Contraceptive efficacy, safety, and acceptability of Amphora® (an acid-buffering vaginal gel) and Conceptrol®

Kurt T. Barnhart, MD, MSCE[1]; Kelly Culwell, MD, MPH[2]; Clint Dart, MS[3]

[1]University of Pennsylvania School of Medicine, Philadelphia, PA; [2]Evofem, Inc., San Diego, CA; [3]Health Decisions Inc, Durham, NC

Introduction

- Multiple factors influence a woman's choice for contraceptives, but no single factor drives preference of use.[1] The availability of reliable contraception tailored to suit women's needs and lifestyles is essential to address the substantial human and financial costs of unintended pregnancy.
- Amphora® (L-lactic acid, citric acid, and potassium bitartrate), a new contraceptive vaginal gel, immobilizes sperm by buffering the vaginal pH so it remains acidic (pH 3.5–4.5) in the presence of alkaline semen.[2,3]

Methods

- This multicenter, open-label, randomized, non-inferiority study assessed the contraceptive efficacy and safety of Amphora compared with Conceptrol (nonoxynol-9, 4%), and was conducted at 49 sites in the United States and 13 sites in Russia. Participants were healthy, sexually active women 18–45 years of age.
- Kaplan-Meier (KM) methods and Pearl Indices were used to assess pregnancy rates. A non-inferiority hypothesis was tested based on the KM method and a non-inferiority delta of 5.5%. The primary endpoint was contraceptive efficacy over 6 months (7 cycles) of Amphora use compared to that of Conceptrol. Key secondary endpoints included self-reported product acceptability and safety assessments.

Results

- A total of 1665 women were randomized to Amphora and 1659 were randomized to Conceptrol. Demographics and baseline characteristics were similar across user groups (Table 1). Disposition of women in the study is shown in Table 2.
- Amphora demonstrated 89.5% and 95.9% contraceptive efficacy at 6 months with typical use (modified intent-to-treat [mITT]) and perfect use (efficacy evaluable [EE]), respectively. KM 6-month cumulative pregnancy percentages for Amphora users were similar to that of Conceptrol users, showing that Amphora was non-inferior to Conceptrol (Table 3).

Table 1. Subject demographics and baseline characteristics

Subject characteristic	Amphora (N=1665)	Conceptrol (N=1659)	Overall (N=3324)
Mean (SD) age, years	27.6 (5.6)	27.6 (5.7)	27.6 (5.6)
Age range, years	18–45	18–45	18–45
Mean (SD) body mass index at enrollment, kg/m^2	27.91 (7.95)	27.76 (7.98)	27.83 (7.93)
Race, n (%)			
Black or African American	471 (28.3)	464 (28.0)	935 (28.1)
White	1031 (62.0)	1030 (62.1)	2061 (62.0)
Other	161 (9.7)	165 (9.9)	326 (9.8)

Table 2. Subject disposition

Study completion status, n (%)	7-cycle study			13-cycle study
	Amphora (N=1665)	Conceptrol (N=1659)	Overall (N=3324)	Amphora (N=341)
Completed the study	788 (47.3)	758 (45.7)	1546 (46.5)	261 (76.5)
Discontinued prematurely	877 (52.7)	901 (54.3)	1778 (53.5)	80 (23.5)
Reasons for discontinuation				
Adverse event	25 (1.5)	28 (1.7)	53 (1.6)	2 (0.6)
Pregnancy	151 (9.1)	136 (8.2)	287 (8.6)	14 (4.1)
Other	701 (42.1)	737 (44.4)	1438 (43.3)	64 (18.8)

Table 3. Kaplan-Meier 6-month cumulative pregnancy percentages for typical use (mITT)* and perfect use (EE)† populations

Amphora				Conceptrol				Difference	95% CI
Analysis group	Pregnancies (n)	Pregnancy percentage (%)	95% CI	Analysis group	Pregnancies (n)	Pregnancy percentage (%)	95% CI		
mITT (N=1259)	111	10.5	8.6, 12.3	mITT (N=1281)	100	10.0	8.1, 11.9	0.5%	–2.2, 3.2
EE (N=1153)	36	4.1	2.7, 5.4	EE (N=1158)	36	4.2	2.8, 5.6	–0.1%	–2.1, 1.8

