

# 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

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**Background.** *Trichomonas vaginalis* is the most prevalent nonviral sexually transmitted infection. We evaluated the efficacy and safety of secnidazole vs placebo in women with trichomoniasis.

**Methods.** Women with trichomoniasis, confirmed by a positive *T. vaginalis* culture, were randomized to single-dose oral secnidazole 2 g or placebo. The primary endpoint was microbiological test of cure (TOC) by culture 6–12 days after dosing. At the TOC visit, participants were given the opposite treatment. They were followed for resolution of infection afterward and offered treatment at subsequent visits, if needed. Fifty patients per group (N = 100) provided approximately 95% power to detect a statistically significant difference between treatment groups.

**Results.** Between April 2019 and March 2020, 147 women enrolled at 10 sites in the United States. The modified intention-to-treat (mITT) population included 131 randomized patients (secnidazole, n = 64; placebo, n = 67). Cure rates were significantly higher in the secnidazole vs placebo group for the mITT population (92.2% [95% confidence interval {CI}: 82.7%–97.4%] vs 1.5% [95% CI: .0%–8.0%]) and for the per-protocol population (94.9% [95% CI: 85.9%–98.9%] vs 1.7% [95% CI: .0%–8.9%]). Cure rates were 100% (4/4) in women with human immunodeficiency virus (HIV) and 95.2% (20/21) in women with bacterial vaginosis (BV). Secnidazole was generally well tolerated. The most frequently reported treatment-emergent adverse events (TEAEs) were vulvovaginal candidiasis and nausea (each 2.7%). No serious TEAEs were observed.

**Conclusions.** A single oral 2 g dose of secnidazole was associated with significantly higher microbiological cure rates vs placebo, supporting a role for secnidazole in treating women with trichomoniasis, including those with HIV and/or BV.

**Clinical Trials Registration.** NCT03935217.

**Keywords.** *Trichomonas vaginalis*; trichomoniasis; secnidazole; women.

Trichomoniasis is the most prevalent nonviral sexually transmitted infection (STI) worldwide, affecting 3.7 million people in the United States (US) [1]. Women with *Trichomonas vaginalis* have a 2- to 3-fold increased risk for acquiring human immunodeficiency virus (HIV) [2] and other STIs [3]. Trichomoniasis is also associated with infertility [4] and adverse birth outcomes

[5]. National guidelines recommend annual screening of women with HIV for trichomoniasis [6].

The 2015 Centers for Disease Control and Prevention's (CDC) sexually transmitted disease treatment guidelines recommend a single 2 g dose of oral metronidazole (MTZ) or tinidazole (TDZ) for *T. vaginalis*-infected women without HIV; for infected women with HIV, MTZ 500 mg orally twice daily for 7 days is preferred [6]. The 2020 American College of Obstetricians and Gynecologists' (ACOG) practice bulletin on vaginitis has recently recommended multidose MTZ for all nonpregnant women [3], based on new clinical trial data [7]. Updated 2021 CDC STI treatment guidelines are pending.

Secnidazole (SEC) is a potent 5-nitroimidazole antibiotic with a longer half-life than MTZ and TDZ [8]. In 2017, SEC was approved by the US Food and Drug Administration (FDA) as the first, single-dose oral treatment for bacterial vaginosis (BV) in women [9, 10]. The 2020 ACOG guidance includes SEC 2 g as an alternative treatment for BV, based on a randomized controlled trial, finding it comparable to 7-day MTZ for BV [3].

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As a treatment for trichomoniasis, single-dose SEC had microbiological cure rates of 93%–96% after 2–3 days of treatment and up to 100% for  $\leq 20$  days of treatment in studies conducted outside the US [11]. We aimed to evaluate the efficacy and safety of single-dose SEC in US-based women with trichomoniasis. We hypothesized that microbiological cure rates would be high after treatment of *T. vaginalis*-infected women with SEC, similar to studies outside the US.

## METHODS

### Study Design

This phase 3, randomized, double-blind, placebo-controlled, delayed-treatment study received institutional review board approval (IntegReview, Austin, Texas; Western Institutional Review Board, Puyallup, Washington; Office of Human Research Ethics, Chapel Hill, North Carolina) for 10 clinical sites in the US (ClinicalTrials.gov identifier NCT03935217). It was designed and monitored in accordance with FDA recommendations and the sponsor's standard operating procedures, which comply with the International Conference on Harmonisation's Good Clinical Practice Guidelines and the Declaration of Helsinki. All patients provided written informed consent or parental/legal guardian consent (when appropriate) before engaging in study-related procedures.

