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Acceptability of and Adherence to an Antiretroviral-Based Vaginal Microbicide among Pregnant Women in the United States

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Abstract

The MTN-008 trial was the first multi-dose study conducted to evaluate the safety of a microbicide gel (2:1 randomized to tenofovir 1% or hydroxycellulose (HEC) placebo gel) during pregnancy. The study aim was to evaluate safety, tolerability and pharmacokinetics of the study products. Procedures included daily gel administration, with Day 0 and Day 6 in clinic, and Days 1–5 at home. Because pregnancy may pose unique challenges to consistent gel use and acceptability, evaluation of adherence and acceptability was a secondary objective of the trial. The study enrolled healthy, HIV-negative, pregnant women aged 18–40 in Pittsburgh, PA and Birmingham, AL, USA in 2 consecutive groups: cohort 1 was 37–39 weeks gestation, cohort 2 was 34–36 weeks. Ninety-one women completed the study (45 and 46 in each cohort, respectively)

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Compliance with Ethical Standards

Conflict of Interest All authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

and were evaluable per protocol. Adherence was evaluated using self-reports: participants completed a web-based computer-assisted self-interview (CASI) at Days 0 and 6 about gel attitudes and behaviors. At Day 6 trained research staff conducted a short interviewer-administered questionnaire with both structured and open-ended questions. Frequencies of quantitative data were tabulated in SAS and descriptive statistics are presented; open-ended textual data were summarized by a behavioral scientist experienced in qualitative analysis. Participants reported generally neutral perceptions of gel characteristics. A small number of women (7–8%) reported pain (6/90), other physical discomfort (7/90), or mental discomfort (7/90) associated with the process of applicator insertion. About 5% reported the same for the gel itself. Two-thirds (61/90) thought the gel was runny, many complained of bothersome gel leakage and several cited this reason for not inserting a full dose. The majority were not worried the gel would cause problems for their pregnancy or babies. Ninety-seven percent (83/86) said they would use the gel in the future if they were pregnant, and 90% (81/90) when nonpregnant. Self-reported adherence was high with 88% (79/90) reporting daily gel use on both the computerized and interviewer-administered questionnaires. The majority (67/90) reported no difficulty with daily use. However, drug was undetectable (<0.31 ng/mL) among 45% (27/60; 95% CI 32–58%) of the women on active product prior to observed dosing at Day 6. The most common reason for reported nonuse (N = 6) was forgetting. Study gel was generally acceptable, but many complained of a runny consistency (61/90) and leakage (83/90). No frequent or strong concerns about the effects of the study gel on the pregnancy/fetus were reported. Self-reported adherence to study gel self-administered at home for 5 days was high, however plasma drug levels suggest actual use may have been considerably lower. Findings from this study can provide insights relevant to use of other antiretroviral-based, vaginally-inserted HIV prevention methods during pregnancy.

Keywords

HIV prevention; Tenofovir; Pregnant; Breastfeeding; Microbicide

Background

HIV risk is increased for women during pregnancy, and there is evidence that viral acquisition during pregnancy may increase the likelihood of subsequent transmission to sexual partners and babies [1–4]. Microbicides are a potential means for women to protect themselves from HIV, and research into their safety and efficacy among women, including pregnant women, is a public health imperative. The Microbicide Trials Network (MTN)-008 trial, conducted at two sites in the United States, was an expanded phase I study, and the first multidose study of the safety and pharmacokinetics of a microbicide gel during pregnancy. Women were to use tenofovir (TFV) 1% gel or placebo for 7 daily doses near term (34–39 weeks) with day 0 and day 6 insertion in clinic, and days 1–5 at home. TFV gel was found to be safe and to produce low serum drug levels among the study sample of term and near-term pregnant women. Adherence to, experiences with, and acceptability of gel use are commonly assessed during later-stage microbicide trials. However, given that adherence to and acceptability of an ARV-based vaginal gel may be influenced in unique ways by pregnancy (for example physical challenges to insertions, or concerns about harming the fetus), these factors were assessed as secondary objectives of the MTN-008 trial.