*mITT=ITT subjects who were 18–35 years of age (inclusive) at enrollment; had ≥1 report of pregnancy status after being enrolled; had diaries indicating they had ≥1 episode of coitus while using the assigned study product; and had ≥1 cycle of diary without any backup contraception or emergency contraception OR experienced an on-study pregnancy; excludes women who became pregnant prior to randomization.

†EE=Subset of the mITT population that includes only those subjects who used the assigned study product correctly for every episode of intercourse for ≥1 menstrual cycle; excludes women who were pregnant prior to randomization.

- Six-month Pearl Indices were also similar between the 2 typical use (mITT) groups, with a Pearl Index of 24.3 (5472 women-months at risk) for the Amphora group and 22.4 (5356 women-months at risk) for the Conceptrol group (difference in Pearl Indices, 1.9 [95% CI: –4.4, 8.2]). For the perfect use (EE) groups, the Pearl Index for the Amphora group was 8.8 (4924 women-months at risk) and 9.1 (4733 women-months at risk) for the Conceptrol group (difference in Pearl Indices, –0.4 [95% CI: –4.5, 3.8]).

Table 4. Summary of AEs in the all-treated population

	Amphora (N=1458)	Conceptrol (N=1477)
AEs leading to early discontinuation, n (%)	23 (1.6)	25 (1.7)
Relationship of AEs, n (%)		
Unrelated	466 (32.0)	468 (31.7)
Possibly related	327 (22.4)	348 (23.6)
Probably related	26 (1.8)	29 (2.0)
Definitely related	14 (1.0)	12 (0.8)
Intensity of AEs, n (%)		
Mild	560 (38.4)	579 (39.2)
Moderate	240 (16.5)	231 (15.6)
Severe	33 (2.3)	47 (3.2)

Table 5. Incidence of AEs (≥5%) in the 7-cycle all-treated population

AE (preferred term), n (%)	Amphora (N=1458)	Conceptrol (N=1477)
Women with ≥1 AE, n (%)	793 (54.4)	857 (58.0)
Urinary tract infection	140 (9.6)	193 (13.1)
Bacterial vaginitis	160 (11.0)	170 (11.5)
Vulvovaginal mycotic infection	156 (10.7)	168 (11.4)
Headache	96 (6.6)	80 (5.4)
Vulvovaginal pruritus	55 (3.8)	76 (5.1)
Nasopharyngitis	76 (5.2)	48 (3.2)

Note: Women could have reported more than 1 AE.

- A higher percentage of Amphora users (83.5%) said they strongly or somewhat liked the product compared with Conceptrol users (79.8%, $P<0.05$). A higher percentage of Amphora users said they would probably or definitely use the product again (87.9%) compared with Conceptrol users (84.2%, $P<0.05$).
- Reported adverse events (AEs) were similar across the 2 groups. Overall, most AEs were mild and unrelated to study product in both the Amphora and Conceptrol groups (Table 4).
- The most commonly reported AEs for both Amphora and Conceptrol users are reported in Table 5.

Conclusions

- **Amphora gel had efficacy similar to Conceptrol for use in preventing pregnancies. Both study products were acceptable and few women had AEs; however, a significantly higher percentage of women who used Amphora liked the method and would use it again compared with women who used Conceptrol.**
- **Amphora gel was shown to be efficacious and well tolerated in a phase 3 clinical study. Amphora provides a valuable option for women and supports both individual and public health goals, including personal control of contraceptive use and the reduction of unwanted or unplanned pregnancies.**

References

1. Mansour D. *Int J Womens Health.* 2014;6:367-375.
2. Amaral E et al. *Contraception.* 2004;70:492-497.
3. Garg S et al. *Contraception.* 2001;64:67-75.

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