03]
Kharsany AB 1993	11	28	15	69	2.5%	2.33 [0.90, 6.02]
La Vecchia C 1986	70	533	39	533	16.0%	1.92 [1.27, 2.89]
Lazenby 2014	4	36	13	288	1.2%	2.64 [0.81, 8.60]
Li CD 2010	51	374	547	6339	24.9%	1.67 [1.23, 2.28]
Liu XX 2015	21	50	7	50	1.9%	4.45 [1.68, 11.81]
Qin Y 2014	55	266	47	362	14.9%	1.75 [1.14, 2.68]
Schiff M 2000	18	93	39	282	7.4%	1.50 [0.81, 2.77]
Silva 2013	5	39	9	302	0.8%	4.79 [1.52, 15.11]
Slattery ML 1989	53	263	21	405	6.2%	4.61 [2.71, 7.86]
Spinillo A 2006	5	145	13	544	2.5%	1.46 [0.51, 4.16]
Vieira-Baptista 2016	4	83	17	539	2.0%	1.55 [0.51, 4.74]
Total (95% CI)		**7715**		**67598**	**100.0%**	**2.06 [1.77, 2.39]**
Total events	346		968			

Heterogeneity: Chi² = 21.14, df = 14 (P = 0.10); I² = 34%

Test for overall effect: Z = 9.36 (P < 0.00001)



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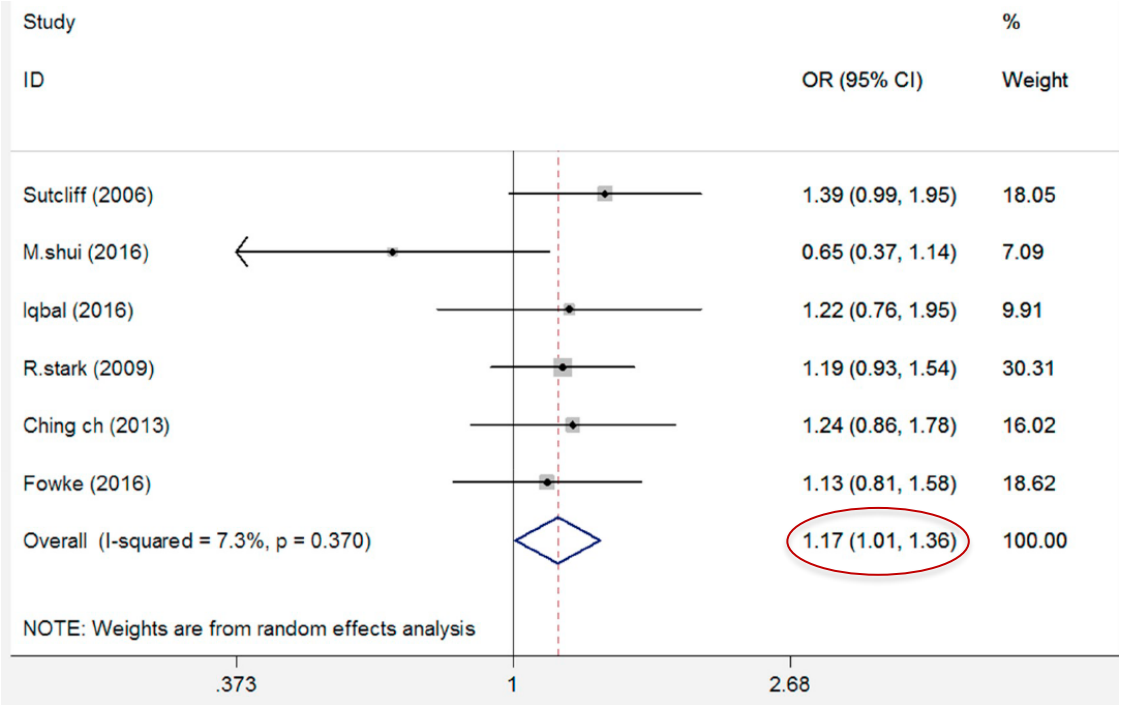
Eur J Obstet Gynecol Reprod Biol 2018;228:166-173

