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Prevalence and Treatment Outcome of Cervicitis of Unknown Etiology

Stephanie N. Taylor, MD^{1,*}, Shelly Lensing, MS², Jane Schwebke, MD³, Rebecca Lillis, MD¹, Leandro A. Mena, MD, MPH⁴, Anita L. Nelson, MD⁵, Anne Rinaldi, BA⁶, Lisa Saylor, BA⁶, Linda McNeil, MA⁶, and Jeannette Y. Lee, PhD²

¹Louisiana State University Health Sciences Center, New Orleans, LA

²University of Arkansas for Medical Sciences, Little Rock, AR

³University of Alabama at Birmingham, Birmingham, AL

⁴University of Mississippi, Jackson, MS

⁵Women's Health Care Clinic/LA Biomedical Institute, Los Angeles, CA

⁶FHI 360, Triangle Park, NC

Abstract

Background—Mucopurulent cervicitis (MPC) is a clinical syndrome characterized by mucopurulent discharge from the cervix and other signs of inflammation. This was a phase III, multi-center study designed to evaluate the effectiveness of placebo versus empiric antibiotic treatment for clinical cure of MPC of unknown etiology at 2 months follow-up. Unfortunately, enrollment was terminated due to low accrual of women with cervicitis of unknown etiology but important prevalence and outcome data were obtained.

Methods—Five hundred seventy-seven women were screened for MPC. Women with MPC were randomized to the treatment or placebo arm of the study and the two arms were evaluated based upon the etiology, clinical cure rates, adverse events (AEs) and rates of pelvic inflammatory disease (PID).

Results—One hundred thirty-one or 23% (131/577) of screened women were found to have MPC. Eighty-seven were enrolled and randomized. After excluding women with sexually transmitted infections and other exclusions, 61% (53/87) had cervicitis of unknown etiology. The overall clinical failure rate was 30% (10/33) and the clinical cure rate was only 24% (8/33). Rates were not significantly different between the arms. There were 24 gastrointestinal (GI) AEs in the treatment arm compared to 1 AE in the placebo arm.

Conclusion—Over half of the cases of MPC were of unknown etiology. Clinical cure rates for the placebo and treatment arms were extremely low, with most women concluding the study with a partial response. Gastrointestinal AEs were higher in the treatment arm.

*Corresponding author. Mailing address: LSU Health Sciences Center, Section of Infectious Diseases, 517 N. Rampart St., New Orleans, LA 70112. Phone: (504) 658-2622. Fax: (504) 568-5979. staylo2@lsuhsc.edu.

Conflicts of Interest – JS – Combe and Medicis.

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Keywords

Mucopurulent Cervicitis; Cervicitis; Trichomonas; Bacterial Vaginosis; Chlamydia; Gonorrhea; Mycoplasma genitalium

Introduction

Mucopurulent cervicitis is a clinical syndrome characterized by the presence of mucopurulent discharge from the cervix and other signs of inflammation such as easily induced cervical bleeding (bleeding that occurs with gentle passage of a cervical swab).¹ In some centers, the presence of 30 white blood cells (WBCs) per oil immersion field on cervical Gram's stain is also used.^{2,3} The diagnostic precision for cervicitis however varies and the predictive value of certain cervical findings suggestive of MPC may also vary.⁴

Commonly, women with MPC are empirically treated for GC and CT. Though associated with cervicitis, GC and CT were identified in only half of cervicitis cases and causes of the remaining cases were unknown in several studies.^{3,5,6} This represents a clinical dilemma in that even with highly sensitive diagnostic tests the etiology of MPC is still unknown in many cases.^{3,5,7-9} Marrazzo, *et al.*² demonstrated that among 1,028 women with either cervical mucopus or easily induced cervical bleeding, only 20% were due to CT or GC detected by culture. Gaydos *et al.*¹⁰ also demonstrated that among 133 women with MPC, 61% had no etiology determined as assessed by NAAT for CT, GC, MG, or *Trichomonas vaginalis* (TV).

