SIDE EFFECTS BY FREQUENCY OF USE WITH EVO100 VAGINAL GEL: RESULTS FROM THE PHASE 2B/3 AMPREVENCE TRIAL

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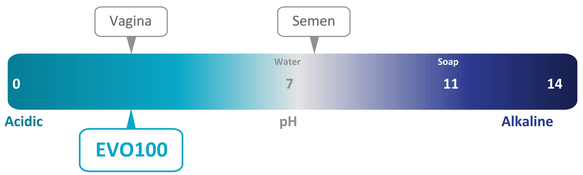
INTRODUCTION

- In 2019, 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]
  - 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]
- EVO100 has subsequently received approval from the FDA for prevention of pregnancy in May 2020 (Phexxi®)[6]

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



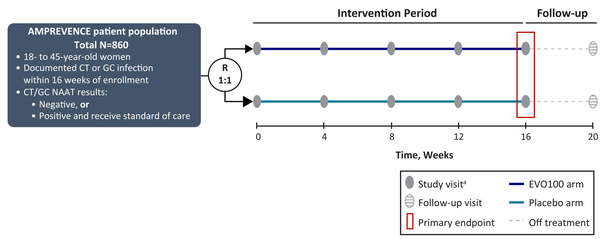
OBJECTIVE

- The objective of the current analysis is to report on genitourinary side effects by frequency of study product use in the AMPREVENCE study

METHODS

- AMPREVENCE (NCT03107377) was a phase 2B/3, placebo-controlled, multicenter study conducted over approximately 16 weeks in women at risk of urogenital CT and GC infection[7]
  - Sexually active, healthy women 18-45 years old who had documented CT or GC infection within 16 weeks of enrollment were randomized 1:1 to receive EVO100 or placebo
  - 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
- Safety was assessed through adverse event (AE) reporting
  - Women who documented any use of study product were included in the safety population

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 tests; R, randomization.

RESULTS

- In total, 860 women were enrolled and 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 product at least once and were included in the safety analysis
- Overall, 159 women (EVO100: n=80; placebo: n=79) had an AE on study, with the most commonly reported AEs being vaginal candidiasis (n=19, 5%), vaginal discharge (n=12, 3%), and urinary tract infection (UTI; n=12, 3%) for EVO100 users; and bacterial vaginosis (n=18, 5%), UTI (n=10, 3%), and vaginal discharge (n=10, 3%) for placebo users (**Table 1**)

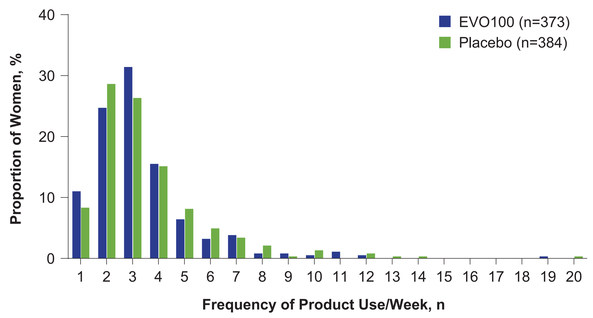
Table 1. Summary of AEs Occurring in ≥2% of Women (Safety Population)

	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 2 or more different AEs within the higher level category.
AE, adverse event.

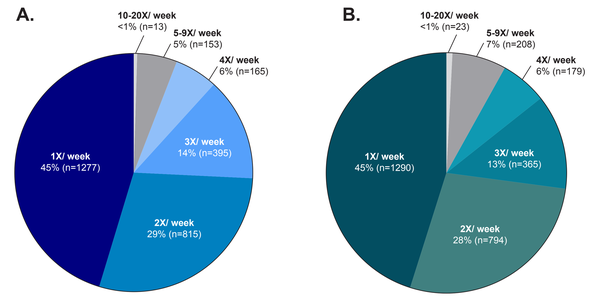
- The maximum frequency of product use in a single week ranged between 1 and 20 times for both arms (**Figure 3**)
  - Most women randomized to EVO100 (31%, 117/373) reported a maximum of 3 uses in a single week
  - Most women randomized to placebo (29%, 110/384) reported a maximum of 2 uses in a single week