T. vaginalis and Risk of Prostate Cancer



Microb Pathog 2019;137:103752

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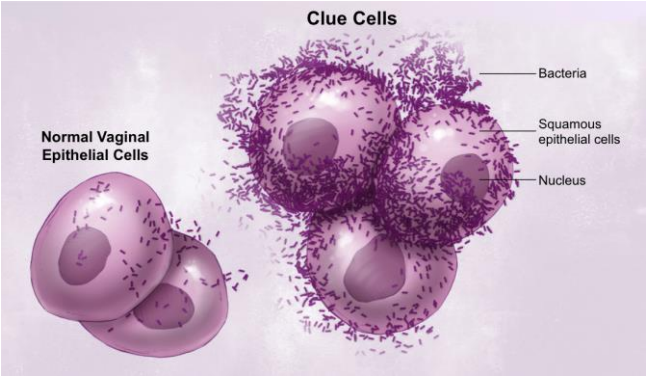
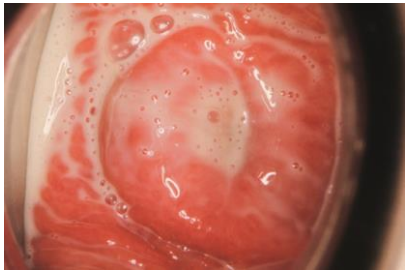
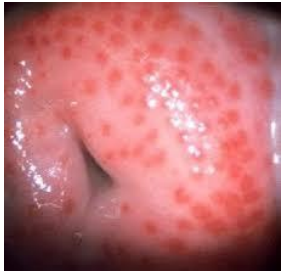
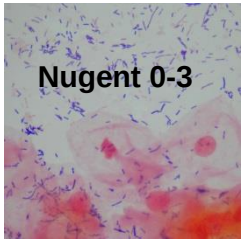
Updates in BV and *T. vaginalis* Diagnosis



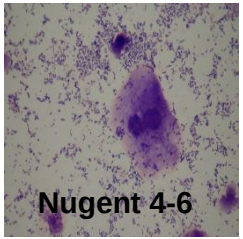


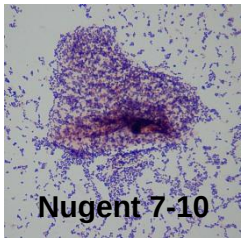


Traditional Diagnosis of BV



- Amsel criteria[1] (clinical criteria)
  - Homogenous vaginal discharge, vaginal pH>4.5, positive whiff test, >20% clue cells/hpf
  - 3 out of 4 criteria needed for diagnosis
  - Sensitivity 37-70%, specificity 94-99% compared to Nugent
- Nugent score[2] (vaginal Gram stain criteria)
  - **0-3**: lactobacillus predominate vaginal microbiota
  - **4-6**: intermediate microbiota with emergence of *G. vaginalis*
  - **7-10**: disappearance of lactobacilli with numerous *G. vaginalis* and strict anaerobes
  - Mainly used in research settings





[1]*Am J Med* 1983;74:14-22; [2]*J Clin Microbiol* 1991;29:297-301; Photos taken by Charles Rivers, PhD, MSPH

BV Molecular Diagnostics

- Advantageous over microscopy and point of care tests as they are based on detection of specific bacterial nucleic acids
- Objective, able to detect fastidious BVAB, enable quantitation, and are ideal for self-collected vaginal swabs
- Most useful in symptomatic women

J Clin Microbiol 2018;56(9)

Markers for Consideration in BV NAAT Tests

- Targeted PCR assays were developed for 17 vaginal bacterial species
  - Species selected based on their abundance in broad-range rRNA gene clone libraries, their initial apparent specificity for BV, or their novelty
- Applied to 264 vaginal fluid samples from 81 subjects with and 183 subjects without BV
- Results compared to Amsel, Nugent

Results compared to Nugent:

Bacterium	Sensitivity (%) (95% CI)		Specificity (%) (95% CI)	
Gardnerella vaginalis	97.3	(90.6 – 99.3)	45.5	(37.5 – 53.6)
Atopobium spp.	95.9	(88.6 – 98.6)	84.6	(77.8 – 89.6)
Megasphaera Type 1	94.5	(86.7 – 97.9)	94.4	(89.4 – 97.1)
Megasphaera Type 2	6.9	(3.0 – 15.1)	100	(97.4 – 100)
BVAB2	80.8	(70.3 – 88.2)	96.5	(92.1 – 98.5)
Either *Megasphaera* Type 1 or BVAB2	95.9	(88.6 – 98.6)	93.7	(88.5 – 96.7)
Lactobacillus crispatus	8.2	(3.8 – 16.8)	6.3	(3.4 – 11.5)
Lactobacillus iners	94.5	(86.7 – 97.9)	11.9	(7.6 – 18.2)

J Clin Microbiol 2007; 45:3270-3276

Current BV NAAT Tests in the U.S. – for use in symptomatic women

5 quantitative multiplex PCR tests are currently available that detect certain BVAB as well as *Lactobacillus* spp.[1-4]

	BD MAX™ Vaginal Panel	Hologic Aptima® BV	LabCorp NuSwab® VG	Quest Diagnostics™ SureSwab® Bacterial Vaginosis	MDL OneSwab® BV Panel PCR w/ Lactobacillus Profiling by qPCR
Regulatory	Market Authorized	Cleared	LDT	LDT	LDT
Gardnerella vaginalis	Y	Y	-	Y	Y
***Lactobacillus* spp.**	Y	Y	-	Y	Y
Atopobium vaginae	Y	Y	Y	Y	Y
BVAB-2	Y	-	Y	-	Y
Megasphaera-1 *(& -2)	Y	-	Y	Y*	Y*
Reported as	BV	BV	Species w/ interpretation guidance for BV	Species w/ interpretation guidance for BV	Species w/ interpretation guidance for BV
Reportable results	POS NEG	POS NEG	Score: Negative for BV (0-1) Indeterminate (2) Positive for BV (3-6)	Not supportive of BV Equivocal Supportive of BV	Normal microflora Transitional microflora Abnormal microflora