Microbicide research is at a promising juncture. The dapivirine vaginal ring has recently been proven safe and effective in two large trials in sub-Saharan Africa [5, 6]. As the ring moves towards licensure and roll-out, its safety, acceptability, and effectiveness among pregnant and lactating women will be an important research priority. Although TFV gel and the dapivirine ring differ in formulation, many of the individual-level (e.g. physical and emotional concerns) and socio-contextual considerations (e.g. male partner attitudes) relevant to acceptability and adherence are similar. This paper offers important preliminary insights about use of, and attitudes towards, an antiretroviral-based, vaginally-inserted method for HIV prevention during pregnancy, and offers a starting point for further research into these topics for other dosing forms and in HIV endemic settings.

Methods

Study Design and Procedures

The MTN-008 study enrolled 98 healthy, HIV-negative, pregnant women aged 18–40 in Pittsburgh, PA and Birmingham, AL, USA between April 2011 and September, 2013. Study participants were neither required, nor precluded, from being sexually active during the study. The primary objectives of the MTN-008 study were to assess safety, tolerability and the pharmacokinetics of 1% tenofovir gel used for 7 days during pregnancy. As indicated above, assessment of adherence to gel for 7 days and its acceptability of use during pregnancy were secondary objectives. Of the women enrolled, 91 completed required study procedures before giving birth, and were classified as “evaluable” by the protocol team. Seven participants were enrolled but nonevaluable: 5 gave birth before completion of study procedures, one was an erroneous enrollment (pre-existing clinical exclusion criteria recognized post-enrollment but prior to dosing), and one withdrew consent. The study enrolled and followed two cohorts, the first of which included 45 pregnant “term” participants between 37 and 0/7 weeks gestation and 39 and 1/7 weeks (inclusive). Following an interim safety review to confirm that there were no safety concerns with the mother or fetus, the targeted sample moved backwards in the gestational period so as to enroll a second cohort of 46 “near term” participants who were between 34 0/7 and 36 6/7 weeks pregnant. Participants in each cohort were randomized in a 2:1 ratio to receive tenofovir 1% gel or placebo, dispensed in pre-filled 4 mL single-use applicators (HTI Plastics).

Gel was administered by a clinician in the clinic on the day of enrollment (Day 0), followed by 5 days of self-administered dosing at home, with the final dose given at clinic on Day 6. At the enrollment visit and at Day 6, participants completed a web-based computer-assisted self-interview (CASI) following a pelvic exam and the administration of gel. Study staff oriented participants to the CASI prior to the baseline interview, and were available nearby to assist with any technical problems. At Day 6, again following a pelvic exam, and the administration of gel, participants completed a follow-up CASI, and research nurses conducted a short interviewer-administered questionnaire that included structured and open-ended questions. Research nurses were trained by the lead social science Investigator on methods of obtaining complete participant responses during open-ended questions. To corroborate self-reported data about gel use, plasma taken prior to directly-observed gel

dosing at Day 6 was assessed for the presence of tenofovir using a previously reported liquid chromatography/tandem mass spectrometry method with a 0.31 ng/mL lower limit of quantitation [7]. Tenofovir concentrations less than 0.31 ng/mL were defined as "undetectable".

Measures

The CASI baseline questionnaire included demographic measures (e.g. age, marital status, race), as well as questions regarding current and previous alcohol use, drug use and sexual behavior. Participants were asked about intravaginal practices, including having ever inserted the following: vaginal douche, personal or sexual lubricant, drying or tightening agents, treatments for vaginal symptoms (e.g. yeast infections), items for contraception, or items for control of menstrual blood flow (e.g. tampons, menstrual cup). For every affirmative response they were further asked how many times they had inserted the item within the past 4 weeks, and if this was more than one time, how many times within the past week.

