EFFICACY AND SAFETY OF A NOVEL VAGINAL PH MODULATOR FOR PREVENTION OF CHLAMYDIA AND GONORRHEA

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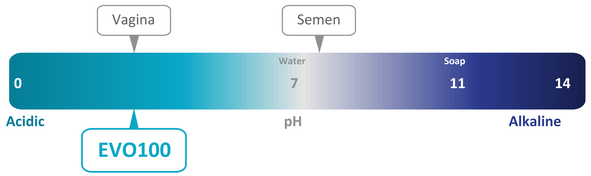
INTRODUCTION

- 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 conditions in the United States, respectively[1]
  - Increasing incidence of CT and GC infection rates suggest that there is an urgent need for new prevention strategies
- It is thought that the naturally acidic vaginal environment can inhibit acquisition of common sexually transmitted infections such as CT and GC[2-6]
  - EVO100 is being developed as an woman-controlled, antimicrobial, pH-modulating investigational vaginal gel for the prevention of sexually transmitted infections.[7,8]
  - EVO100 contains 3 active ingredients, L-lactic acid (1.76%), citric acid (1%), and potassium bitartrate (0.4%), 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[9,10]

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



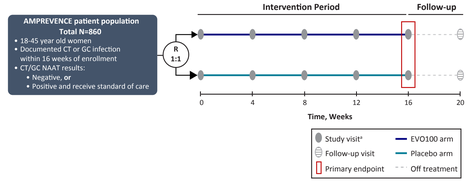
AIM

- To determine if EVO100 reduces the risk of urogenital CT and GC infection in healthy, sexually active women

METHODS

- AMPREVENCE (NCT03107377) was a double-blinded, placebo-controlled, randomized phase 2B/3 trial conducted at 50 US sites with a 16-week intervention period (**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 and completed standard of care treatment with subsequent negative test prior to enrollment
  - Women were instructed to administer a single prefilled applicator of study drug intravaginally before each episode of intercourse
  - Women used diaries to record timing of product administration, coital information, and side effects
- The primary efficacy outcome was the incident infection of CT during the intervention period
  - The secondary outcome was the incident infection of GC during the intervention period
- Study visits were scheduled every 4 weeks (Visits 2 to 5) to obtain repeat CT/GC nucleic acid amplification test (NAAT), to review diaries, and to collect adverse event (AE) and concomitant medication information
  - A follow-up visit (Visit 6) 4 weeks after the last intervention visit was scheduled for post-intervention assessment

Figure 2. AMPREVENCE Study Design



[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.

- All randomized women constituted the intent-to-treat (ITT) population
- A subset of women in the ITT population who were negative for CT and GC infection at enrollment and reported use of the study product were part of the modified intent-to-treat (mITT) population
  - This analysis eligible population (mITT) included women with known infection status through the end of the treatment phase and no use of prohibited antibiotic medications
- Women who documented any use of study product were included in the Safety population

RESULTS

- In total, 860 women were randomized 1:1 to receive EVO100 (n=426) or placebo (n=434)
  - There were 764 women (EVO100: n=376; placebo: n=388) who used the study drug at least once and were included in the safety analysis
- Baseline characteristics were similar between treatment arms (**Table 1**)

Table 1. Baseline Demographics and Disease Characteristics of Enrolled Women (ITT Population)

	ITT		
	EVO100 n=426	Placebo n=434	Total N=860
Age in years, mean (SD)	27.8 (7.1)	27.5 (6.7)	27.7 (6.9)
BMI at screening (kg/m^2, mean [SD])	29.1 (8.2)	28.7 (7.8)	28.9 (8.0)
Race/Ethnicity, n (%)			
White	228 (53.5)	239 (55.1)	467 (54.3)
Black or African American	185 (43.4)	173 (39.9)	358 (41.6)
American Indian/Alaska Native	3 (0.7)	2 (0.5)	5 (0.6)
Native Hawaiian or Pacific Islander	0	2 (0.5)	2 (0.2)
Asian	5 (1.2)	9 (2.1)	14 (1.6)
Other	5 (1.2)	9 (2.1)	14 (1.6)
Not Hispanic or Latina	291 (68.3)	286 (65.9)	577 (67.1)
Vaginal pH, mean (SD)	4.5 (0.7)	4.6 (0.8)	4.5 (0.8)

N=number of women in the treatment group analysis set; n=number of women in the specified category with non-missing values.
BMI, body mass index; ITT, intent-to-treat.