LDT = laboratory developed test

Not published

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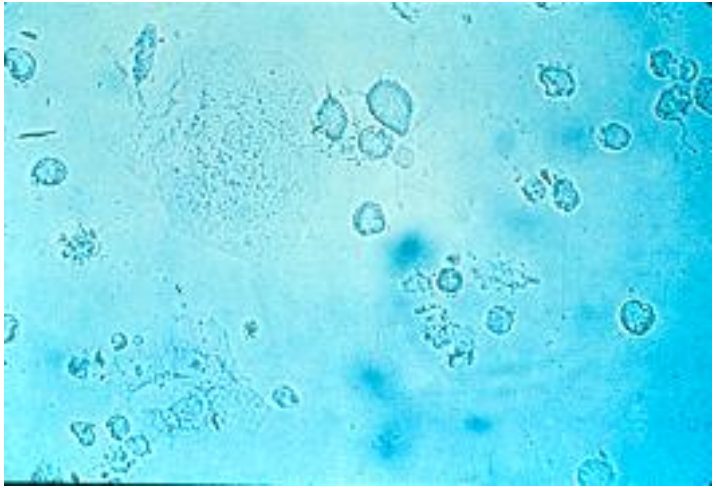
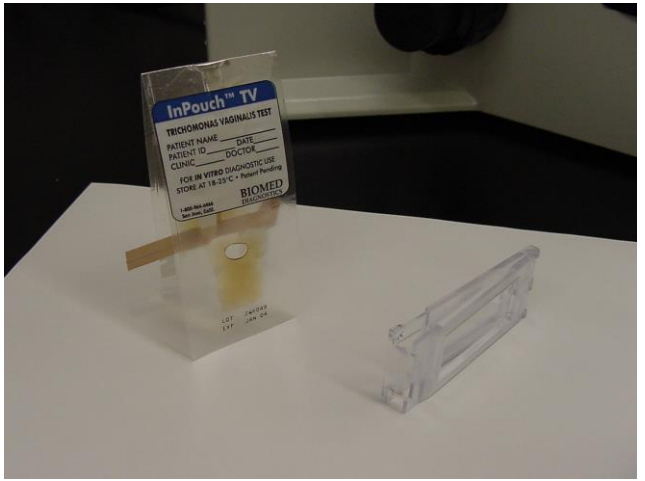
[1]*J Clin Microbiol* 2012; 50: 2321-2329; [2]*Obstet Gynecol* 2017; 130:181–189; [3]*J Clin Microbiol* 2016; 54:1017–1024; [4]*J Clin Microbiol* 2020;58(2):e01643-19

Traditional *T. vaginalis* Diagnosis: Wet Mount and Culture



- Point-of-care test
- Must be performed in 10-20 minutes after specimen collection or trichomonads will lose viability
- Sensitivity 44-68%; Specificity 100%



- Need to inoculate InPouch within 1 hour of specimen collection (women: urine; men: urethral swab, urine sediment, semen)
- Requires incubation at 37ºC
- Sensitivity 44%–75%; Specificity 100%

Sex Transm Infect 2013; 89: 434–438; *Int J Curr Microbiol Appl Sci* 2016; 5:731–741

Hologic Aptima *T. vaginalis* NAAT - 2011

- The first *T. vaginalis* NAAT FDA-approved for use in women
  - Can be used on vaginal swab, endocervical swab, ThinPrep Pap, and urine specimens
- Sensitivity 95-100%; Specificity 98-100%
- Assay performance similar in asymptomatic and symptomatic women
- Requires central lab processing; results not available in real-time
- Not FDA-approved for use in men; needs to be internally validated prior to being used in patient care

J Clin Microbiol 2011; 49:4106–11

BD ProbeTec Qx *T. vaginalis* NAAT[1] - 2014

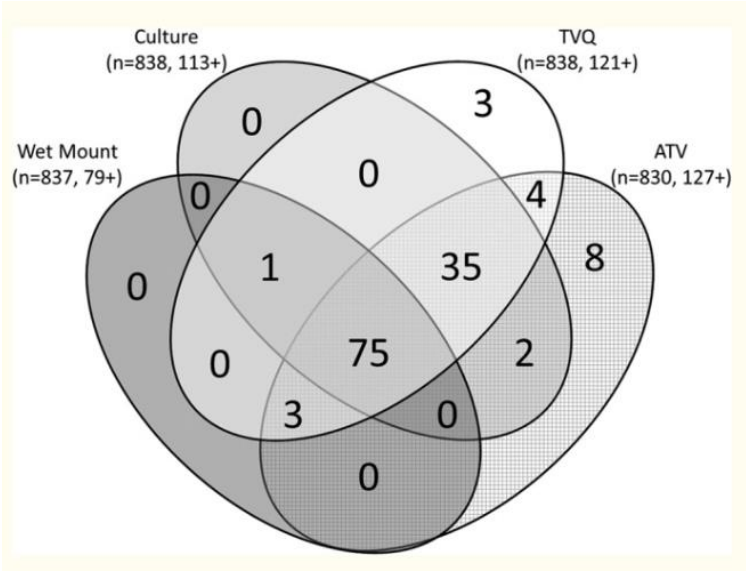
FDA-approved for use in women-vaginal specimens (patient or clinician-collected)