The issue of empiric therapy for cervicitis is further complicated by recent evidence that other organisms, particularly MG and TV, are associated with non-CT/non-GC MPC.^{7,11} Additionally, the potential role of bacterial vaginosis (BV) in the etiology of MPC has been demonstrated.^{1,12,13,14}

The social and relationship consequences of misdiagnosing a sexually transmitted infection (STI) and overuse of antibiotics are also problems associated with empiric therapy for MPC. A central question underlying this study was whether or not increased unnecessary empiric antibiotic treatment puts women at greater risk than a strategy of screening with nucleic acid amplification tests (NAATs) and treating only those who are positive for known pathogens. The diagnosis of MPC that may ultimately be non-CT/non-GC creates unnecessary stress and social consequences for women and their partners.¹⁵ Additionally, a more pressing public health concern is overuse of antibiotics which contributes to antibiotic resistance.^{16,17,18}

This phase III randomized, double-blinded, non-inferiority study was designed to evaluate the effectiveness of placebo versus empiric antibiotic treatment with a single dose of cefixime 400 mg and azithromycin 1 gm¹⁹ in achieving clinical cure at 2 months of follow-up among women with MPC of unknown etiology. Secondary objectives included comparison of PID case rates and AEs; exploration of the role of BV and MG in the persistence of MPC; evaluation of the MG cure rate; and presentation of the outcome data at 2-3 weeks after enrollment. To evaluate these objectives, the study planned to randomize 772 women with equal allocation to placebo and treatment arms; however, due to low accrual of women with cervicitis of unknown etiology the Data Safety and Monitoring Board (DSMB) recommended that the trial be closed. We describe the etiology, clinical cure rates, AEs and rates of PID in women enrolled in this trial.

Materials and Methods

Participants were enrolled from four sites: New Orleans, LA; Birmingham, AL; Jackson, MS; and Los Angeles, CA. Women 18 years of age were invited to sign a screening consent prior to physical examination. If clinical MPC (cervical mucopus and/or easily induced cervical bleeding) was found, standard of care and research specimens were collected. Screened women with clinical MPC were then considered for enrollment in the randomized treatment trial if they were willing to provide written informed consent, abstain from sexual intercourse or use condoms during the entire study, abstain from using vaginal products during the entire study and met none of the exclusion criteria presented in Table 1. In an attempt to study the natural history of untreated BV and its association with MPC, women with symptomatic BV were excluded because they had to be treated for BV.

The research definition of cervicitis was cervical mucopus and/or easily induced cervical bleeding, and the presence of ≥ 30 WBCs per oil immersion field on cervical Gram's stain. Cervical Gram's stains, which were sent to the LSU Infectious Diseases Research laboratory for reading, were not available at the time of enrollment. Enrolled women whose baseline specimens were positive for GC or CT by NAAT run in local labs, those who had < 30 WBCs, or were positive for TV by InPouch (BioMed, White City, OR) were discontinued from the study and treated according to local standard of care after unblinding the treatment assignment (Table 1).

Women were diagnosed with bacterial vaginosis if they met 3 of the following 4 Amsel's criteria: vaginal pH > 4.5 , fishy amine odor with the addition of 10% KOH to vaginal discharge, a thin homogenous discharge, and $\geq 20\%$ clue cells on wet prep.²⁰

Women had follow-up visits at 2-3 weeks and at 2 months. Definitions of clinical outcomes are presented in Table 2.

Study participants were randomized equally to treatment with cefixime and azithromycin or placebo, stratifying the randomization by clinical center. All medications were over-encapsulated and appeared the same so that participants and clinicians were blinded to treatment.

This study was approved by the Institutional Review Board of each institution.

Specimen collection, transport and storage

Three endocervical and four vaginal swabs were collected and processed as outlined in Table 3. Specimens for future use were stored at -70°C and shipped on dry ice to the LSU Research laboratory. Specimens for CT/GC testing by APTIMA Combo 2 (Gen Probe, San Diego, CA) were held at room temperature prior to testing. Specimens for MG/TV Gen-Probe testing were shipped on cold packs weekly to LSU and then frozen at -70°C until tested at 2 to 3 month intervals.

