IMPACT OF PRODUCT ADHERENCE AND CONDOM USE ON RATES OF UROGENITAL INFECTION WITH CHLAMYDIA TRACHOMATIS OR NEISSERIA GONORRHOEAE IN THE AMPREVENCE PHASE 2B/3 CLINICAL TRIAL

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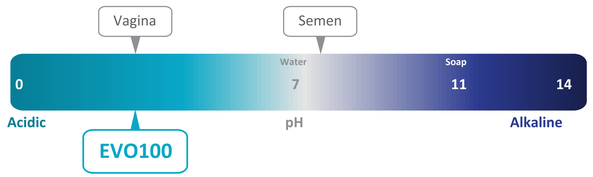
INTRODUCTION

- In 2017, the United States Centers for Disease Control and Prevention reported that *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (GC) were the first and second most common notifiable sexually transmitted infections in the United States, respectively[1]
  - Despite availability of male and female condoms for the prevention of sexually transmitted infections, the increasing incidence of CT and GC infection rates suggest that there is an urgent need for new prevention strategies
- EVO100 (L-lactic acid, citric acid, and potassium bitartrate) was developed as a woman-controlled, antimicrobial, pH-regulating investigational vaginal gel for the prevention of sexually transmitted infections[2,3]
  - EVO100 has acid-buffering properties and is able to maintain the acidic vaginal environment (pH 3.5–4.5) even in the presence of alkaline semen (**Figure 1**)
  - In preclinical testing, EVO100 showed microbicidal activity against CT and GC, without impacting native lactobacilli species in the vaginal mucosa[4,5]
- AMPREVENCE (N=860) was a double-blinded, placebo-controlled, multicenter, phase 3 study based in the United States conducted over approximately 16 weeks in women age 18–45 years who were at risk of CT or GC infection
  - AMPREVENCE met its primary and secondary efficacy endpoints, with significantly lower CT and GC infection rates in women receiving EV100 than placebo users; there was a 50% reduction of risk in CT infection and 78% reduction of risk in GC infection following 16 weeks of EVO100 use compared with placebo[6]
  - EVO100 was safe and well tolerated with most side effects being mild to moderate

Figure 1. EVO100 Has Unique Acid-buffering Properties and Can Maintain the Acidic Vaginal Environment



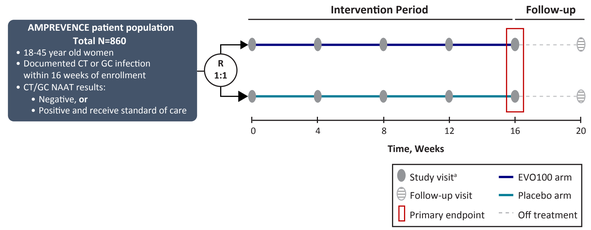
AIM

- The objective of this analysis was to assess the effects of adherence and condom use during the phase 2b/3 AMPREVENCE study on urogenital CT or GC infection

METHODS

- AMPREVENCE (NCT03107377) was a double-blinded, placebo-controlled, randomized phase 2b/3 trial conducted at 50 US sites over approximately 16 weeks (**Figure 2**)
  - Sexually active, healthy women aged 18–45 with documented CT or GC infection within 16 weeks preceding the Enrollment Visit (Visit 1) or found to be positive at the screening visit were enrolled
  - Women administered one prefilled applicator of study product intravaginally ≤1 hour before each act of intercourse
  - Women were counseled to address individual risk factors and advised on correct and consistent use of male condoms for prevention of sexually transmitted infections; condom use only was not an acceptable form of contraception for this study
  - Women used diaries to record timing of study product administration and condom use with each act of intercourse
  - Diaries entries were reviewed at each study visit

Figure 2. AMPREVENCE Study Design



Diary entries were reviewed at each study visit. [a]Women visited the clinic for screening (Visit 0 [Weeks -6 to 0]), for enrollment (Visit 1 [Week 0]), and during the intervention period at Visit 2 (Week 4), Visit 3 (Week 8), Visit 4 (Week 12), and Visit 5 (Week 16). The post-intervention/follow-up visit occurred at Week 20.
CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; NAAT, nucleic acid amplification test; R, randomization.

- Exploratory analyses on the efficacy evaluable (modified intent-to-treat [mITT]) population examined if CT and GC infection rates differed between treatment groups by adherence rates
  - The efficacy eligible population (mITT) included women with known infection status through the end of the treatment phase and no use of prohibited antibiotic medications
  - Using diary data, the rate of adherence was calculated as the number of times the product was used by the number of coital events
  - Product adherence was summarized in "≥20%", "≥40%", "≥60%", "≥80%", and "100%" subgroups
- Additionally, the impact of condom use on CT and GC infection were also explored
  - Mean condom usage rate was calculated as the ratio of number of coital acts with a male condom to the total number of coital acts during study treatment
  - CT and GC infection rates by treatment group and condom usage rate (none, low, high) were analyzed
  - Low condom use was defined as women who had a rate that was less than or equal to the 50th percentile calculation of women using condoms
  - Results were summarized using descriptive statistics