Requires central lab processing; results not available in real-time

Has superior performance vs. wet mount ($p < 0.001$); equivalent to the Aptima *T. vaginalis* NAAT ($p = 0.09$)

Not FDA-approved for use in men; needs to be internally validated

*BD CTGCTV2 assay is recently approved for *T. vaginalis* diagnosis in men using urine samples, with 97.9% sensitivity and 99.7% specificity while also detecting chlamydia or gonorrhea coinfection simultaneously[2]



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[1]*J Clin Microbiol* 2014;52(3):885-9; [2]*Sex Transm Dis* 2021;48(2):134-40

Cepheid Xpert® *T. vaginalis* NAAT - 2018

- FDA-approved *T. vaginalis* NAAT for use in both women and men at the point-of-care
- Multi-center study using the Xpert® *T. vaginalis* Assay to test specimens from women and men
  - 1,867 women and 4,791 men
- In women, performance of the Xpert Assay compared to culture and Aptima *T. vaginalis* NAAT
- Sensitivity and specificity for combined female specimens (first catch urine, self-collected vaginal swabs, and clinician-collected endocervical swabs): 99.5-100% and 99.4–99.9%
- For male first catch urine, sensitivity and specificity were 97.2% and 99.9%, compared to culture
- Assay can provide on-demand results in 65 minutes or less, with early termination for positive results ~ 40 minutes → diagnosis in real time (uses smaller instrumentation)

For *in vitro* diagnostic use

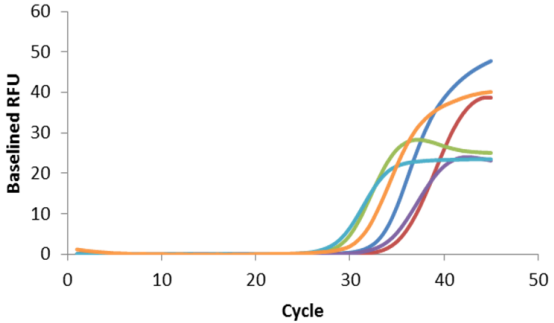
J Clin Microbiol 2018; 24;56(2)

Roche Cobas® TV/MG assay

- Performed on the Cobas® 6800/8800 platform
- Recently FDA-approved for *T. vaginalis* diagnosis in women and men (male urine)
- Can also reliably detect the presence of *Mycoplasma genitalium* infection
- Samples used for chlamydia/gonorrhea testing can also be used for *T. vaginalis* and *M. genitalium* testing, when appropriate, in the same run
  - **Note:** Screening for *M. genitalium* is not currently recommended in any population (2021 CDC STI Treatment Guidelines)

Expert Review of Molecular Diagnostics 2020; 20(4): 381-6

Abbott Alinity m STI Assay*



Picture is for illustrative purposes

Pathogen	Target
C. trachomatis	Ribosomal (r) RNA
N. gonorrhoeae	OPA gene DNA
T. vaginalis	Ribosomal (r) RNA
M. genitalium	Ribosomal (r) RNA
Internal control	RNA target unrelated to target sequences
Cellular control	Beta Globin (BG)

DETECT AND DIFFERENTIATE 4 PATHOGENS IN ONE REACTION
< 115 MIN TO FIRST RESULT

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*Not yet FDA Approved - CE marked and available outside the US

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Updates in Treatment of BV and *T. vaginalis*

Updates in BV Treatment in Non-Pregnant Women

- **3 new BV medications are now FDA-approved and available in the U.S.**
  - Clindesse 2% intra-vaginal cream X 1 dose (FDA-approved 2004 but not available in US until recently)[1]
  - Metronidazole 1.3% vaginal gel X 1 dose (FDA-approved April 2014)[2,3]
  - Secnidazole 2 g oral granules X 1 dose (FDA-approved September 2017)[4,5]
    - Longer ½ life (17 hours) vs. oral MTZ (7-8 hours)
    - No data in pregnant women
- There are no data suggesting superior efficacy of these newer medications to currently recommended BV therapies

[1]*Infect Dis Obstet Gynecol 2005;13:155-160;* [2]*J Low Genit Tract Dis* 2015; [3]*Sex Transm Dis* 2015; 42(7): 376-81; 19(2): 129-34; [4]*Obstet Gynecol* 2017; 130(2): 379-386; [5]*Am J Obstet Gynecol* 2017;217(6):678.e1-678.e9

2021 Recommended and Alternative BV Treatment Regimens

Recommended Regimens for Bacterial Vaginosis

Metronidazole 500 mg orally 2 times/day for 7 days

or

Metronidazole gel 0.75% one full applicator (5 g) intravaginally, once daily for 5 days

or

Clindamycin cream 2% one full applicator (5 g) intravaginally at bedtime for 7 days

Alternative Regimens

Clindamycin 300 mg orally 2 times/day for 7 days

or

Clindamycin ovules 100 mg intravaginally once at bedtime for 3 days*

or

Secnidazole 2 g oral granules in a single dose†

or

Tinidazole 2 g orally once daily for 2 days

or

Tinidazole 1 g orally once daily for 5 days

* Clindamycin ovules use an oleaginous base that might weaken latex or rubber products (e.g., condoms and diaphragms). Use of such products within 72 hours after treatment with clindamycin ovules is not recommended.

