

EFFICACY AND SAFETY OF A VAGINAL pH-REGULATOR: RESULTS FROM THE PHASE 3, AMPOWER CLINICAL TRIAL

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BACKGROUND

- Evofem's investigational vaginal pH-regulator (VPR™), is a novel, non-hormonal, woman-controlled, water-based, petroleum-free, nonoxynol-9-free vaginal gel being studied for prevention of pregnancy and sexually transmitted infections
- Provides acidic pH buffering, thereby maintaining the acidic vaginal environment to immobilize sperm, even in the presence of alkaline semen^{1,2} (Figure 1)
- Has bioadhesive and viscosity-retaining properties designed to contribute to the effectiveness of the gel

Figure 1. Acidic pH Buffering by Vaginal pH-Regulator (VPR)



- Here we present primary results from the confirmatory, phase 3 AMPOWER clinical trial (NCT03243305); the primary endpoint was 7-cycle cumulative pregnancy percentage with typical-use
- The design of AMPOWER had to meet strict criteria as specified by the Food and Drug Administration (FDA)
- Definitions of typical- and perfect-use in contraceptive clinical trials such as AMPOWER differ from those in real-world setting
- In the clinical trial setting:
- Typical-use includes cycles with inconsistent or incorrect use and sexual intercourse occurring at least once/month
- Perfect-use includes cycles in which directions for use are followed exactly and consistently, no additional methods of contraception are used, and sexual intercourse is reported at least once/ month
- Only cycles with lengths of 21-35 days are permitted to be included in the analysis
- In real-world setting, usage definitions do not depend on factors such as menstrual cycle length, use of concomitant contraceptives, or intercourse frequency specifically³

METHODS

- AMPOWER was a single-arm, open-label study conducted at 112 sites within the United States
- All sites obtained IRB approval and all participants provided informed consent
- Eligibility criteria:
- Healthy, monogamous, sexually active participants aged 18-35 years with normal cyclic menses of length 21-35 days
- Willing to engage in intercourse ≥ 3 times per cycle
- Willing to use the study drug as the only method of contraception over the course of the study
- Participants were instructed to administer a single prefilled applicator of study drug intravaginally before every act of vaginal sex
- After application, one dose of VPR is effective immediately, will last up to one hour, and provides protection for one act of vaginal sex
- An additional dose of VPR was to be applied for every act of vaginal sex; if more than one act of vaginal sex happened within one hour, an additional dose was to be applied before each act

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- Participants used eDiaries to record timing of product administration, coital information, and side effects
- Endpoints:
- Primary: 7-cycle cumulative pregnancy percentage with typical-use calculated by the Kaplan-Meier method
- Each of the 7 menstrual cycles had to meet rigorous criteria, per FDA guidance, to be evaluable as follows:
- Cycles 0-6 for participants enrolled \geq 21 days prior to start of next menses, or Cycles 1-7 for participants who enrolled <21 days prior to start of next menses
- Cycles in which no backup contraception or emergency contraception was used or in which participants became pregnant
- Cycles with length of 21-35 days or in which a participant was pregnant
- Cycles where at least one entry of diary was recorded or in which the participant was pregnant
- Cycles where at least one act of intercourse was recorded
- Cycles that started on or before date of last study product use + 7 days
- [For the perfect-use analysis, cycles had to meet all the above criteria as well as be ones in which the eDiaries indicate that study drug was used correctly for every act of intercourse during that cycle; perfect-use analyses are ongoing and will be presented in a subsequent
- Secondary: efficacy measured by the Pearl Index, adverse events (AEs), pregnancy outcomes
- Exploratory: participant satisfaction, sexual satisfaction, pregnancy intendedness, dosing time deviations for study drug-associated pregnancies

RESULTS

- Analysis populations:
- N=1384 in intent-to-treat (ITT) population
- N=1182 in primary efficacy analysis, modified ITT (mITT) population
- N=1330 used at least 1 application of study product and were included in safety population
- In total, 1.7% of study participants discontinued due to AEs
- Baseline characteristics and mean number of prior pregnancies for the ITT population are shown in Table 1