In contrast to the FDA approval of tinidazole for trichomoniasis, which was based on a literature-focused New Drug Application submission, in this circumstance, the FDA required a single, placebo-controlled trial for the approval of SEC to treat trichomoniasis. To ensure patient safety, the investigators, in collaboration with the FDA, adopted a delayed-treatment study design, similar to FDA guidance on uncomplicated urinary tract infection studies [12]. Because there is no evidence that a 1- to 2-week delay in treatment for trichomoniasis is associated with significant health risks, the study design was approved by both local (academic) and central institutional review boards. Out of an abundance of caution, the investigators agreed on a trial protocol that was more stringent than the current standard of care, which recommends retesting for *T. vaginalis* at 3 months [6]. In the current trial, test of cure (TOC) was performed 6–12 days after treatment, with additional follow-up if needed to ensure successful treatment. In addition, the investigators counseled patients on the need for partner therapy and the importance of abstinence during the study to prevent reinfection.

### Participants

Eligible patients were adult females or postmenarchal adolescent girls  $\geq 12$  years of age in general good health. An initial diagnosis of *T. vaginalis* was determined by a positive wet mount, positive OSOM Trichomonas Rapid Test (Sekisui Diagnostics, Burlington, Massachusetts), or a positive *T. vaginalis* nucleic acid amplification test (NAAT; within the past 30 days) for

which treatment had not yet been initiated. Patients diagnosed with *T. vaginalis* based on a Pap smear were not excluded; however, these patients were required to have *T. vaginalis* confirmed with 1 of the other diagnostic tests mentioned above. Patients agreed to abstain from vaginal intercourse, vaginal penetration (eg, sex toys), or use of any vaginal products (eg, spermicides, tampons, vaginal douches, lubricants) until after study completion. Patients were counseled to notify all sexual partners within the past 60 days to be treated as contacts to trichomoniasis. Based on data from in vitro studies [13], and as noted in the package insert [14], SEC does not have an alcohol consumption restriction. Patients were excluded if they were pregnant (owing to placebo-controlled study design) or lactating, had symptomatic vulvovaginal candidiasis or an active genital herpes outbreak, received a course of antibacterial or antifungal therapy within the past 14 days, or had a known allergy to nitroimidazoles. Patients with chlamydia or gonorrhea via positive NAAT test at enrollment were included in the safety population; however, they were not included in the modified intention-to-treat (mITT) analysis, as per the direction of the FDA. Women with HIV and those with BV (based on all 4 Amsel criteria per FDA trial guidance: presence of homogeneous, white/gray vaginal discharge;  $\geq 20\%$  clue cells per high-power field on wet mount; positive whiff test; vaginal pH  $\geq 4.7$ ) [15] were not excluded.

### Procedures

Eligible patients were randomly assigned (1:1) to SEC 2 g or matching placebo in a double-blinded manner. Before study start, biostatisticians generated a randomization list assigning kit numbers to 1 of the 2 treatment groups. This list was used by the study sponsor to package study drug into treatment kits. Randomization was stratified by site and clinical symptoms of trichomoniasis at baseline (present/absent).

At visit 1 (baseline), patients completed assessments including demographics, medical history (including presence of genital symptoms), vital signs, urine pregnancy testing, and a physical examination. A pelvic examination was performed to assess genital signs and to collect vaginal specimens for pH, wet mount, potassium hydroxide whiff test, InPouch *T. vaginalis* culture (BioMed Diagnostics, White City, Oregon), and gonorrhea/chlamydia NAAT (Roche HC/Chlamydia Collection Kit [Cobas PCR Media Uni Swab]). SEC oral granules or matching placebo oral granules were mixed in approximately 4 ounces of unsweetened applesauce and administered under direct observation. The matching placebo contained the same ingredients as the active formulation with the exception of SEC. Both SEC and the placebo were packaged in white packets with blinded packaging and labeling so they were indistinguishable. Patients were evaluated 6–12 days later at visit 2 for TOC.