The CASI follow-up questionnaire explored the participants' experiences using the gel during the prior 6 days, including a daily adherence record, reasons for non-use, and gel and applicator acceptability. Participants' willingness/likelihood to use in the future, gel use problems, partner's reaction, sexual behavior and pleasure, condom use and intravaginal product use other than the study gel were also explored. Reasons for non-use included a pre-specified list of potential reasons for non-use commonly reported in previous studies, as well as an open-ended "other, specify" option.

The acceptability of the microbicide gel was measured through both broad-based and detailed questions in the CASI instrument. To assess overall acceptability, participants were asked: "*Overall how much do you like the study gel?*" and asked to rank their responses from 1 to 10, with 1 being "dislike very much" and 10 being "like very much". Scaled items were labelled at both anchors, and the middle of the scale was labelled "neither like nor dislike". Further questions asked in greater detail about attitudes towards the gel's physical characteristics: "*How much do you like the (color/taste/smell/consistency)?*" using the same response scale. The frequency and experiences of physical and emotional discomfort from both the applicator and the gel were individually explored through a series of questions as follows: "*How often did the insertion of the gel applicator cause you any (pain/physical discomfort/mental or emotional discomfort such as worries, fears, guilt or any other unpleasant feelings)?*" with categorical responses of: every time/some of the times/none of the times. Physical discomfort was parenthetically qualified as "not including pain" to capture, for example, physical discomfort with reaching around or under the pregnant belly to insert the gel vaginally. The same set of questions about applicators were repeated in reference to the gel itself (e.g. "*how often did the gel itself cause you any pain*"). For responses other than "none", respondents were subsequently asked to describe how much the pain/physical discomfort/emotional discomfort bothered or concerned her, and the level of intensity of the experience, both on ten-point scales.

The interviewer-administered semi-structured questionnaire measured the participant's overall experiences and feelings using gel during the trial in greater, open-ended, depth. For example, participants were asked to describe any pain, physical discomfort or emotional

challenges they faced, any worries or concerns they had; their experiences using the prescribed amount of gel; use at the same time every day; and other worries, likes, or dislikes using the gel during pregnancy. Open-ended responses were recorded verbatim unless too lengthy, in which case staff summarized key points. Additionally, a structured section of the interview-administered questionnaire asked to what extent participants were worried about the physical, mental or emotional concerns or experiences she encountered or she perceived in her partner.

Analysis—Open-ended textual data were imported into an Excel spreadsheet and summarized thematically by a behavioral scientist experienced in qualitative analysis. CASI data were summarized using SAS. There was inadequate power to conduct analyses of the association between acceptability and adherence among the subset of women on active gel with PK data (N = 60), therefore only descriptive statistics are presented. As described above, many CASI-based questions asked participants to indicate attitudes about the gel on a 10-point scale. For the purposes of this analysis, some scaled responses were summarized into mean and median values, while others were concatenated into 3 categories: 1–3 (e.g., disliked), 4–7 (e.g., “neutral” or neither liked nor disliked), or 8–10 (e.g., liked).

Results

Demographics

Characteristics of the study sample are presented in Table 1. Approximately two-thirds (64%, 58/91) were under 25 years old, and the majority (80%; 72/90) had completed high school or higher. Most women were single and heterosexual, and the majority (78%; 71/91) racially identified as black. The current pregnancy was the first pregnancy for a substantial minority (40%; 37/90). Additional data about participants’ employment, student and insurance status, as well as risk behavior and vaginal practices are detailed in Table 1.