Efficacy

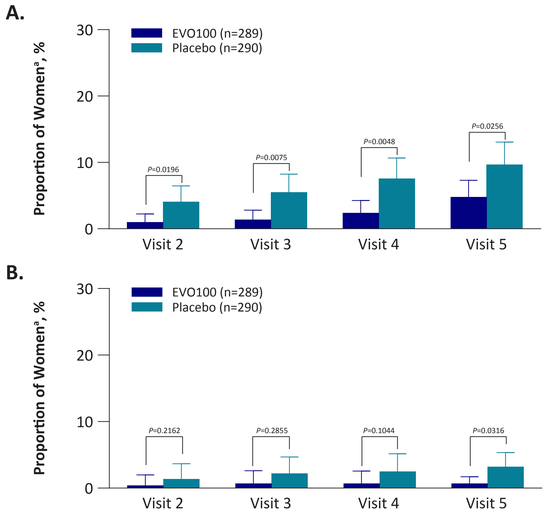
- Among women eligible for CT analysis, 4.8% (14/289) receiving EVO100 compared with 9.7% (28/290) of placebo users experienced CT infection during the study (P=0.03), representing a significant reduction in the relative risk of 50% (**Table 2**)
- For GC, the infection rate was 0.7% (2/280) in the EVO100 arm compared with 3.2% (9/277) in the placebo arm (P=0.03), representing a relative risk reduction of 78%
- At each visit throughout the study, the incident CT infection rate was significantly lower in women treated with EVO100 compared with women treated with placebo (**Figure 3**)
  - Similarly, lower rates of GC infection were observed in women treated with EVO100 versus placebo users at each study visit but other than visit 5 these differences were not significantly different due to low numbers of infections at each visit

Table 2. Summary of the Proportion of Women with CT and GC Infection During the Study (mITT Population)

	mITT[a]			
	EVO100 n=364	Placebo n=383	Rate Difference	*P*-value[b]
CT-analysis–eligible population[c], n	289	290		
Women without CT infection, n (%)	275 (95.2)	262 (90.3)		
Women with CT infection, n (%)	14 (4.8)	28 (9.7)	-4.8	0.0256
95% CI for rate and rate difference	(2.4, 7.3)	(6.3, 13.1)	(-9.0, -0.6)	
GC-analysis–eligible population[c], n	280	277		
Women without GC infection, n (%)	278 (99.3)	268 (96.8)		
Women with GC infection, n (%)	2 (0.7)	9 (3.2)	-2.5	0.0316
95% CI for rate and rate difference	(0, 1.7)	(1.2, 5.3)	(-4.8, -0.2)	

N=number of women in the treatment group analysis set; n=number of women in the specified category.
[a]Percentage (%) based on number of women in row category within each treatment category.
[b]Two-sided *P*-value based on Chi-Square test or Fisher's exact test (if any cell count is <5).
[c]To be eligible for efficacy analysis, a woman must have had known infection status through end of the treatment phase, no use of prohibited antibiotic medications, and no earlier on-study CT or GC infection.
CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; mITT, modified intent-to-treat.

Figure 3. Incident CT (A) and GC (B) Infection by Study Visit (mITT Population)



Two-sided *P*-value based on Chi-Square test or Fisher's exact test (if expected cell count is <5). [a]Proportion of women reporting positive CT or GC infection in CT- or GC-analysis–eligible population in each study arm.
CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; mITT, modified intent-to-treat.

Safety

- Overall, 20.8% of women experienced an AE during the study (**Table 3**)
- Across both arms, there were similar rates of all-cause AEs (EVO100: 21.3%; placebo: 20.4%)
  - Treatment-related AE rates were also similar (EVO100: 7.2%; placebo: 7.5%)
- The most common AEs in each arm were:
  - EVO100: vulvovaginal candidiasis (5.1%), vaginal discharge (3.2%), and urinary tract infection (3.2%)
  - Placebo: bacterial vaginosis (4.6%), urinary tract infection (2.6%), and vaginal discharge (2.6%)
- Few women discontinued due to AEs in either arm (EVO100, 1.1%; placebo, 1.5%)
- No treatment-related serious AEs were reported

Table 3. Summary of AEs Occurring in ≥2% of Women (Safety Population)

	Safety[a]		
	EVO100 n=376	Placebo n=388	Total N=764
Any AE, n (%)[b]	80 (21.3)	79 (20.4)	159 (20.8)
Gastrointestinal disorders, n (%)	3 (0.8)	13 (3.4)	16 (2.1)
Infections and infestations, n (%)[c]	50 (13.3)	49 (12.6)	99 (13.0)
Bacterial vaginosis	11 (2.9)	18 (4.6)	29 (3.8)
Urinary tract infection	12 (3.2)	10 (2.6)	22 (2.9)
Vulvovaginal candidiasis	19 (5.1)	8 (2.1)	27 (3.5)
Reproductive and breast disorders, n (%)[c]	29 (7.7)	21 (5.4)	50 (6.5)
Vaginal discharge	12 (3.2)	10 (2.6)	22 (2.9)
Vulvovaginal discomfort	8 (2.1)	4 (1.0)	12 (1.6)
Any serious AEs, n (%)[a,b]	2 (0.5)	3 (0.8)	5 (0.7)
Discontinuation due to an AE, n (%)[a,b]	4 (1.1)	6 (1.5)	10 (1.3)

N=number of women in the treatment group analysis set; n=number of women in the specified category with non-missing values.
[a]Percentage (%) based on number of women in row category within each treatment category.
[b]AEs were coded by Medical Dictionary for Regulatory Activities (version 20.1) by system organ class and preferred term.
[c]Totals for the number of women at a higher level may not equal the sum of lower levels since women may have reported two or more different AEs within the higher level category.
AE, adverse event.

CONCLUSIONS

- 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
- EVO100 was generally safe and well tolerated with most side effects being mild to moderate

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DISCLOSURES

BTC: Research, Evofem Biosciences, Inc.
SM: Employee, ICON Clinical Research LLC, which received funding from Evofem Biosciences, Inc. to help conduct this study
KC, BH: Employee, Evofem Biosciences, Inc.

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