At visit 2 (TOC), patients were queried about treatment-emergent adverse events (TEAEs) and assessed for clinical

symptoms of trichomoniasis. A provider obtained an additional vaginal specimen for *T. vaginalis* culture. At this visit, patients received the opposite treatment from baseline (ie, SEC if they had received placebo at baseline or placebo if they had received SEC at baseline) under direct observation by study staff. Patients with a microbiological cure, defined as negative *T. vaginalis* by InPouch culture at visit 2, were subsequently discharged from the study. Patients with a positive *T. vaginalis* culture from visit 2 were asked to return for a third visit, 7–12 days later, for an additional assessment, including determination of the need for additional therapy. A fourth visit (7–12 days after visit 3) was scheduled at the investigator's discretion if a repeat *T. vaginalis* culture at visit 3 was positive. Patients who had a positive culture at visit 3 and visit 4 were offered treatment, based upon the investigator's discretion and per standard of care [6]. InPouch cultures were examined daily for 5 days over a 7-day period to reduce the possibility of false-negative results [16].

The primary efficacy endpoint was microbiological cure at visit 2 (TOC). The trial was designed to limit the possibility of unprotected sex resulting in reinfection, which would become more likely the longer the interval between treatment and TOC. The InPouch culture was selected as the diagnostic TOC based on its relatively high sensitivity (81%–94%) [17, 18], allowing for a TOC visit within 1 week. We did not perform a *T. vaginalis* NAAT for TOC as the optimal timing of this highly sensitive test is 3–4 weeks after treatment. Use of this test within 3 weeks after treatment may have detected remnant trichomonal nucleic acid, leading to false-positive test results [19]. In addition, the use of *T. vaginalis* NAAT for TOC would have required patients to remain sexually inactive for as much as 4 weeks, which was considered impractical.

### Statistical Analysis

Assuming microbiological cure rates of 75% [7] and 40% [20] with SEC and placebo, respectively, a sample size of 100 patients (50 patients/group) provided approximately 95% power to demonstrate a statistically significant between-treatment-group difference using a 2-sided, 2-sample comparison of proportions at the  $\alpha = .05$  level of significance. Assuming an attrition rate of 30%, 144 patients needed to be randomly assigned to SEC or placebo.

The primary efficacy endpoint was compared between the active and placebo treatment groups using a 2-sided Cochran-Mantel-Haenszel test (stratified by the presence/absence of clinical symptoms of trichomoniasis at baseline, HIV status, and BV status) at the  $\alpha = .05$  level of significance. As required by the FDA and determined a priori, the primary efficacy analysis was based on the mITT population, defined as all randomized patients who had a positive *T. vaginalis* culture at baseline and a negative chlamydia and gonorrhea NAAT at baseline. Secondary efficacy endpoint analysis was based on the per protocol (PP) population, defined as patients in the mITT population who received

their assigned study medication and had a TOC visit. Post hoc efficacy analyses of the microbiological cure rate at TOC compared SEC- vs placebo-treated patients (1) with trichomoniasis who were symptomatic and those who were asymptomatic, (2) infected with HIV, and (3) with BV at baseline. All analyses were performed using SAS software version 9.4 (SAS Institute, Cary, North Carolina).

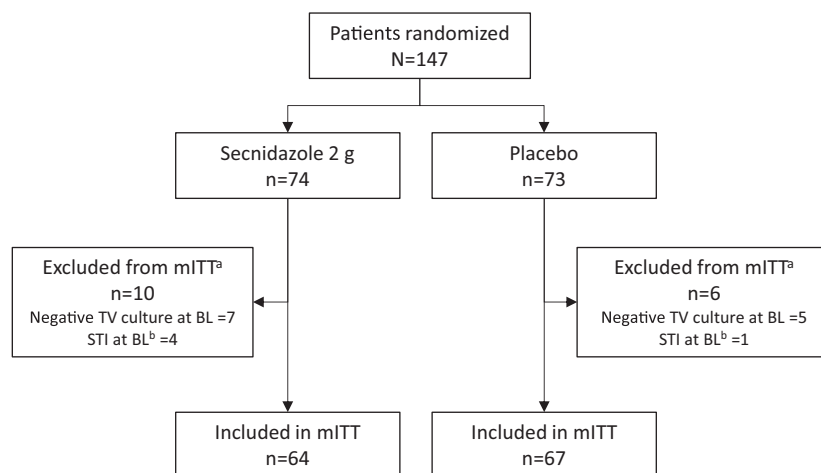
Safety endpoints included the incidence, severity, and relationship to study medication of TEAEs, serious TEAEs, and TEAEs leading to discontinuation. Vital signs, physical examinations, and clinical laboratory tests also were assessed. Safety endpoints were evaluated using the safety population, defined as all randomized patients who received any study-related medication.