Sample Size Estimation

The primary efficacy outcome was MPC clinical cure rates at 2 months. This was a non-inferiority trial designed to reject the null hypothesis that placebo control is inferior to empiric therapy for MPC. Under the assumption that the clinical cure rate is 75% for the empirical treatment group, a 10% non-inferiority margin (i.e., no more than a 10% lower cure rate in the placebo group) at the one-sided 0.05 significance level with 85% power required 270 study participants in each arm (for a total of 540 participants) using an unpooled Z-test using a normal approximation. It was anticipated that approximately 30% of enrolled study participants would not meet requirements for the per protocol population, so

the plan was to enroll 772 participants. To be included in the per protocol population, participants had to receive treatment or placebo, have primary outcome data, and no major protocol deviations. Since it was expected that only 23% of screened patients would meet the criteria for MPC, the trial planned to screen 3,356 women.

Statistical Analysis

To describe participant characteristics and lab results, frequencies and percentages as well as means and standard deviations were computed. Consistent with the test of non-inferiority, asymptotic two-sided 90% confidence limit for the difference in clinical cure rates (placebo minus treatment) were computed so that the lower limit could be examined relative to the non-inferiority margin of -10%. Participant characteristics were compared according to arm using t-test, or chi-square or Fisher's exact tests. The associations between arm and AEs at the subject level and between age group and lab results were investigated using chi-square or Fisher's exact tests. Analyses were performed using SAS version 9.3

Results

The participant flow is presented in Figure 1. Between March 2010 and May 2011, 577 women provided screening consent. Of these, 131 women (23%) met the clinical definition of cervicitis with 41 screening failures and 3 choosing not to enroll. While 87 women (66%) completed the enrollment consent and process, 45 women (52%) were enrollment failures or discontinued early due to CT, GC or TV infections or other protocol withdrawal criteria. After removing nine women who were lost to follow-up, 33 women were evaluable for clinical cure at 2 months. Reasons for screen failure, enrollment failure and early discontinuation among women with MPC are outlined in Table 4. Since the study closed early due to slow accrual with 11% of the targeted sample size enrolled, precision and power were low.

Baseline Characteristics of Enrolled Women

Among enrolled women, the baseline prevalence of CT was 17% (15/86), GC 2% (2/86), MG 13% (11/85), and TV 16% (14/87, which includes wet mount, InPouch, and NAAT). Note that one woman's original test CT and GC results were lost by the lab, and 2 women's MG samples were not sent to the lab (protocol deviations). Among all women with MPC, 22% (29/131) had TV by some method, and 11% (14/131) had TV by wet mount only (note that wet mount testing was the only TV test at screening). Of the 44 women in the treatment arm, 37 (84%) were negative for CT and GC. Of the 43 women assigned to the placebo arm, 33 (77%) were negative for CT and GC. By the protocol definition, 63% (55/87) of enrolled women were found to have MPC of unknown etiology, and when TV or MG via NAAT was also considered, 61% (53/87) were found to have MPC of unknown etiology (not GC, CT, TV or MG).

For enrolled women, age group (<25 vs. > 25 years) was not associated with MPC of unknown etiology with 58% of younger women having MPC of unknown etiology at enrollment as compared to 64% of older women ($p=0.534$). Similarly, age group was not associated with CT (20 vs. 14%), GC (2 vs. 2%), or TV by any test (19 vs. 13%), respectively (all $p>0.40$).

Tables 5 and 6 outline the socio-demographic, baseline physical exam characteristics and clinical findings of the 55 women who met eligibility criteria. No significant arm differences were detected except for a higher proportion of women with mucopus discharge in the placebo group and a higher proportion of women with easily induced bleeding in the treated arm. None of the women had symptomatic BV or PID at enrollment. There was one case of

PID on follow-up in a woman randomized to the treatment arm who was negative for CT, GC, TV, MG and BV. She met criteria for clinical failure and was discontinued at the first follow-up visit so there is no clinical information for the final two month visit. The average time to treatment for women randomized to the placebo arm and subsequently found to have GC or CT [12% (10/87)] was 6.3 (SD, 2.6) days from enrollment. This time frame included the time to get the CT or GC results back from the laboratory, contact the women and the time for women to return to the clinic for treatment.