Figure 3. Maximum Frequency of Study Product Use in a Single Week Among EVO100 and Placebo Users in AMPREVENCE (Safety Population)



- Overall, EVO100 and placebo were used for 2818 and 2859 weeks, respectively (**Figure 4**)
  - There were 1277 and 1290 weeks where EVO100 or placebo was used once/week, respectively

Figure 4. Frequency of On-Study Use of EVO100 (n=2818) (A) and Placebo (n=2859) (B) Per Week



- Study weeks were analyzed to determine if there was an association between the incidence of genitourinary symptoms and frequency of product use
- Of 1277 and 1290 study weeks where EVO100 or placebo was used once/week, respectively, the rate of AEs/week was similar for EVO100 (n=19, 1%) and placebo (n=18, 1%) (**Table 2**)
  - For women reporting once-weekly usage, the most commonly reported AE was vaginal candidiasis (n=8, <1%) for EVO100 and bacterial vaginosis (n=6, <1%) for placebo

Table 2. Summary of Genitourinary Symptoms in Study Weeks with 1 Use/Week of Study Product (Safety Population)

	EVO100 (n=376)	Placebo (n=388)
Study Product Used 1X/Week		
Number of study weeks	1277	1290
Number of genitourinary symptoms, n (%)	19 (1)	18 (1)
Genitourinary Symptoms, n (%)		
Vulvovaginal candidiasis	8 (0.6)	1 (0.1)
Bacterial vaginosis	0	6 (0.5)
Urinary tract infection	4 (0.3)	2 (0.2)
Vulvovaginal discomfort	3 (0.2)	1 (0.1)
Vaginal discharge	1 (0.1)	2 (0.2)
Genital herpes	0	2 (0.2)
Dyspareunia	0	1 (0.1)
Urogenital trichomoniasis	0	1 (0.1)
Vaginal infection	0	1 (0.1)
Vaginal odor	1 (0.1)	1 (0.1)
Vulvovaginal burning sensation	1 (0.1)	0
Vulvovaginal dryness	1 (0.1)	0

- Of 1541 and 1569 weeks where EVO100 or placebo was used ≥2/week, respectively, the rate of AEs/week was similar for EVO100 (n=18, 1%) and placebo (n=17, 1%) use (**Table 3**)
  - The most commonly reported AE with ≥2/week product use was vaginal candidiasis (n=3, <1%) for EVO100 and vaginal discharge (n=4, <1%) for placebo
- Overall, similar rates of AEs/week were observed for EVO100 and placebo users who used the study product once/week or ≥2/week

Table 3. Summary of Genitourinary Symptoms in Study Weeks with ≥2 Use/Week of Study Product (Safety Population)

	EVO100 (n=376)	Placebo (n=388)
Study Product Used ≥2X/Week		
Number of study weeks	1541	1569
Number of genitourinary symptoms, n (%)	18 (1)	17 (1)
Genitourinary Symptoms, n (%)		
Vaginal discharge	2 (0.1)	4 (0.3)
Vulvovaginal candidiasis	3 (0.2)	3 (0.2)
Vulvovaginal discomfort	2 (0.1)	3 (0.2)
Bacterial vaginosis	2 (0.1)	2 (0.1)
Urinary tract infection	2 (0.1)	2 (0.1)
Vulvovaginal burning sensation	3 (0.2)	0
Dyspareunia	0	2 (0.1)
Genital herpes	1 (0.1)	0
Kidney infection	0	1 (0.1)
Pelvic pain	1 (0.1)	0
Vulvovaginal dryness	1 (0.1)	0
Vulvovaginal erythema	1 (0.1)	0

CONCLUSIONS

- The increasing rates of CT and GC infection are an urgent public health concern
  - 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 in women receiving EVO100 than placebo users
- In AMPREVENCE, the incidence of AEs was similar between EVO100 and placebo and did not increase with more frequent use of either product

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DISCLOSURES

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

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