Acceptability

Ease and Difficulties with Use—Pregnant women in this study reported being very comfortable inserting their gel at home as directed by staff. In the CASI questionnaire, less than 10% of women reported instances of the gel applicator causing pain (6/90), physical (7/90) or emotional discomfort (7/90). In semi-structured interviews, one participant described experiencing pain inserting the applicator, but not with applicator removal, and another said the applicator insertion hurt on the first day but subsequently this resolved when she “didn’t stick it in as far”. Only two participants noted physical discomfort inserting the gel applicator, one of whom described that the way the baby was lying made bending over awkward, and she overcame this discomfort by having her boyfriend insert the applicator. Women used a variety of postures to insert the gel, including standing with both feet on the ground (27%), standing with one foot up (20%), squatting (21%), sitting (17%) or lying on their backs (15%). The majority of participants reported no physical difficulties inserting the gel as instructed and in open-ended questionnaires, several compared the process to the simplicity of tampon insertion (see Table 3). Remembering to use gel daily was noted by a few participants (7%; 6/90) as the only difficulty they faced, often because they were tired or busy with work. While some used cell phone reminders or integration of the new procedure

into their bathroom routines, the majority described no problems simply remembering to use it for the short study duration without specific reminder mechanisms. As one participant summarized:

> It is easy to use. It is small so you can carry it around. It's like 1–2 and you're done, it's not a long process. It didn't affect me in any way, I just added putting it in everyday to my daily schedule.
>
> (Pittsburgh, 26 years old)

Gel Consistency—In CASI questionnaires, women were asked their opinions about the physical characteristics of the gel during their 6 days of use. In general, while most did not find the gel too sticky (84%; 76/90), a substantial proportion of women did find it "a little runny" (49%; 44/90) or "too runny" (19%; 17/90). Consistent with this finding, 92% (83/90) experienced gel leakage some or every time it was used, of which 69% (57/90) said it leaked somewhat, and 30% (25/90) felt it leaked "a lot". In semi-structured interviews, several women provided additional detail about their perceptions of gel consistency, describing it as "slimy" and "gross". As one participant from Pittsburgh elaborated: "It was like I was peeing myself". Panty liners were provided by the study; however, some complained that they had to use multiple liners to soak up the gel, and the feeling of leakage into their underwear caused some discomfort during the day.

Concerns with Gel Use: Physical, Emotional, Partner-Related—Women were asked on a scale of 1–10 to rank their level of worry about several aspects of gel use, with "1" being "not at all" and 10 being "a lot". Mean responses for concerns about the gel causing problems for her pregnancy, the baby, her overall health or her main partner's health were all less than 3, with median scores of "1" (Table 2), indicating a very low level of concern. Few participants reported concerns about gel side effects, and those who did described these worries as minor or short-lived.

In semi-structured interviews, no one reported having concerns about the effect of the gel on their babies.

That said, four women noted that their male partners had expressed at least some initial concerns about the safety of the gel for the baby.

> No, he just was initially worried for me and our baby, but we went over the packet (informed consent) together and he felt fine then.
>
> (Birmingham, 27 years old)

Two other participants relayed their partners' health-related concerns that were more specific to pregnancy. The first concern was that the blood draws required for the study would exacerbate her anemia, and the second was that the gel might prematurely initiate the onset of labor. One male partner was reported to insist on condom use during the study period to protect himself from potentially harmful side effects of gel exposure. In general, however, the majority of women reported that their male partners knew about the gel and had no concerns or worries.

Overall Liking of the Gel and Willingness to Use in the Future—When asked in the CASI questionnaire how much they liked the gel overall on a scale of one to ten, women's mean ranking was 6.7 (median 6, range 2–10), suggesting moderate acceptability of the product.

While the majority of women were not worried about getting HIV (median 1, mean 3.9, range 1–10); they did feel it was very important to prevent HIV when pregnant (median 10, mean 9.8, range 1–10; see Table 2)., and the majority said they would use the gel in the future when nonpregnant (90%, 81/90) or pregnant (97%, 83/86) if it was proven effective In semi-structured interviews, although there were varied preferences for dosing, woman provided feedback that they would use it or recommend it to others in the future because it was easy to use and the benefits outweighed the detriments, as described in the following interview excerpts:

- If it really works like it should I would recommend to others and would like to use it myself. One little thing to prevent something so serious. Would rather put gel in than take a pill. Easier than a tampon and smaller. (Pittsburgh, 20 years old)
- I feel like it was a bit drippy. Don't know if they could thicken it. (Each time) I used a pantyliner and it was full. It was kinda gross—dripped the whole day. If it was for HIV prevention, I would use it. Pros outweigh the cons. I might not use it in the a.m. but just prior to having sex. (Pittsburgh, 23 years old)
- It was okay. It was not something I'd use every day because I'm married and we don't use protection. But if I had a friend who had multiple partners, I would probably recommend it because it's simple and easy to use. (Birmingham, 33 years old)
- It's clear and had no odor, so (my) partner does not have to know (I) used it… (the gel) would be helpful for women, especially overseas, who want to keep their using the gel a secret. (Birmingham, 27 years old)
- It will be easy for women to use in the future. The only hard part is remembering to take it, like it is with birth control pills. (Birmingham, 30 years old)

Use of Gel/Adherence—The majority (88%; 79/90) of women reported in both their computerized interviews and interviewer-administered questionnaires that they had inserted the gel on each day of the 5-day dosing period at home. Further, almost all (96%; 85/90) of these women reportedly used the full amount of gel in the applicator, and most women assessed their ability to insert gel as instructed as excellent (60%; 53/90), very good (24%; 21/90) or good (13%; 12/90). By contrast, drug was undetectable in plasma (<0.31 ng/mL) among 45% (27/60; 95% CI 32–58%) of the women on active product (N = 60) prior to observed dosing at Day 6. Participant's adherence and self-reported adherence and use experiences are reported in Table 3.

Discussion

The MTN-008 study was the first study to evaluate use of daily TFV gel among pregnant women at term and near term. It is important to study the safety of microbicide candidates in pregnant populations for several reasons. Pregnancy is common among women of childbearing age in HIV endemic areas, and sexual activity is common among pregnant women. Thus HIV acquisition risk exists, and although inconclusive, some evidence suggests that pregnancy may exacerbate this risk [1, 8–10]. Topical antiretroviral-based microbicides could offer an important strategy for women to protect themselves during pregnancy, and as promising candidates move through the development pipeline, their safety, pharmacokinetics and effectiveness will need to be evaluated among pregnant women in a stepwise fashion (working backwards in the gestation period) as was done here. Parallel to this clinical research, it will be important to assess if and how attitudes and behaviors might change over the course of the perinatal period, and how these are affected by male partners, peers, family and community members, as well as cultural beliefs and other factors.

In addition to showing a favorable safety, tolerability and drug absorption (PK) profile [11], the data reported here suggest that the gel was moderately acceptable and that self-administration was feasible and perceived as simple for at least 5 days at home. While this period of time is not long, it is encouraging that women in late-stage pregnancy reported few physical problems with insertion, and that difficulties with the initial “uptake” period of using a new product were minimal. In the CASI questionnaires and the semi-structured interviews, women reported high and consistent gel use. However, the plasma drug levels suggest that actual use was lower, as 45% had undetectable pre-dose TFV levels in this study at Day 6, compared to 21% with undetectable levels in MTN-001, a similar study in non-pregnant women [7]. While some of this difference could be related to dilutional effects of pregnancy (potentially both increased plasma volume and increased vaginal secretions), the PK parameters on Day 0, 8 h after observed dosing, were observed to be similar between this pregnant cohort and nonpregnant comparators [11]. The challenges of suboptimal adherence and accurate product use reporting in HIV prevention method research have been well documented in other recent microbicide studies [12–15]. In the VOICE trial, as with other microbicide studies, a variety of social and contextual factors influenced women’s ability and willingness to consistently use products on a daily basis [16]. Reasons included fear of side effects, distrust of research, and influence of peers including male partners, as well as beliefs about the potency and safety of antiretrovirals [6, 16]. Importantly, the most common barriers to adherence of these candidates were not dependent on dosing modality (e.g. gel), and thus may be translatable to other formulations. Real-time drug level monitoring with feedback to participants during trial implementation—a strategy now being used in microbicide studies to monitor and encourage high adherence using “objective” biomarkers should be considered in future research with pregnant women [5, 17].