## RESULTS

### Patient Disposition and Characteristics

Between 23 April 2019 and 18 March 2020, 147 women with trichomoniasis (SEC = 74, placebo = 73), identified by a positive wet mount (n = 119), OSOM Trichomonas Rapid Test (n = 112), or *T. vaginalis* NAAT (n = 60) were enrolled at 10 clinical sites in the United States. One hundred thirty-one women (SEC = 64, placebo = 67) were included in the mITT population (Figure 1). In the mITT population, 57 patients had positive *T. vaginalis* InPouch test results at visit 2, and 54 of these 57 patients had negative *T. vaginalis* InPouch test results at visit 3. This corresponds to a 94.7% success rate for SEC.

Eight percent (12/147) of randomized patients were excluded due to a negative *T. vaginalis* culture at baseline; 3.4% (5/147) of patients had a positive gonorrhea/chlamydia NAAT. One hundred nineteen patients were included in the PP population (SEC = 59, placebo = 60) (Figure 2). In addition to the above-mentioned exclusions, 7.5% (11/147) of patients were excluded from the PP population because their TOC visit did not occur within the 6- to 12-day window (Figure 2). Of the 12 patients excluded from both the mITT and PP populations due to a negative *T. vaginalis* culture at baseline, 6 had a positive NAAT (within 30 days of visit 1) at enrollment, 2 had positive wet mounts and positive OSOMs, 1 had a positive wet mount, and 1 had a positive wet mount and positive NAAT. Four patients did not return for TOC at visit 2. One patient withdrew owing to a TEAE, 2 withdrew consent, and 1 was contacted by phone multiple times and sent a certified letter in the mail. She acknowledged receipt of this letter but chose not to return. In the mITT population, the mean age was 37.7 years (standard deviation, 11.19 years; range, 15–65 years), and 90.8% were African American (Table 1). The majority of patients (84.7%) had genital symptoms, and among those, 43.5% had abnormal genital itching, 78.6% had abnormal vaginal discharge, and 63.4% had abnormal odor.



Abbreviations: BL, baseline; CT, *Chlamydia trachomatis*; mITT, modified intent-to-treat population; NAAT, nucleic acid amplification test; NG, *Neisseria gonorrhoea*; STI, sexually transmitted infection; TV, *Trichomonas vaginalis*.

<sup>a</sup>Patients could have multiple reasons for exclusion.

<sup>b</sup>CT/NG by NAAT.

**Figure 1.** Modified intention-to-treat population and reasons for exclusion. <sup>a</sup>Patients could have multiple reasons for exclusion. <sup>b</sup>*Chlamydia trachomatis/Neisseria gonorrhoeae* by nucleic acid amplification test. Abbreviations: BL, baseline; mITT, modified intention-to-treat; STI, sexually transmitted infection; TV, *Trichomonas vaginalis*.

### Efficacy

In the mITT population, the microbiologic cure rate at TOC was significantly higher ( $P < .001$ ) in the SEC vs placebo group (92.2% [95% confidence interval {CI}: 82.7%–97.4%] vs 1.5%

[95% CI: .0–8.0%]) (Table 2). In the PP population, the cure rate at TOC also was significantly higher ( $P < .001$ ) in the SEC vs placebo group (94.9% [95% CI: 85.9%–98.9%] vs 1.7% [95% CI: .0–8.9%]). There were no significant demographic differences