RESULTS

Measurement of Treatment Adherence

- Women reported a mean (SD) 16 (14.7) mean coital events (EVO100: 15.7 [13.5]; placebo: 16.3 [15.8]) during the 16-week treatment phase
- As assessed from women's diaries, adherence was similar between both treatment arms; 66% of women using EVO100 and 67% of women using placebo had treatment adherence ≥80% (**Table 1**)

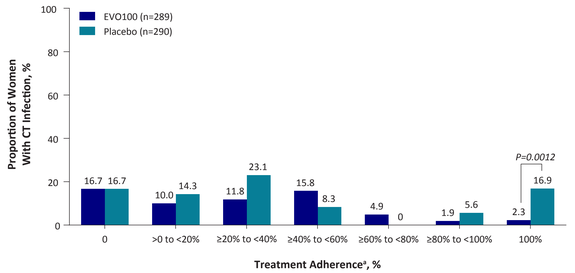
Table 1. Summary of Treatment Adherence (mITT population)

Study product adherence, n (%)[a,b]	mITT		
	EVO100 n=364	Placebo n=383	Total N=747
0%	12 (3.3)	18 (4.7)	30 (4.0)
>0% to <20%	10 (2.7)	9 (2.3)	19 (2.5)
≥20%	20 (5.5)	16 (4.2)	36 (4.8)
≥40%	28 (7.7)	27 (7.0)	55 (7.4)
≥60%	49 (13.5)	49 (12.8)	98 (13.1)
≥80%	127 (34.9)	151 (39.4)	278 (37.2)
100%	114 (31.3)	107 (27.9)	221 (29.6)
Missing	4	6	10

[a]From women's diary entries, adherence was calculated as the ratio of the number of times the product was properly used to all coital events recorded during the treatment phase.
[b]For frequency result of adherence, each group was deemed mutually exclusive.
mITT, modified intent-to-treat.

- EVO100 users with 100% adherence were significantly less likely to acquire a CT infection compared with women using placebo (2.3% vs 16.9%, respectively; *P*=0.0012) (**Figure 3**)
  - Among women with ≥20%, ≥40%, 60%, or ≥80% adherence rates, no significant differences were found in the proportion of women with CT infections between women treated with EVO100 and placebo
- No difference was seen in rates of GC infection between women using EVO100 (1/87) or placebo (0/70) who were 100% adherent, or among those with ≥20%, ≥40%, 60%, or ≥80% adherence rates

Figure 3. EVO100 users with 100% adherence were significantly less likely to acquire a CT infection compared with women using placebo

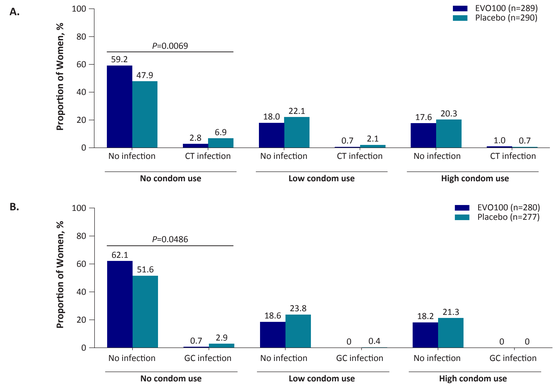


[a]Treatment adherence subgrouping was based on those who were eligible for CT analysis.
CT, *Chlamydia trachomatis*, mITT, modified intent-to-treat.

Condom Use

- The mean (SD) condom usage rate was similar among EVO100 and placebo users (24.5% [39.7] vs 26.7% [40.2], respectively)
- CT infection rates were significantly lower among EVO100 users (2.8%) compared with placebo users (6.9%; *P*=0.0069) when no condom usage was reported (**Figure 4A**)
  - No significant differences in CT infection rates were observed among women with low (*P*=0.4639) or high (*P*=0.6644) condom use between EVO100 or placebo users
- EVO100 users had significantly lower GC infection rates (0.7%) compared with placebo users (2.9%; *P*=0.0486) among women reporting no condom use (**Figure 4B**)
  - No significant difference in GC infection rates were observed among women with low condom use between EVO100 or placebo users (*P*=1.0000)
  - There were no reported GC infections among EVO100 or placebo users reporting high condom use

Figure 4. A) CT and B) GC infection rates by condom usage rates (mITT population)



Low condom use was defined as women who had a rate greater than 0 and ≤50th percentile of condom usage across all women. CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; mITT, modified intent-to-treat.

CONCLUSIONS

- The increasing rates of CT and GC infection are urgent public health concerns
  - EVO100 is a woman-controlled, antimicrobial, pH-regulating investigational vaginal gel that is effective in reducing the risk of CT and GC infection, with significantly lower rates of CT and GC infection women receiving EVO100 than placebo users
- Adherence rates impacted the proportion of women with CT infections, but did not significantly affect GC infections, possible due to the overall small number of infections in each adherence sub-group
- Women were counseled during the trial per standard of care to use condoms consistently, however, reported condom use was quite low
  - In women who reported no condom use, EVO100 was associated with even lower rates of CT and GC infection versus placebo

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DISCLOSURES

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