Follow-up Outcomes

The initial projected proportion of patients who would not meet the criteria for the per protocol population was 30%; however, the actual proportion was 62% after STIs, symptomatic BV, other exclusion criteria and participants lost to follow-up were included in the calculation.

The two week and two month follow-up visit outcomes by arms are presented in Table 7. At two months the clinical cure rate was 33% in the placebo arm and 19% in the treated arm, such that the clinical cure rate was 14% higher in the placebo group, but the corresponding 90% confidence interval was -12.2 to 40.7%. Hence we were unable to reject the null hypothesis that the clinical cure rate for the no treatment arm was worse than the rate for the treated arm by 10% or more (i.e., non-inferiority was not supported). The overall clinical cure rate was 4% (2/45) at 2 weeks and 24% (8/33) at 2 months. The overall clinical failure rate was 42% (19/45) at 2 weeks and 30% (10/33) at 2 months, and did not significantly differ by arm.

Role of BV and MG in MPC

BV (symptomatic and asymptomatic) was noted in 36 of 131 women (28%) with clinical MPC at baseline. Twenty-two of these women (17%) were screen failures due to symptomatic BV. At the first follow-up visit, 14 of 41 women (34%) who were negative for CT, GC, MG, and TV still had asymptomatic BV alone. Only one woman with asymptomatic BV had a clinical cure. At the second follow-up visit, 8 of 32 women (25%) still had asymptomatic BV alone and four of the eight women (50%) still had evidence of persistent cervicitis.

Five (9%) of the 55 women who met all enrollment criteria based on initial lab results were positive for MG in the endocervical specimen at baseline (2 in placebo arm/3 in treatment arm). Four cleared the infection by the second follow-up visit (1 in placebo arm did not clear). In the vaginal samples, six women (11%) were positive at baseline (3 in placebo arm/3 in treatment arm). Two women cleared the infection (2 in the placebo arm and 2 in the treatment arm did not clear). Clearing MG from the cervix or vagina did not have any clear impact on clinical response. Only 1 woman in the treatment arm who cleared the cervical infection had a clinical cure. Three women who cleared the infection from the cervix or vagina had clinical failures or partial responses.

Adverse Events

There were no grade 3 or higher AEs in this study, and GI events were the most common. There were 24 GI AEs in 11 women (25%) in the treatment arm compared to 1 GI adverse event in 1 woman (2%) in the placebo group ($p=0.002$).

Discussion

This multi-center trial of mucopurulent cervicitis of unknown etiology provides prevalence and outcome data from the screening for MPC in 577 women at high risk for STIs. The 23%

prevalence of clinical MPC was consistent with Ryan, *et al.*²¹ who reported a prevalence of 22%. Willmott²² reported a 32% prevalence based upon mucopurulent discharge alone and Gaydos, *et al.* reported a prevalence of 41% in women with cervical discharge and/or friability alone.²³ The prevalence of cervicitis in the current study is also in contrast to Brunham *et al.* who found that cervicitis was common among 100 randomly selected women and reported a prevalence of 40%.³ In his study though, Brunham used >10 WBCs per oil immersion field on cervical Gram's stain and yellow pus on swab test in his definition. In addition, 30 WBCs per oil immersion field was used in the research definition for this study instead of >10 WBCs.

Sixty-one percent (61%) of enrolled women in the current study had MPC of unknown etiology (negative for CT, GC, TV and MG by NAAT). Gaydos, *et al.* also reported that 61% of women with cervicitis had no organism isolated using PCR for TV/MG and NAAT for CT/GC.¹⁰ Only 16 women (18%) in this study were withdrawn with GC and/or CT at baseline. This was consistent with Gaydos, *et al.* who found 22% of women with cervicitis had CT and GC using NAATs for CT and GC.²³ Schwebke and Marrazzo also found that only 24% and 20% of women, respectively, had cervicitis associated with CT and GC but used culture techniques.^{1,2} These data support the practice of screening with NAATs and delaying treatment until laboratory results are known in settings where women can be contacted for treatment in a timely fashion. The data do not support repeating a course of antibiotic therapy for women with persistent cervicitis when no treatable organisms were found on the initial screening.