† Oral granules should be sprinkled onto unsweetened applesauce, yogurt, or pudding before ingestion. A glass of water can be taken after administration to aid in swallowing.

2021 CDC STI Treatment Guidelines

Cost of BV Treatments

Table 2. Dosing and Cost of Current BV Treatments

Medication	Doses	Cost*	Patient Savings Card
MTZ 500 mg po BID X 7 days	14	$7.80	
MTZ gel 0.75% (7.5mg/g), one full applicator (5g), daily X 5 days	5	$36.50	
Clindamycin cream 2%, one full applicator (5g), daily at bedtime X 7 days	7	$35.75	
TIN 2 g orally once daily X 2 days	2	$18.37	
TIN 1 g orally once daily X 5 days	5	$21.27	
Clindamycin 300 mg po BID X 7 days	14	$10.58	
Clindamycin ovules 100 mg intra-vaginally qhs X 3 days	3	$171.56	Patient assistance programs may be available[£]
Clindesse vaginal cream 2%, sustained release formulation, single dose	1	$139.19	Eligible patients pay the first $25 and get up to $75 off their co-pay or out-of-pocket expenses[µ]
MTZ intra-vaginal gel 1.3% (65 mg of MTZ in 5g of gel), single dose	1	$179.40	Insured patients pay as little as $25, cash-paying patients pay as little as $55[β]
SEC 2 g oral granules once	1	$272.30	Insured and cash-paying patients pay $25[€]

Black font = current recommended BV therapies; **Navy font = current alternative BV therapies**; **Red font = new BV therapies**

- Clindesse Patient Savings Card: Eligible patients pay the first $25 and get up to $75 off their co-pay or out-of-pocket expenses
- MTZ 1.3% Vaginal Gel Patient Savings Card: insured patients pay as little as $25, cash-paying patients pay as little as $55
- SEC Patient Savings Card: Insured and cash-paying patients pay $25
- SEC Patient Assistance Program: US citizens at or below 150% of Family Poverty level get medication delivered for free

GoodRx.com

Safety and Efficacy of a Novel Vaginal Anti-infective, TOL-463, in the Treatment of Bacterial Vaginosis and Vulvovaginal Candidiasis: A Randomized, Single-blind, Phase 2, Controlled Trial

Jeanne M Marrazzo ✉, Julia C Dombrowski, Michael R Wierzbicki, Charlotte Perlowski, Angela Pontius, Dwyn Dithmer, Jane Schwebke

Phase 3 trial currently enrolling

Clin Infect Dis 2019;68(5):803-809

Partner Treatment for BV – not currently recommended by CDC

Male Partner Treatment Trials of Women with BV

Study, year	N	Treatment of women	Treatment of men	Comparator	Primary outcome
Swedberg et al, 1985[31]	64	Oral MTZ 2 g single dose or oral MTZ 500 mg BID x 7 days	Oral MTZ 2 g single dose or oral MTZ 500 mg BID x 7	Standard of care	Culture negative for G. vaginalis and improved vaginal symptoms at 21 days: 68% vs 64% (RR=1.06; 95% CI: 0.74-1.52)
Vejtorp et al, 1988[32]	106	Oral MTZ 2 g on days 1 and 3	Oral MTZ 2 g on days 1 and 3	Placebo	Clinically diagnosed BV at 5 wks: 25% vs 29% (RR=0.85; 95% CI: 0.45-1.61)
Mengel et al, 1989[36]	98	Oral MTZ 2 g single dose or Oral MTZ 500 mg BID x 7 days	Oral MTZ 2 g single dose	Placebo	Symptoms and clinical cure of BV at 2, 5, and 8 wks: BV on vaginal Gram stain at 2 and 5 wks. No point estimates reported.
Moi et al, 1989[33]	190	Oral MTZ 2 g on days 1 and 3	Oral MTZ 2 g on days 1 and 3	Placebo	Relapse of clinically diagnosed BV at 12 wks: 21.1% vs 15.8% (RR=1.33; 95% CI: 0.73-2.44)
Vutyanavich et al, 1993[34]	106	Oral TIN 2 g single dose	Oral TIN 2 g single dose	Placebo	Clinical cure rate of BV at 4 wks: 71.6% vs 63.2% (RR=1.13; 95% CI: 0.95-1.35)
Colli et al, 1997[35]	139	2% clindamycin vaginal cream qhs x 7 days	Clindamycin 150 mg orally QID x 7 days	Placebo	Clinically diagnosed BV recurrence at 12 wks: 31.9% vs 30.0% (RR= 1.06; 95% CI: 0.65-1.75)