The ranking of the TFV and matched placebo gel in this study was, on average, a 6.7 out of ten, suggesting moderate acceptability, and the majority of women said they would use it in the future to prevent HIV, whether they were pregnant or not. Nevertheless, several participants complained of a runny consistency and leakage that made them uncomfortable. The viscosities of the tenofovir and placebo gels used in this study have previously shown

comparability to over-the-counter lubricants such as KY Jelly and Astroglide Gel [18]. Nevertheless, feelings of runniness and leakage may be exacerbated in pregnant women experiencing increased vaginal discharge, highlighting the importance of studying special populations. Gel leakage and excess lubrication have been reported as a concern by men and women in other microbicide studies [19, 20], and while some have reportedly favored added lubrication, others have disliked how extra “wetness” changes the feeling of sex or reveals gel usage to partners. In this study, many women inserted gel in the morning, whereas in other studies such as VOICE, insertion at night was common [16]. In future studies or demonstration projects where gel is used, problems related to leakage could potentially be overcome by allowing dosing schedules to vary based on individual preferences for lubrication during sex, sleeping and bathing schedules. Formulation changes in the gel itself could also enhance acceptability among a wider group of women, however in order to know what to modify, more studies assessing end-user preferences for delivery platforms (and the modifiable specific aspects of each platform) are needed.

Contrary to our expectations, no frequent or strong concerns about the effects of the study gel on the pregnancy/fetus were reported by participants. This may have been due to their late stage of pregnancy. Additionally, those who came forward and enrolled in the MTN-008 study are likely to differ in their attitudes from other pregnant women in these study communities (i.e. women who were concerned, likely did not enroll). Further work is needed on acceptability of vaginal gel use during pregnancy among the general population of pregnant women in areas where gel use for HIV prevention would be likely. Several women did report that their male partners were concerned about side effects of the gel and other issues, and this finding reinforces the need for researchers to acknowledge male partners influence, while supporting women’s agency to autonomously use products. Indeed, several dimensions of gel acceptability explored in this study may be translatable to other vaginally inserted antiretroviral-containing HIV prevention products, such as the dapivirine vaginal ring, and should be considered in future research on product use during pregnancy. For example, male partner concerns, and attitudes about how use of the product might impact the baby, women’s comfort and ability to physically insert/remove something intravaginally in late-stage pregnancy.

Aside from the selectivity of the study population, several additional potential limitations must be considered for these data. First, plasma PK results suggest that fewer women may have used gel than verbally reported, and thus reported experiences and attitudes with the gel were potentially based on less actual experience than anticipated. All participants received two doses in the clinic; thus, even women who never used the gel at home still could report on their acceptability of the gel from clinic exposure. The inconsistency of plasma drug levels with self-reporting of home dosing suggest a high degree of social desirability bias in adherence reporting, and this bias may have similarly distorted reporting on gel acceptability. That said, many participants did openly complain about gel characteristics such as leakage. This expanded phase I study was conducted in the United States and it is unknown to what degree these attitudes are relevant to pregnant women in other parts of the world with a higher prevalence of HIV, particularly Africa where microbicides will first be deployed if proven effective. Beliefs about using any “medicine” and inserting anything intravaginally—either while pregnant or otherwise—are culturally-defined and differ across

settings. It will be important to continue to evaluate attitudes in other settings if and when vaginal products are approved for further testing and use. Open-ended interviews were conducted by clinic nurses, which may have introduced bias.