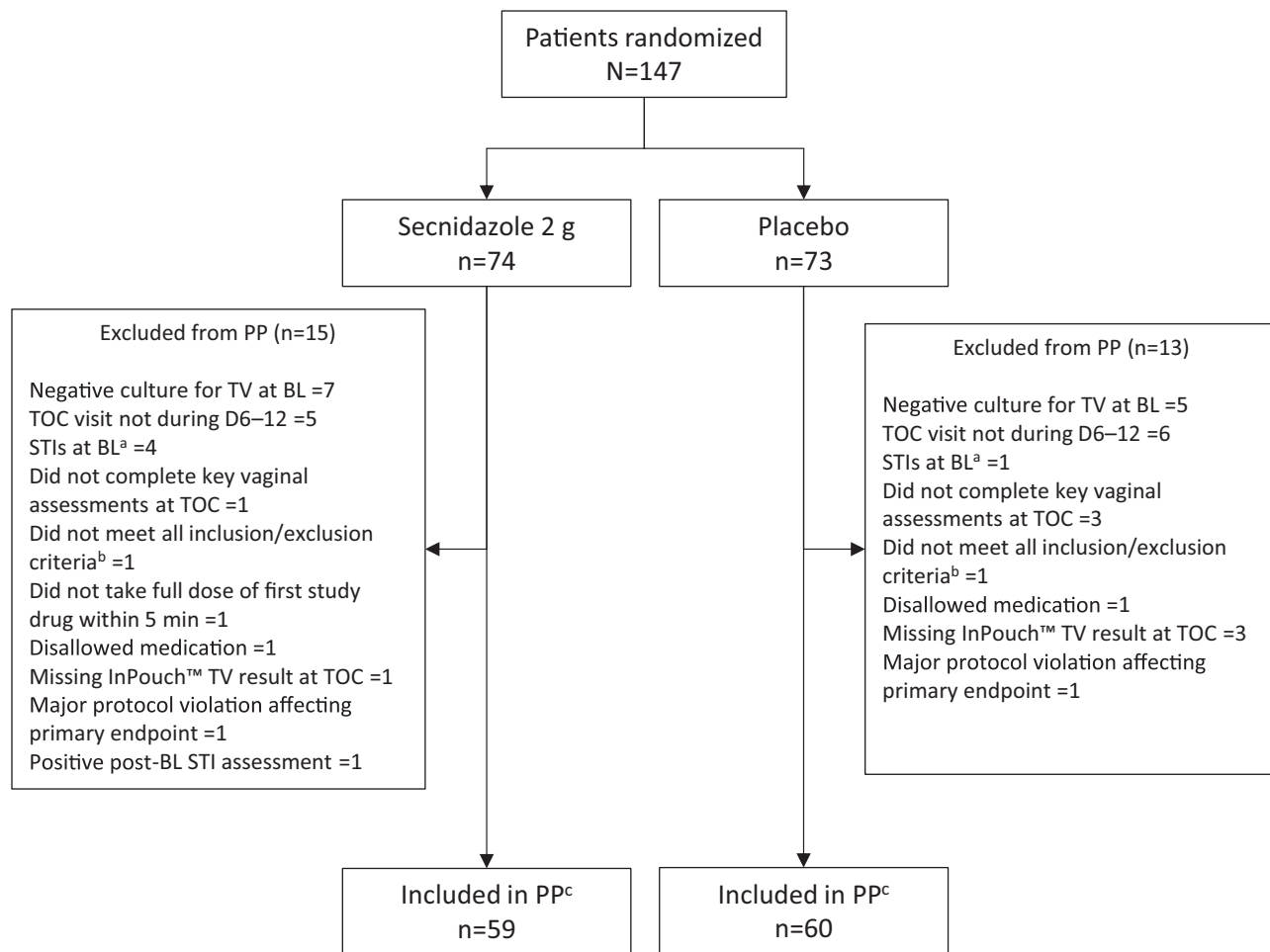
**Table 1. Baseline Characteristics (Modified Intention-to-Treat Population)<sup>a</sup>**