Table1. Adapted from Mehta et al[30]; CI, confidence interval; MTZ, metronidazole; qhs, at bedtime; QID, 4 times daily; RR, risk ratio; TIN, tinidazole

Adapted from Mehta, *Sex Transm Dis* 2012; Table taken from Muzny *Contemporary Ob/Gyn* August 2018 Educational Supplement

Only one trial reported that male partner treatment had an effect on recurrent BV in female partners…

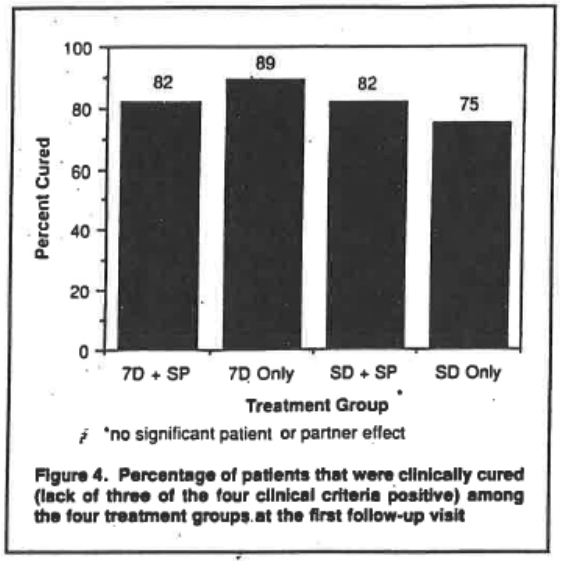

Figure 4. Percentage of patients that were clinically cured (lack of three of the four clinical criteria positive) among the four treatment groups at the first follow-up visit

At 2 weeks, there was no clear difference in clinical cure rate of BV by arm

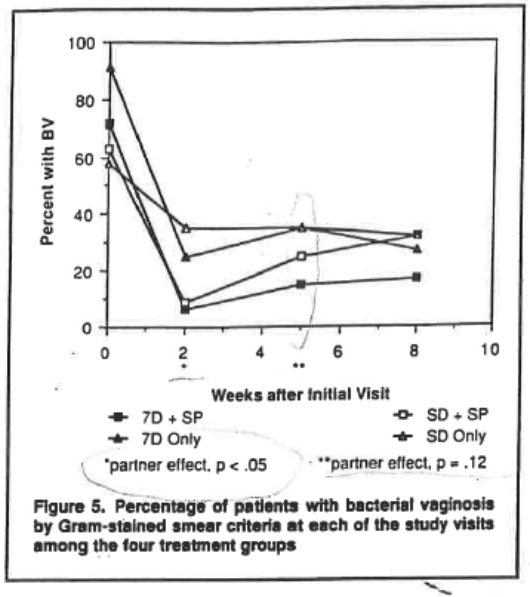

Figure 5. Percentage of patients with bacterial vaginosis by Gram-stained smear criteria at each of the study visits among the four treatment groups

However, at 2 and 5 weeks, women whose partners were treated had less BV by vaginal Gram stain

And at 8 weeks, women whose partners were treated were more likely to report resolution of their BV symptoms

However, results were presented graphically and effect sizes were not stated!!!

J Fam Pract 1989;28(2):163-171

But…prior male partner treatment trials had multiple limitations…

- In all trials, the study drug was delivered to the male by the female and no measures of compliance were noted
- Trials had insufficient power to detect reasonable effect sizes
- Randomization methods were deficient or insufficiently reported
- Adherence to therapy in men was infrequently reported
- Many of the treatment regimens used in the trials, including single-dose 2 gram metronidazole, would now not be considered effective therapy for BV

Sex Transm Dis 2012;39(10):822-30

Clinical Infectious Diseases

MAJOR ARTICLE

Treatment of Male Sexual Partners of Women With Bacterial Vaginosis: A Randomized, Double-Blind, Placebo-Controlled Trial

- This study minimized several of the limitations of prior male partner treatment trials
  - Sufficient power calculation
  - Randomization of men face-to-face to the currently recommended MTZ 500 mg orally twice daily for 7 days
  - Improved monitoring of male partner adherence (pill bottle review)

Clin Infect Dis 2020; e-published online 12/31/20

Unfortunately, similar to prior studies, this trial also found that male partner treatment with metronidazole did not reduce BV recurrence in female partners.

Table 2. Analysis of Primary Outcome

	BV Treatment Failure,[a] % (n/N)	
	Intent-to-Treat Population (n = 214)	Per-Protocol Population[b] (n = 133)
Population/arm		
Metronidazole	81 (87/107)	72 (50/69)
Placebo	80 (86/107)	75 (48/64)
Two-sided *P* value[c]	>.999	.844

Abbreviation: BV, bacterial vaginosis.

