INCORPORATING DIRECT PATIENT HEALTH OUTCOMES INTO CLINICAL TRIALS FOR THE PREVENTION OF UROGENITAL CHLAMYDIA TRACHOMATIS INFECTION: ANALYSIS OF A NOVEL ENDPOINT IN A CLINICAL TRIAL OF EVO100 (EVO-003)

P-720

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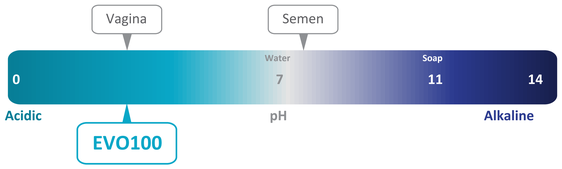
INTRODUCTION

- 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 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



- AMPREVENCE was a phase 2B/3 trial that evaluated EVO100 for the prevention of CT and 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[7]
  - Women's sexual satisfaction with EVO100 over the course of the study was an exploratory outcome
- Water-based lubricants such as EVO100 are associated with increased sexual pleasure and satisfaction[3,8]

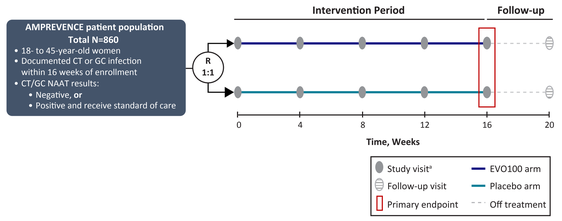
OBJECTIVE

- To assess the utility and performance of EVO100 for the prevention of CT and GC using a novel composite endpoint that combines rates of CT and GC infection and patient reported overall sexual satisfaction

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

Figure 2. AMPREVENCE Study Design

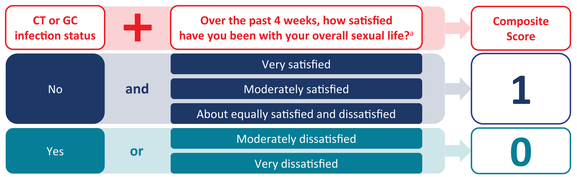


Diary entries were reviewed at each study visit. [a]Women visited the clinic for screening (Visit 0 [Weeks -6 to 0]), for enrollment (Visit 1 [Week 0]), and during the intervention period at Visit 2 (Week 4), Visit 3 (Week 8), Visit 4 (Week 12), and Visit 5 (Week 16). The post-intervention/follow-up visit occurred at Week 20.

CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*; NAAT, nucleic acid amplification tests; R, randomization.

- Vaginal swabs were collected at all visits and specimens were centrally assessed for CT/GC by nucleic acid amplification tests
- Overall sexual satisfaction was an exploratory endpoint, assessed with the Female Sexual Function Index (FSFI) overall satisfaction question administered at Enrollment (Visit 1) and Visit 5
  - The FSFI overall satisfaction question asked, "Over the past 4 weeks, how satisfied have you been with your overall sexual life?"
    - Response options included: "very satisfied", "moderately satisfied", "about equally satisfied and dissatisfied", "moderately dissatisfied", and "very dissatisfied"
  - Responses of "very satisfied", "moderately satisfied", or "about equally satisfied and dissatisfied" indicated that overall sexual satisfaction was improved or not impaired
  - Responses of "moderately dissatisfied", and "very dissatisfied" indicated that overall sexual satisfaction was impaired
- The composite endpoint was scored as follows (**Figure 3**):
  - A composite score of 1 was given for women who did not have CT/GC infection ***and*** had reported improvement or no impairment in overall sexual satisfaction
  - A composite score of 0 was given for women who had CT/GC infection ***or*** reported impaired overall sexual satisfaction

Figure 3. Composite Endpoint Scoring



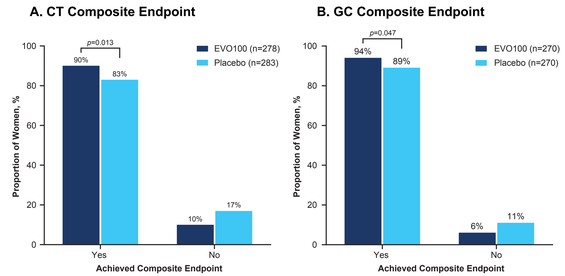
[a]Question 16 from the Female Sexual Function Index.

- Additional sensitivity analyses assessed the proportion of women achieving the composite endpoints in a subset of women who were ≥80% or 100% adherent to the study treatment
- The proportion of those achieving composite endpoints with EVO100 or placebo were compared using Chi-squared test for superiority, with a two-sided 5% type I error rate (α=0.05)
- To assess the proportion of CT-evaluable women who maintained or improved sexual satisfaction at Visit 5 compared with their sexual satisfaction reported at baseline, the overall sexual satisfaction responses were scaled from 0 (lowest/worst) to 100 (highest/best)
  - Additional analysis included women who reported at least a 25 point (ie, 1 category or more) improvement in overall sexual satisfaction

RESULTS

- AMPREVENCE enrolled 860 women randomized 1:1 to receive EVO100 (n=426) or placebo (n=434)
  - A total of 764 women reported at least one use of study drug (Safety population)
  - Overall, 579 and 557 women were included in the CT- and GC-analysis eligible population, respectively, of whom 561 and 540, respectively, provided responses to the overall sexual satisfaction assessment (FSFI question 16)
- In this analysis, there were 262 and 269 women randomized to EVO100 and placebo, respectively, who provided responses to the FSFI overall sexual satisfaction question (**Figure 4**)
- Among women evaluated for CT infections, more women in the EVO100 arm (89.9%) achieved successful composite endpoints compared with women in the placebo arm (82.7%, p=0.013) (**Figure 4**)
- Among women evaluated for GC infections, more women in the EVO100 arm (93.7%) achieved successful composite endpoints compared with women in the placebo arm (88.9%, p=0.047)