Table 1. Baseline Characteristics and Obstetric History (ITT)

| Characteristic | VPR (N=1384) |
|--|-----------------|
| | |
| BMI, kg/m² (SD) | 28.7 (8.1) |
| Race/Ethnicity | |
| White | 69.0% |
| Black | 25.1% |
| Other | 5.9% |
| Non-Hispanic or non-Latino | 58.2% |
| Hispanic or Latino | 41.3% |
| Number of prior pregnancies (SD) | 2.5 (1.8) |
| Values are means unless otherwise specified. | |

BMI, body mass index; VPR, vaginal pH-regulator.

Immediately prior to enrollment, a total of 969 (70%) participants reported use of any contraceptive; the 3 most common contraceptive methods were non-hormonal and included: male condom (56.9%, 787/1384), withdrawal method (14.2%, 196/1384), and rhythm method (5.1%, 70/1384) (Figure 2)



Figure 2. Contraceptive Methods Used Immediately Prior to Enrollment in ≥1% (ITT)

For the primary efficacy analysis in the mITT population, 7-cycle cumulative pregnancy percentage with typical-use was 13.7% (95% CI; 9.9, 17.4), which met the prespecified primary endpoint of having upper bound 95% CI ≤21 (**Table 2**)

Table 2. Primary Efficacy Outcome (mITT)

| Method | VPR (N=1182) |
|--|---------------------------|
| Cumulative pregnancy percentage via Kaplan-Meier | |
| Typical-use | 13.7% (95% Cl; 9.9, 17.4) |

The most common treatment-emergent adverse events were vulvovaginal burning sensation (20.0%, 266/1330), vulvovaginal pruritus (11.2%, 149/1330), urinary tract infection (5.7%, 76/1330), vulvovaginal pain (3.8%, 51/1330) and vulvovaginal mycotic infection (2.9%, 38/1330) (Table 3)

Table 3. Treatment-Emergent Adverse Events in ≥1% (Safety Population)

| Preferred Term | VPR (N=1330) |
|-----------------------------------|--------------|
| Vulvovaginal burning sensation | 266 (20.0) |
| Vulvovaginal pruritus | 149 (11.2) |
| Urinary tract infection | 76 (5.7) |
| Vulvovaginal pain | 51 (3.8) |
| Vulvovaginal mycotic infection | 38 (2.9) |
| Bacterial vaginosis | 37 (2.8) |
| Nasopharyngitis | 35 (2.6) |
| Vaginal discharge | 23 (1.7) |
| Influenza | 19 (1.4) |
| Vulvovaginal discomfort | 18 (1.4) |
| Nausea | 17 (1.3) |
| Upper respiratory tract infection | 17 (1.3) |
| Headache | 14 (1.1) |
| Vaginal hemorrhage | 14 (1.1) |

Fourteen participants (1.1%) experienced a serious adverse event with only one event (cystitis, 0.1%) considered treatment-related

More participants reported being "very satisfied" or "satisfied" with the study method (Visit 4: 89.5%, 734/820), compared with their previous birth control method before enrollment (46.5%, 616/1325) (Figure 3)



Figure 3. Percentage of Participants Very Satisfied/Satisfied With Study Product (Safety Population)

CONCLUSIONS

- The investigational VPR is a novel, non-hormonal, woman-controlled gel that can be used "in the moment" to prevent pregnancy, providing users with an important new contraceptive option
- In this large phase 3 study, VPR was found to be safe and effective in preventing pregnancy
- With a 7-cycle cumulative pregnancy percentage for typical-use of 13.7% (upper bound 95% CI; 17.4), the study met the prespecified primary endpoint
- Most participants (>85%) were very satisfied/satisfied with VPR

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ACKNOWLEDGEMENTS

The study was sponsored by Evofem Biosciences, Inc. Medical writing assistance was provided by PharmaWrite, LLC (Princeton, NJ, USA) and funded by Evofem Biosciences, Inc. (San Diego, CA, USA).

DISCLOSURE

PC: Evofem Inc., consultant BH: Evofem Inc., employee