[a]Participants with recurrence/persistence through the third follow-up visit (day 112–119) were added to the cumulative failures for the study. Participants who did not return for their test-of-cure visit were also considered treatment failures.

[b]Includes women whose partners completed treatment and excludes pre-existing protocol violations of entry criteria.

[c]Fisher's exact test. Note: In the intent-to-treat population, 51 who did not attend the last visit were treated as failures; this includes 31 without any BV testing and 20 with negative BV tests at follow-up visits 1 and/or 2.

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Potential Reasons for Negative Finding of Most Recent BV Male Partner Treatment Trial

- BV treatment failure rate high in both arms
  - Women in both arms were likely heavily BV experienced and had persistent BV biofilm on their vaginal mucosa that was insufficiently eradicated with oral MTZ
- Lack of female and male adherence to multi-dose MTZ occurred in some couples
  - Consider use of single dose oral Secnidazole 2 grams in future partner treatment trials
- Oral MTZ may not have effectively cleared BV-associated bacteria (BVAB) from the penile microbiome and/or prostatic or seminal vesicle reservoirs
  - Phase 3 trial underway in Australia to evaluate the efficacy of oral MTZ 400 mg twice daily and topical 2% clindamycin cream to the glans penis and upper shaft twice daily, both for 7 days

Clin Infect Dis 2020; e-published online 12/31/20

2021 Recommended and Alternative *T. vaginalis* Treatment Regimens

Recommended Regimen for Trichomoniasis Among Women

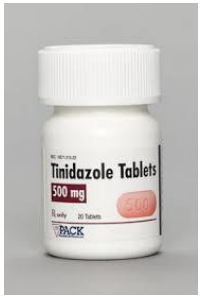
Metronidazole 500 mg orally 2 times/day for 7 days

Recommended Regimen for Trichomoniasis Among Men

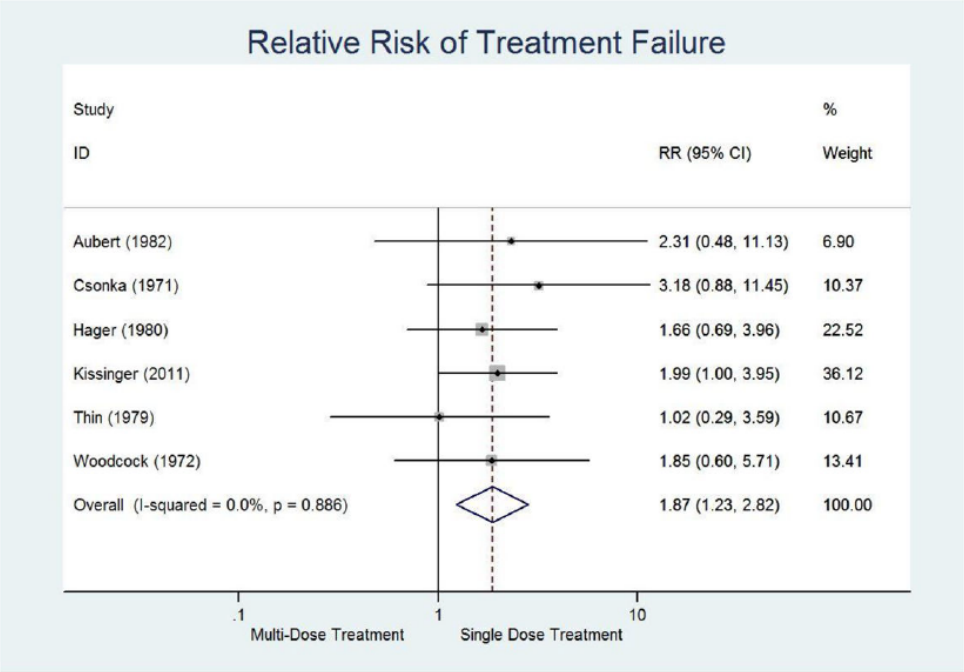
Metronidazole 2 g orally in a single dose

Alternative Regimen for Women and Men

Tinidazole 2 g orally in a single dose



Single-dose compared to multi-dose metronidazole for the treatment of trichomoniasis in women: A meta-analysis



The pooled risk ratio indicated higher treatment failure for single dose MTZ compared to multi-dose MTZ: 1.87 (95% confidence interval, 1.23-2.82; p<0.01)

Sex Transm Dis 2017;44(1):29-34

Single-dose versus 7-day-dose metronidazole for the treatment of trichomoniasis in women: an open-label, randomised controlled trial

Patricia Kissinger, Christina A Muzny, Leandro A Mena, Rebecca A Lillis, Jane R Schwebke, Laura Beauchamps, Stephanie N Taylor, Norine Schmidt, Leann Myers, Peter Augostini, William E Secor, Martina Bradic, Jane M Carlton, David H Martin