Characteristic	Secnidazole 2 g (n = 64)	Placebo (n = 67)	Overall (N = 131)
<b>Age, y</b>			
Mean (SD)	36.9 (11.3)	38.4 (11.12)	37.7 (11.19)
Median (range)	34.5 (19–65)	39.0 (15–65)	36.0 (15–65)
<b>Race, No. (%)</b>			
American Indian/Alaska Native	1 (1.6)	1 (1.5)	2 (1.5)
Asian	1 (1.6)	0	1 (0.8)
Black/African American	59 (92.2)	60 (89.6)	119 (90.8)
Native Hawaiian/Other Pacific Islander	0	0	0
White	3 (4.7)	6 (9.0)	9 (6.9)
Other	0	0	0
<b>Ethnicity, No. (%)</b>			
Not Hispanic or Latino	62 (96.9)	65 (97.0)	127 (96.9)
Hispanic or Latino	2 (3.1)	2 (3.0)	4 (3.1)
<b>Weight, kg, mean ± SD</b>			
Weight, kg, median (range)	90.4 (25.9)	92.4 (26.7)	91.4 (26.3)
BMI, kg/m <sup>2</sup> , mean ± SD	33.8 (9.4)	34.1 (9.3)	34.0 (9.3)
BMI, kg/m <sup>2</sup> , median (range)	32.2 (17.7–63.5)	31.2 (19.5–62.3)	31.6 (17.7–63.5)
<b>Trichomoniasis symptoms<sup>b</sup>, No. (%)</b>			
Present	56 (87.5)	55 (82.1)	111 (84.7)
Absent	8 (12.5)	12 (17.9)	20 (15.3)
<b>Bacterial vaginosis, No. (%)</b>			
Bacterial vaginosis, No. (%)	21 (32.8)	17 (25.4)	38 (29.0)
<b>HIV positive, No. (%)</b>			
HIV positive, No. (%)	5 (7.8)	4 (6.0)	9 (6.9)

Abbreviations: BMI, body mass index; HIV, human immunodeficiency virus; SD, standard deviation.

<sup>a</sup>Data are means ± SDs or n (%), unless otherwise specified.

<sup>b</sup>Vaginal itching, discharge, and/or odor.



Abbreviations: BL, baseline; CT, *Chlamydia trachomatis*; D, day; NAAT, nucleic acid amplification test; NG, *Neisseria gonorrhoea*; PP, per-protocol population; STI, sexually transmitted infection; TOC, test of cure; TV, *Trichomonas vaginalis*.

<sup>a</sup>CT/NG by NAAT.

<sup>b</sup>Patient did not abstain from sexual intercourse during the study.

<sup>c</sup>Patients could have multiple reasons for exclusion.

**Figure 2.** Per-protocol population and reasons for exclusion. <sup>a</sup>*Chlamydia trachomatis*/*Neisseria gonorrhoeae* by nucleic acid amplification test. <sup>b</sup>Patient did not abstain from sexual intercourse during the study. <sup>c</sup>Patients could have multiple reasons for exclusion. Abbreviations: BL, baseline; PP, per protocol; STI, sexually transmitted infection; TOC, test of cure; TV, *Trichomonas vaginalis*.

between patients who were not cured (ie, at visit 2 in the SEC group and at visit 3 in the placebo group) and those who were cured (data not shown).

In the subgroup of patients with vaginal symptoms at baseline, the microbiological cure rate at TOC was 92.9% (95% CI: 82.7%–98.0%) in the SEC group; no patient in the placebo group had a negative *T. vaginalis* culture at TOC ( $P < .001$ ; Table 3). In women with HIV, 100% (4/4) had a microbiological cure at TOC; no patient in the placebo group had a negative *T. vaginalis* culture at TOC. In patients with BV at baseline, the microbiological cure rate at TOC was 95.2% (95% CI: 76.2%–99.9%) in the SEC group; no patient in the placebo group had a negative *T. vaginalis* culture at TOC ( $P < .001$ ).

### Safety

In the safety population, TEAE rates were lower in the SEC vs placebo group. All TEAEs were mild. Only 1 patient in the SEC group discontinued due to mild nausea and productive cough. There were no serious TEAEs (Table 4).

### DISCUSSION

The results of this study demonstrate the superiority of SEC vs placebo for the treatment of trichomoniasis. Importantly, SEC was superior to placebo in patients with trichomoniasis and vaginal symptoms and in those with HIV and/or BV. Although prior studies have shown trichomoniasis is

**Table 2. Microbiological Cure at Test-of-Cure Visit (Modified Intention-to-Treat Population)**

Status at TOC Visit	Secnidazole 2 g (n = 64)	Placebo (n = 67)
Microbiological cure <sup>a</sup> , No. (%)	59 (92.2) <sup>b</sup>	1 (1.5) <sup>b</sup>
95% exact binomial CI	82.70–97.41	.04–8.04
P value <sup>c</sup>	<.001	

Abbreviation: CI, confidence interval; TOC, test of cure.