In this study the prevalence of CT was 17%, GC 2%, MG 13%, and TV 16%. When women who were excluded due to trichomonas were included, 22% of all women with MPC had TV by some method (11% had TV by wet mount only). Gaydos, *et al.* found a prevalence of 11% CT, 4.6% GC, 19% MG and 15% TV by NAAT in women with MPC.¹⁰

No woman randomized to the placebo arm with delayed treatment for CT or GC developed PID. In a paper describing the natural history of untreated CT, Geisler, *et al.* reported 2% (2/97) of women had PID when treatment occurred 3 weeks after screening.²⁴ Hook, *et al.*²⁵ reported that 3% (3/100) of women with a median time to treatment of 14 days developed PID and Bachmann, *et al.*²⁶ reported that 4.5% (2/67) of women developed PID after being screened in the emergency room and returning for treatment (time between screening and treatment was not reported). In the current study, the average time to treatment was 6.3 days. Delay in treatment was not a problem. All women with CT and GC were contacted and treated.

Several studies have demonstrated the possible association of BV with cervicitis or cervical inflammation.^{1, 12-14, 27-29} Bacterial vaginosis (symptomatic and asymptomatic) was noted in 28% (36/131) of women with clinical MPC. At the first follow-up visit, 14 of 41 women (34%) who were negative for CT, GC, MG, and TV still had asymptomatic BV alone and only one woman had a clinical cure. At the second follow-up visit, 8 of 32 women (25%) still had asymptomatic BV alone and four of the eight women (50%) still had evidence of persistent cervicitis. In this cohort of women with MPC, these data also suggest BV plays a role in MPC.

Adverse events, overuse of antibiotics and antibiotic resistance are challenges involved with the practice of empiric therapy such as that used for MPC.¹⁷⁻¹⁹ In this study, of forty-four women in the treatment arm, 37 (84%) were negative for CT or GC. Of the forty-three women assigned to the placebo arm, 33 (77%) were negative for CT or GC. Therefore, antibiotics were only necessary for 16 (18%) women who were positive for CT or GC at baseline in both the placebo and treatment arms combined and represented overuse of

antibiotics using the empiric therapy approach. There are risks of adverse events (AEs) when empiric therapy is practiced. In this study there were 24 GI AEs in 11 women in the treatment arm compared to only 1 GI AE in 1 woman in the placebo arm. Though the numbers are small, this information lends support to the practice of initially screening with NAATs and treating only when test results are available if proper follow-up can be established. This practice is used in some family planning clinics. In addition, some have suggested using age as a criterion for the use of empiric therapy. Marrazzo, *et al.* presented data suggesting that treatment of MPC for presumed CT or GC infection may not be routinely indicated in women 25 years and older under certain conditions.² The CDC STD Treatment Guidelines recommend treating women with MPC at high risk for CT (e.g., those 25 years, those with new or multiple sex partners and those who engage in unprotected intercourse), especially if follow-up cannot be ensured.¹⁹

At two weeks follow-up, 43/45 women (96%) with MPC of unknown etiology had evidence of persistent cervicitis with only 2 clinical cures. At two months follow-up, 26/33 women (79%) had signs of persistent MPC of unknown etiology with only 7 (21%) clinical cures. This was well below our original assumption of a 75% clinical cure rate. Antibiotics targeting GC and CT were not necessary for most cases of MPC. Antibiotics to cover bacterial vaginosis were not included in this study but a possible association of MPC and BV was recognized. This could have also contributed to the low cure rates. Schwebke, *et al* demonstrated that resolution of cervicitis was more frequent among women who received metronidazole gel (used to treat BV) than those who received placebo.¹ Unfortunately, in the current study there was low power to conclude non-inferiority due to insufficient accrual and that was a limitation of this study.