Figure 4. Proportion of Women Achieving Composite Endpoints With EVO100 or Placebo Use in CT- and GC-Analysis Eligible Population[a,b]



[a]Includes women who were included in the CT-analysis eligible population and had evaluable patient reported overall sexual satisfaction assessment. [b]Includes women who were included in the GC-analysis eligible population and had evaluable patient reported overall sexual satisfaction assessment. CT, *Chlamydia trachomatis*; GC, *Neisseria gonorrhoeae*.

- Among CT-analysis eligible women who reported improvements or no impairments to their sexual satisfaction and had treatment adherence of ≥80%, more women in the EVO100 group achieved successful composite endpoints compared with women in the placebo group (92.6% vs 84.5%; p=0.011) (**Table 1**)
  - Similarly, among women who were 100% adherent to study treatment, more EVO100 users achieved successful composite endpoints compared with placebo (91.9% vs 75.9%; p=0.005)

Table 1. Proportion of Women Achieving Composite Endpoints With EVO100 or Placebo Gel Use by Adherence Rates Among Women Who Reported Improvements or No Impairments With Their Sexual Satisfaction[a]

	EVO100	Placebo	Pearson Chi-Square
Treatment Adherence ≥80%, n	190	206	
Achieved composite endpoint, n (%)	176 (92.6)	174 (84.5)	0.011
Did not achieve composite endpoint, n (%)	14 (7.4)	32 (15.5)	
Treatment Adherence 100%, n	86	83	
Achieved composite endpoint, n (%)	79 (91.9)	63 (75.9)	0.005
Did not achieve composite endpoint, n (%)	7 (8.1)	20 (24.1)	

[a]Includes women who provided responses of "very satisfied", "moderately satisfied", or "about equally satisfied and dissatisfied" to the overall sexual satisfaction assessment.

- Change in overall sexual satisfaction from baseline was assessed on a continuous scale (ie, 0=lowest/worst to 100=highest/best) (**Table 2**)
  - Among CT-analysis eligible women, numerically more EVO100 users maintained or improved their overall sexual satisfaction as a continuous score and had no CT infection compared with placebo users (75.2% vs 67.7%; p=0.052)
  - Additionally, more EVO100 users reported meaningful improvements (≥25 point improvement) in their overall sexual satisfaction score and had no CT infection compared with placebo users (28.4% vs 20.4%; p=0.028)

Table 2. Proportion of Women Achieving Composite Endpoints Who Reported Stable or Improvements in Overall Sexual Satisfaction From Baseline

	EVO100	Placebo	Pearson Chi-Square
Maintained or Improved[a], n	278	279	
Achieved composite endpoint, n (%)	209 (75.2)	189 (67.7)	0.052
Did not achieve composite endpoint, n (%)	69 (24.8)	90 (32.3)	
≥25 Point Improvement, n	278	279	
Achieved composite endpoint, n (%)	79 (28.4)	57 (20.4)	0.028
Did not achieve composite endpoint, n (%)	199 (71.6)	222 (79.6)	

[a]Includes women who reported stable or improved overall sexual satisfaction compared with baseline.

CONCLUSIONS

- In this study, we evaluated both CT/GC infection as well as patient reported overall sexual satisfaction outcomes as a composite endpoint
  - Use of EVO100 resulted in a reduction in CT/GC infection rate and maintenance or improvements in overall sexual satisfaction compared with placebo gel
  - This result was more pronounced among women who were more adherent with the study treatment
  - More EVO100 users reported a meaningful improvement in their overall sexual satisfaction and did not report CT infection on study compared with placebo gel users
- Assessing how EVO100 can prevent CT/GC infections and its impact on overall sexual satisfaction as a composite endpoint provides important information related to patient counseling

REFERENCES

1. National overview - sexually transmitted disease surveillance, 2019. Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/std/statistics/2019/overview.htm.
2. Garg S, et al. *Contraception*. 2001;64:67-75.
3. Bayer LL, Jensen JT. *Contraception*. 2014;90:11-18.
4. Pilipenko V, et al. Poster presented at the International Society for Sexually Transmitted Diseases Research, July 11-14, 1999 [poster #143].
5. Spencer SE, et al. *J Infect Dis*. 2004;189:410-419.
6. Drug approval package: PHEXXI. Food and Drug Administration. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/nda/2020/208352Orig1s000TOC.cfm
7. Chappell BT, et al. *Am J Obstet Gynecol*. 2021;doi:10.1016/j.ajog.2021.03.005.
8. Herbenick D, et al. *J Sex Med*. 2011;8:202-212.

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DISCLOSURES

JHP: Consultant, Arrevus, Bavarian Nordic, Celularity, DaVolterra, Eicos, Eli Lilly, Evofem Biosciences, Inc., Eyecheck, Fuji, Gilead, GlaxoSmithKline, Johnson & Johnson, Microbion, Mustang, OPKO, Otsuka, Romark, Shinogi, Vir. **RM:** Consultant, Evofem Biosciences, Inc., Heron, Johnson and Johnson Vision Care, Taiho. **TS:** Consultant, Evofem Biosciences, Inc. **KC:** Former employees, Evofem Biosciences, Inc. **BH:** Employee, Evofem Biosciences, Inc.

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