In conclusion, in this study population of pregnant women, aside from concerns about the gel consistency and leakage, the use of this microbicide product for HIV prevention resulted in few problems related to physical pain, discomfort or concerns about safety for the mother or fetus. Complaints about the gel being too runny, might be mitigated by behavioral modifications such as timing and technique for applicator insertion. Although results of the PK analysis indicate that a substantial proportion of active arm participants were not adherent, the majority of women in this study reported they would use it in the future if proven effective, suggesting that TFV gel—or another candidate—could be more acceptable to pregnant women once efficacy data is available and the product is licensed for use. Indeed, there is not necessarily a linear relationship between acceptability and adherence (e.g. one may dislike a product but use it), thus low adherence or over-reporting of adherence does not mean a product was disliked. Further, nonuse of an investigational product of unknown efficacy during a trial does not mean that a product would not be liked or used if proven effective. The quantitative and qualitative evaluation of women's attitudes and experiences using antiretroviral-based vaginal products during different stages of pregnancy and across cultural contexts, is critical to a comprehensive understanding of their public health potential.

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Table 1

Characteristics of the study population at enrollment, N = 91

	N	%
Age		
Under 25	58	63.7
25 and over	33	36.3
Race/ethnicity		
White, non-Hispanic	13	14.3
Black, non-Hispanic	71	78.0
Mixed race, Hispanic	1	1.1
Mixed race, non-Hispanic[a]	6	6.6
Education		
Less than 12 years	18	20.0
12 years	44	48.9
More than 12 years	28	31.1
Parity		
0	37	41.1
1	26	28.9
2 or more	27	30.0
Employment		
Full -time	22	24.4
Part-time	12	13.3
Unemployed	56	62.2
Student status		
Full or part-time	15	16.7
Non student	75	81.3
Sexuality		
Straight/heterosexual	80	88.9
Other	10	11.1
Insurance		
Not public	12	13.3
Public	78	86.7
Marital status		
Single	74	82.2
Married	10	11.1
Separated	2	2.2
Divorced	1	1.1
Engaged	3	3.3
# days consumed alcohol/week (prior to pregnancy)		
Less than 3	84	93.3
3 or more	6	6.7
Ever smoked, ingested or inhaled recreational drugs	31	34.4

	N	%
Ever injected recreational drugs	1	1.1
Ever exchanged sex for food, shelter, money or drugs	0	0
Ever used any intravaginal product[b]	85	94.4
Ever used douche in vagina	53	58.9
Ever used sexual lubricant	35	38.9
Ever put something in vagina to treat symptoms	40	44.4
Ever put something in the vagina for contraception	24	26.7
Ever put something in the vagina for menstrual control (e.g. tampons, menstrual cup) menstrual	72	80.0

Sample includes 91 women deemed “evaluable” per study protocol, of 98 women total who enrolled but did not complete procedures. Denominators are less than 91 for some variables due to missing information

[a] 3 participants marked Black and White, 1 marked: Black, White and Native American, 1 marked Asian and White, 1 wrote in “biracial”

[b] This is a created variable that includes Individuals who answered “yes” to use of one or more of the products described in non-bold text underneath

Table 2

Acceptability of and experiences with the gel during 7-day use period

Characteristic	Cohort 1 37–39 weeks gestation (N = 44)[a]	Cohort 2 34–36 weeks gestation (N = 46)	Total (N = 90)[a]
Gel feels too runny			
Yes, too runny	4 (9%)	13 (28%)	17 (19%)
A little too runny	25 (57%)	19 (41%)	44 (49%)
No, not runny	15 (34%)	14 (30%)	29 (32%)
Gel feels too sticky			
Too sticky	1 (2%)	3 (7%)	4 (4%)
A little too sticky	2 (5%)	8 (17%)	10 (11%)
No, not sticky	41 (93%)	35 (76%)	76 (84%)
Gel leaked from vagina—frequency			
Every time	24 (55%)	29 (63%)	53 (59%)
Some of the time	16 (36%)	14 (30%)	30 (33%)
None of the time	4 (9%)	3 (7%)	7 (8%)
Quantity of gel leakage from vagina			
A lot	9 (23%)	16 (37%)	25 (30%)
Somewhat	30 (75%)	27 (63%)	57 (69%)
Not at all	1 (3%)	–	1 (1%)
Insertion of applicator caused pain			
Ever	2 (5%)	4 (9%)	6 (7%)
Never	42 (95%)	42 (91%)	84 (93%)
Insertion of applicator caused any other physical discomfort			
Ever	1 (2%)	6 (13%)	7 (8%)
Never	43 (98%)	40 (87%)	83 (92%)
Insertion of applicator caused mental/emotional discomfort			
Ever	1 (2%)	6 (13%)	7 (8%)
Never	43 (98%)	40 (87%)	83 (92%)