Idiopathic MPC appears to be a persistent condition that does not appear to respond to the antibiotics used to treat CT and GC. An important finding in this study is that none of the women with persistent evidence of idiopathic MPC developed upper tract findings or PID. The literature is limited in reports with recommendations on how to manage persistent cervicitis. Nyirjesy reviewed prolonged antibiotic courses and ablative therapy and concluded that there were no data regarding the effectiveness of these procedures.⁹ Paavonen, *et al.* reported persistent or recurrent cervicitis at 3 months in 23% of a group of women treated with doxycycline and 33% of a group treated with amoxicillin.³⁰ These cases were all negative for GC, CT, TV, genital mycoplasma, and *Gardnerella vaginalis*. In the current study, 30% of women had complete clinical failure at 2 months follow-up. There is no evidence in the literature to support aggressive procedures or prolonged antibiotic courses, and this study demonstrates the difficulty of completing a comparative trial of empiric therapy in women with cervicitis of unknown etiology.

Using current NAAT diagnostic capabilities, the number of women with cervicitis of unknown etiology and clinical failure is quite intriguing. Clearly other unknown organisms or elements are involved and there is an intrinsic inflammatory response. As new diagnostic methods are developed to identify previously unknown organisms in the microbial flora of the vagina and cervix,^{31,32} perhaps we will gain a better understanding of cervicitis of unknown etiology and develop improved research and treatment strategies.

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Figure 1. Participant Flow

*Some lab results were not available until after the participant was randomized. Participants who were enrollment failures were discontinued.

Table 1
Protocol-Specified Screening Exclusion Criteria and Early Discontinuation Criteria at Enrollment

<u>Screening Exclusion Criteria</u>	
1	Signs and symptoms of PID
2	History of PID
3	Ectopic pregnancy or recurrent cervicitis (3 or more episodes in the prior year or written documentation of cervicitis within the past 30 days)
4	Motile trichomonas on wet mount examination
5	Symptomatic bacterial vaginosis
6	Use of vaginal products in past 48 hours
7	Chronic renal diseases
8	Current use of probenecid
9	Nursing mothers
10	Colitis or coagulopathy
11	Allergy to cephalosporins, penicillin or macrolides
12	Latex allergy
13	Serious underlying infection, including HIV
14	Concomitant infection requiring antibiotics
15	Menstruation at time of screening visit
16	Active herpes outbreak at the time of screening
17	Positive urine pregnancy test
18	Women who would require antibiotic treatment due to known or suspected GC or CT in a sexual partner
19	Use of systemic antibiotics (oral or intravenous), antivirals vaginal antibiotics, vaginal antifungal, or oral antifungal use within 30 days of study enrollment
<u>Early Discontinuation Reasons at Enrollment</u> <u>(Enrollment Failure Based on Baseline Specimen)</u>	
1	GC or CT positive or indeterminate at enrollment
2	<30 WBCs at enrollment
3	TV positive (In Pouch) at enrollment

Table 2
Clinical Outcome Definitions

Clinical Cure	• Absence of cervical mucopus and easily induced cervical bleeding and • < 30 WBCs per oil immersion field on cervical Gram's stain
Partial Response	• Persistent cervical mucopus and/or easily induced cervical bleeding with < 30 WBCs, or • 30 WBCs in the absence of both cervical mucopus and easily induced cervical bleeding
Clinical Failure	• Persistent cervical mucopus and/or easily induced cervical bleeding and 30 WBCs or • Signs of pelvic inflammatory diseases including cervical, fundal or adnexal tenderness