- HIV-negative women recruited between October 2014 – April 2017 from 3 STD clinics: New Orleans, LA, Jackson, MS, and Birmingham, AL
- Randomized 1:1 to 2 gram oral MTZ vs. MTZ 500 mg po BID X 7 days
- Primary outcome: *T. vaginalis* infection by intent-to-treat at test of cure (TOC), 4 weeks after completion of treatment - diagnosed by NAAT and/or culture
- Analysis of primary outcome also stratified by BV status (defined by Nugent score)

Lancet Infect Dis 2018; 18(11):1251-9

--Of 1,028 patients assessed for eligibility, **623 were randomly assigned to treatment groups**
--Self-reported adherence was 99% in the single dose group and 96% in the 7-day dose group; side effects were similar by group; the most common being N/V, HA

	7-day-dose metronidazole group	Single-dose metronidazole group	7-day-dose vs single-dose difference (95% CI)	Relative risk (95% CI)	p value*
Primary outcome analyses by intention to treat†					
Trichomonas vaginalis infection at test-of-cure	34/312 (11%)	58/311 (19%)	−7·8 (−2·2 to −13·3)	0·55 (0·34 to −0·70)	<0·0001
Among patients with bacterial vaginosis at baseline	16/125 (13%)	26/125 (21%)	−8·0 (−12·8 to −20·8)	0·59 (0·43 to 0·80)	0·0002
Among patients without bacterial vaginosis at baseline	13/139 (9%)	24/140 (17%)	−7·8 (−0·2 to −15·8)	0·57 (0·45 to 0·71)	<0·0001
Sensitivity analyses of primary outcome					
All missing TOC results reclassified as negative	29/312 (9%)	51/311 (16%)	−7·1 (−1·9 to −12·4)	0·57 (0·45 to 0·71)	<0·0001
All missing TOC results reclassified as positive	71/312 (23%)	92/311 (30%)	−6·8 (−0·1 to −13·7)	0·77 (0·70 to 0·85)	<0·0001
T vaginalis culture results as outcome‡	22/269 (8%)	41/270 (15%)	−7·0 (−1·3 to −12·7)	0·54 (0·39 to 0·75)	0·0002
NAAT and *T vaginalis* culture results as outcome‡	29/270 (11%)	51/270 (19%)	−8·2 (−2·2 to −14·1)	0·57 (0·45 to 0·71)	0·008

TOC=test-of-cure. NAAT=nucleic acid amplification test. *Relative risks and p values were derived from generalised estimating equation (GEE) analysis. †Missing data imputed using the fully conditional method in SAS. ‡In the per-protocol population.

Table 2: **Primary outcome and sensitivity analyses**

BV status had no effect on the relative risk

Lancet Infect Dis 2018; e-published online 10/5/18

Pharmacokinetic and Pharmacodynamic Effects of Metronidazole May Account for the Superior Efficacy of Multidose Therapy Among Women With Trichomoniasis

Davey Legendre, PharmD, Christina A. Muzny, MD, MSPH,† and Patricia Kissinger, PhD‡*

(1) MTZ inactivation may be occurring by certain BV-associated bacteria in the vaginal microbiota → lower drug concentrations at the site of infection; treatment success may depend upon saturating these “sponge” organisms with multi-dose therapy
(2) Accumulation of a MTZ metabolite may contribute to treatment success, particularly in the setting of multi-dose therapy

Sex Transm Dis 2019; 46 (1): 751-752

Clin Infect Dis. 2021 Mar 26;ciab242. doi: 10.1093/cid/ciab242. Online ahead of print.

Efficacy and Safety of Single Oral Dosing of Secnidazole for Trichomoniasis in Women: Results of a Phase 3, Randomized, Double-Blind, Placebo-Controlled, Delayed-Treatment Study

Christina A Muzny [1], Jane R Schwebke [1], Paul Nyirjesy [2], Gregory Kaufman [3], Leandro A Mena [4], Gweneth B Lazenby [5], Olivia T Van Gerwen [1], Keonte J Graves [1], Janeen Arbuckle [1], Belvia A Carter [6], Connette P McMahon [7], Scott Eder [8], Jackie Shaw [3], Brajesh Pandey [3], Steven E Chavoustie [9]

Table 2. Microbiological Cure at TOC Visit (mITT)

	Secnidazole 2 g (n=64)	Placebo (n=67)
Microbiological cure[a], n (%)	59 (92.2)[b]	1(1.5)[b]
95% exact binomial CI	82.70–97.41	0.04–8.04
P-value[c]	<.001	

Abbreviations: CI, confidence interval; mITT, modified intent-to-treat population; TOC, test of cure.
[a]InPouch™ *T. vaginalis* test negative for *T. vaginalis*.
[b]Patients with no test results were assumed to be positive (numbers imputed: secnidazole = 1; placebo = 3).
[c]*P* value vs. placebo from a Cochran-Mantel-Haenszel test adjusted for clinical symptoms (present/absent) of trichomoniasis at baseline.

SEC FDA-approved for treatment of trichomoniasis in U.S. women and men - June 30, 2021

Clin Infect Dis 2021; e-published online ahead of print 3/26/21

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Knowledge that will change your world

Thank you!

Questions/Comments?