	Median (mean, range)
Overall how much did you like the study gel (from: 1, not at all, to 10, a lot)	6 (6.7, 2–10)
How worried gel would cause problems for…(from: 1, not at all, to 10, a lot)	
Pregnancy	1 (2.3, 1–10)
Baby	1 (2.6, 1–10)
Overall health	1 (1.8, 1–10)
Main partner's health	1 (1.5, 1–10)
How worried about getting HIV (from: 1, not at all, to 10, a lot)	1 (3.9, 1–10)
How important to you to prevent HIV when pregnant (from: 1, not at all, to 10, very)	10 (9.8, 1–10)
How comfortable with insertion of gel at home (from: 1, not at all, to 10, very)	9 (8.6, 1–10)

[a]One evaluable participant did not complete the CASI follow-up questionnaire

Table 3

Adherence and use experiences

PK results (active arm only)	**Cohort 1 37–39 weeks gestation (N = 29)**	**Cohort 2 34–36 weeks gestation (N= 31)**	**Total (N = 60)**
Drug detectable	17 (59%)	16 (52%)	33 (55%)
Drug not detectable	12 (41%)	15 (48%)	27 (45%)
Behavioral questionnaires	Cohort 1 37– 39 weeks gestation (N = 44)[a]	Cohort 2 34 – 36 weeks gestation (N = 46)	Total (N = 90)[a]
Number of days inserted gel at home[b]			
Never	–	1 (2%)	1 (1%)
1–4	4 (9%)	6 (13%)	10 (11%)
5 or more[a]	40 (91%)	39 (85%)	79 (88%)
Most important reason for not inserting study gel at home[c]			
Not applicable, I used the gel every day	35 (80%)	32 (71%)	67 (75%)
Inserted at clinic	5 (11%)	5 (11%)	10 (11%)
I forgot	3 (7%)	3 (7%)	6 (7%)
I physically could not insert it	–	1 (2%)	1 (1%)
I didn't like the feeling of the gel	–	–	–
I did not have the gel with me	1 (2%)	1 (2%)	2 (2%)
My sexual partner did not want me to use it	–	–	–
I was scared it could be bad for me or my baby	–	–	–
Other[d]	–	3 (%)	3 (%)
Used less than full amount at home[c]			
Ever	3 (7%)	1 (2%)	4 (4%)
Never	41 (93%)	44 (98%)	85 (96%)
Self-perceived ability to use gel as instructed at home[c]			
Very poor	–	–	–
Poor	–	1 (2%)	1 (1%)
Fair	–	2 (4%)	2 (2%)
Good	6 (14%)	6 (13%)	12 (13%)
Very good	8 (18%)	13 (29%)	21 (24%)
Excellent	30 (68%)	23 (51%)	53 (60%)
Inserted the gel at approximately the same time every day			
Yes	38 (86%)	40 (87%)	78 (87%)
No	6 (14%)	6 (13%)	12 (13%)
			Median (mean, range)
How easy/difficult to insert the gel at the same time every day (from: 1 difficult, to 10, easy)			9 (8.4, 1–10)

[a] One evaluable participant did not complete the CASI follow-up questionnaire

[b] Includes 10 participants who inserted gel at clinic during the home-dosing period

[c] Among 89 participants who used gel at home

[d] 1 participant described timing too close to previous dose, 1 was told by PI not to dose, 1 response unclear