Table 3
Specimen Collection

Vaginal Swabs 1-4	Endocervical Swabs 1-3
Trichomonas culture via InPouch (Biomed, White City, OR)	Assessment of clinical MPC (yellow pus or blood noted on swab) and Gram's stain. This swab was then placed in a dry tube and later frozen for future molecular studies.
Wet mount for the detection of motile TV and clue cells, pH, KOH preparation for the detection of candidiasis, and whiff test	GC/CT testing (Aptima Combo 2, Gen-Probe, San Diego, CA)
TV and MG assay using Gen-Probe Aptima collection kit	Placed in Gen-Probe transport medium for later testing at 2 to 3 month intervals by the Gen-Probe TV analyte-specific reagent assay and the Gen-Probe MG research-use-only assay. No treatment or withdrawal decisions were made using these assay results.
Swab for future molecular studies	

Table 4
Reasons for screen failure, enrollment failure, and early discontinuation among women with MPC

Screen failures	N=41 women
Symptomatic BV	22
Trichomonas on wet mount	13
Infection requiring antimicrobial therapy/expected use	6
Requires antibiotic treatment due to GC or CT in partner	3
Symptoms of PID	2
OTC vaginal hygiene products in past 48 hrs	2
Unwilling to abstain from sex/use condoms	1
Unable to follow the protocol	1
History of PID, ectopic pregnancy or recurrent/recent cervicitis	1
Breast feeding	1
Taken antibiotics, antifungals in last 30 days	1
Total reasons *	53
Enrollment failures (based on baseline lab)	N=32 women
Positive for Gonorrhea	2
Positive for Chlamydia	15
Trichomonas (in pouch)	10
<30 WBC on Gram stain	10
Total reasons *	37
Early discontinuation (based on follow-up lab or reason)	N=13 women
Positive for Chlamydia	2
Trichomonas (Wet prep)	1
Systemic antibiotics	5
Symptomatic BV	2
Pregnancy	1
Withdrawal of consent	1
Unable to comply with follow-up	1
Total reasons	13

* Number of reasons does not add up to the number of women since 12 subjects had 2 reasons for screen failure, and 3 women had 2 reasons and 1 woman had 3 reasons for enrollment failure.

Table 5
Baseline Socio-Demographic Characteristics of Women with MPC

	Women with MPC Meeting All Enrollment Criteria			p-value*
	Placebo N=25	Cefixime + Azithromycin N=30	Both Arms Combined N=55	
Age in years, mean (SD)	25.8 (6.3)	25.8 (6.6)	25.8 (6.4)	0.997
Marital status, %				0.233
Married / Living Together	0	10	5	
Divorced / Never Married / Widowed	100	90	95	
Hispanic, %	16	13	15	1.000
Race				0.230
Black or African American	88	70	78	
White or Caucasian	12	23	18	
Other	0	7	4	
Highest grade/level of school completed, %				0.313
High school or less	60	46	53	
Some college or vocational certificate	36	37	36	
College degree or higher	4	17	11	
Clinic				0.488
STD	88	80	84	
Family Planning	12	20	16	

* T-test or chi-square test comparing Placebo and Cefixime+Azithromycin arms.

Table 6
Baseline Physical Exam Findings for Women Meeting All Enrollment Criteria

	Placebo N=25	Cefixime + Azithromycin N=30	Both Arms Combined N=55	p-value
Vaginal Discharge, %				0.397
None	12	27	20	
Scant (Visible on vaginal wall only)	56	40	47	
Moderate (Pools on Speculum)	28	33	31	
Large (Visible at Introitus)	4	0	2	
Mucopus Discharge, %	100	77	87	<.001
Easily induced bleeding, %	24	53	40	0.027
Ectopy, %	16	23	20	0.498
Swab Test Positive, %	52	63	58	0.396
Asymptomatic BV, %	32	14	22	0.109

* Chi-square test comparing Placebo and Cefixime+Azithromycin arms

Table 7
Clinical Outcome at First and Second Follow-Up Visits

	Placebo	Cefixime + Azithromycin	Both Arms Combined
First follow-up (2 weeks): Evaluable participants	N=18	N=27	N=45
Outcome, %			
Clinical failure	28	52	42
Partial response	72	41	53
Clinical cure	0	7	4

Second follow-up (2 months): Evaluable participants	N=12	N=21	N=33
Final Outcome, %			
Clinical failure	17	38	30
Partial response	50	43	45
Clinical cure	33	19	24