<sup>a</sup>InPouch *Trichomonas vaginalis* test negative.

<sup>b</sup>Patients with no test results were assumed to be positive (numbers imputed: secnidazole = 1; placebo = 3).

<sup>c</sup>P value vs placebo from a Cochran-Mantel-Haenszel test adjusted for clinical symptoms (present/absent) of trichomoniasis at baseline.

asymptomatic in 70%–85% of cases [21], patients can present with symptoms including yellow-to-green frothy vaginal discharge, abnormal vaginal odor, pruritus, irritation, and/or dysuria [3]. Thus, single-dose SEC may be an effective option for symptomatic and asymptomatic trichomoniasis in women.

National guidelines have traditionally recommended a single, 2 g dose of oral MTZ or TDZ as the preferred treatment of trichomoniasis in women, with oral MTZ 500 mg twice daily (BID) for 7 days as an alternative regimen [6]. In 2010, results of a randomized, open-label trial of a single oral dose of MTZ 2 g vs the 7-day MTZ 500 mg BID regimen in women with HIV and trichomoniasis demonstrated microbiological cure rates of 83.2% vs 91.5%, 6–12 days after treatment [22]. These results led to the CDC recommendation to use the multidose MTZ regimen for trichomoniasis in women with HIV [6]. In 2018, similar results were reported from a randomized, open-label trial of single- vs multidose MTZ for trichomoniasis in women without HIV. Microbiological cure rates at TOC were 81.4% and 89.1% in the single- and multidose MTZ groups [7]. Hence, the 2020 ACOG practice bulletin on vaginitis now recommends the multidose MTZ regimen as the preferred regimen for trichomoniasis in nonpregnant women [3]. Updated 2021 CDC STI treatment guidelines are anticipated later this year.

As providers move toward multidose MTZ as the preferred regimen for all women with trichomoniasis, our findings also support the use of single-dose SEC. With efficacy rates for the treatment of trichomoniasis comparable to those of multidose MTZ [7, 22], SEC has favorable attributes that may provide advantages over other options. In vitro studies of *T. vaginalis* isolates [14] showed that the minimal lethal concentration of SEC is 56% lower compared with MTZ. SEC also differs from other 5-nitroimidazoles with a notably longer half-life (17 hours) vs MTZ (7–8 hours) and TDZ (12 hours) [23]. Single-dose options are convenient and likely to improve adherence overall, especially in populations at risk for noncompliance [24]. Of note, compliance with multidose MTZ has been low (50%–63%) in some studies [25]. Factors that may impact adherence include gastrointestinal complaints, treatment duration, and lifestyle restrictions. In 1 study, 23% of patients reported nausea in the single-dose and multidose MTZ groups [7]. In our study, 2.7% of patients reported nausea with SEC. Additionally, SEC does not have an alcohol restriction based on data from in vitro studies [13, 14].

In our study, cure rates were 92%–100% in the overall population and in subgroups of women with genital symptoms, HIV, and/or BV. Previous research showed that trichomoniasis treatment significantly decreases HIV viral load and viral shedding and may reduce HIV transmission [6, 26–28]. Although only 4 patients had HIV, our finding that all were cured is reassuring, and larger clinical trials in this patient population are warranted to confirm these results. Moreover, coinfection of BV and *T. vaginalis* is common, with rates of 60%–80% [29]. Thus, a single treatment for BV and trichomoniasis may have multiple benefits.

A potential limitation of this study was the use of *T. vaginalis* culture to achieve a shorter timeframe to TOC. Although InPouch may be less sensitive than NAAT [21], the accuracy in this study was high as supported by the low placebo responder rate (~1%). Other limitations include the lack of long-term follow-up and the exclusion of men and pregnant women. However, 2 non-US-based

**Table 3. Microbiological Cure by Presence of Clinical Symptoms and Human Immunodeficiency Virus or Bacterial Vaginosis Status at Baseline<sup>a</sup> (Modified Intention-to-Treat Population)**

Status at Baseline	Secnidazole 2 g (n = 64)		Placebo (n = 67)		P Value <sup>b</sup>
	Symptoms Present	Symptoms Absent	Symptoms Present	Symptoms Absent	
Microbiological cure <sup>c</sup> , % (no./No.)	92.9 (52/56)	87.5 (7/8) <sup>d</sup>	0 (0/55) <sup>d</sup>	8.3 (1/12)	<.001
95% CI	82.7–98.0	47.4–99.7	.0–6.5	.2–38.5	<.001
Microbiological cure <sup>c</sup> , HIV, % (no./No.)	100 (4/4)	...	0 (0/4)	...	NC
Microbiological cure <sup>c</sup> , BV, % (no./No.)	95.2 (20/21)	...	...	0 (0/17) <sup>d</sup>	<.001
95% CI	76.2–99.9	...	...	.0–19.5	

Abbreviations: BV, bacterial vaginosis; CI, confidence interval; HIV, human immunodeficiency virus; NC, not calculated.

<sup>b</sup>Post hoc analysis.

<sup>c</sup>P value vs placebo from a Cochran-Mantel-Haenszel test adjusted for clinical symptoms (present/absent) of trichomoniasis at baseline.

<sup>d</sup>InPouch *Trichomonas vaginalis* test negative.

<sup>e</sup>Patients with no test results were assumed to be positive (numbers imputed: secnidazole [symptoms absent] = 1; placebo [symptoms present] = 3; placebo [symptoms absent] = 1).

**Table 4. Summary of Treatment-Emergent Adverse Events<sup>a</sup> (Safety Population)**

TEAE	Secnidazole 2 g (n = 74)		Placebo (n = 73)	
	Patients <sup>b</sup> , No. (%)	Events, No.	Patients <sup>b</sup> , No. (%)	Events, No.
Any TEAE	11 (14.9)	13	16 (21.9)	20
Nausea	2 (2.7)	2	3 (4.1)	3
Abdominal pain	1 (1.4)	1	1 (1.4)	1
Diarrhea	1 (1.4)	1	2 (2.7)	2
Vomiting	1 (1.4)	1	1 (1.4)	1
Vulvovaginal candidiasis	2 (2.7)	2	0	0
Vulvovaginal mycotic infection	1 (1.4)	1	0	0
Trichomoniasis	0	0	2 (2.7)	2
Productive cough	1 (1.4)	1	0	0
Upper-airway cough syndrome	1 (1.4)	1	0	0
Myalgia	1 (1.4)	1	0	0
Back pain	0	0	1 (1.4)	1
Headache	1 (1.4)	1	5 (6.8)	5
Vulvovaginal pruritus	1 (1.4)	1	0	0
Dysmenorrhea	0	0	2 (2.7)	2
Irregular menstruation	0	0	1 (1.4)	1
Thirst	0	0	1 (1.4)	1
Pruritus	0	0	1 (1.4)	1

Abbreviation: TEAE, treatment-emergent adverse event.

<sup>a</sup>Includes all TEAEs during the primary phase (start date on or before the test-of-cure visit).

<sup>b</sup>Patients experiencing multiple TEAEs are counted only once within a given cell.

studies of SEC for trichomoniasis in patients, including a small subgroup of men, showed cure rates of 91.7%–100% at 2–20 days after treatment [30, 31]. Although our study did not include pregnant women, and data on the use of SEC during pregnancy are limited, reproductive preclinical toxicology studies have shown no evidence of toxicity, and SEC is not contraindicated during pregnancy [14, 32]. The CDC recommends that trichomoniasis treatment be considered for symptomatic pregnant women, regardless of pregnancy stage [6]. Finally, 5-nitroimidazole susceptibility testing was not performed on trichomonas isolates in the study; thus, we cannot comment on any resistance that potentially may have been present.

Study strengths include high cure rates for SEC (92%–95%), low placebo responder rates, minimal dropouts, a favorable TEAE profile, and treatment success in women with and without clinical symptoms, HIV, and/or BV.

In conclusion, this study demonstrated that a single dose of SEC 2 g was efficacious and well tolerated in women with trichomoniasis and in those with trichomoniasis and comorbid HIV and/or BV. If approved by the FDA for the treatment of trichomoniasis, SEC will be the only single oral-dose medication available for the treatment of BV and *T. vaginalis*. Future studies should be considered in pregnant women and those with persistent *T. vaginalis* infection, including the use of SEC multidose regimens.

## Notes

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