Title
Adherence in a Phase 3 Trial of a Multipurpose Vaginal pH-Regulator vs Nonoxynol-9 [2M]

Permalink
https://escholarship.org/uc/item/7hb9x42x

Journal
Obstetrics & Gynecology, 133

ISSN
0029-7844

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Publication Date
2019-05-01

DOI
10.1097/01.aog.01.aog.0000559275.01255.0d

Peer reviewed
3:00 PM–4:00 PM
CONTRACEPTION/FAMILY PLANNING
A Data-Driven Evaluation of the Size and Content of Expanded Carrier Screening Panels [1M]
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INTRODUCTION: The American College of Obstetricians and Gynecologists (ACOG) proposed seven criteria for expanded carrier screening (ECS) panel design. To ensure that screening for a condition is sufficiently sensitive to identify carriers and reduce residual risk of non-carriers, one criterion requires a per-condition carrier rate greater than 1-in-100. However, it is unestablished whether this threshold corresponds with a loss of clinical detection. The manner in which these criteria are interpreted and implemented could have an appreciable effect on the ability of ECS to detect at-risk couples. Yet, there has been no data-driven evaluation of the impact of these criteria.

METHODS: Carrier rates and at-risk couple rates were calculated in 56,281 patients who underwent a 176-condition ECS and evaluated for panels satisfying various criteria. Condition-specific clinical sensitivity was estimated via simulation. This study was exempt from IRB oversight.

RESULTS: Different interpretations of the 1-in-100 criterion have variable impact: a compliant panel would include between 3 and 38 conditions, identify 11%-81% fewer at-risk couples, and detect 36%-79% fewer carriers than a 176-condition panel. We found no conspicuous change in the ratio of the marginal panel carrier rate relative to the marginal at-risk couple rate that would motivate a 1-in-100 carrier-rate threshold. Simulations suggest that the clinical detection rate remains >84% for conditions with carrier rates as low as 1-in-1000, with detection rates sensitive to condition-specific variant-frequency distributions, which we have compiled.

CONCLUSION: The 1-in-100 criterion should be reconsidered because it limits at-risk couple detection without substantially easing the burden of testing partners of carriers.

Financial Disclosure: Rotem Ben-Shachar disclosed the following—Myriad Women’s Health: Employment, Ownership Interest includes stock, stock options, patent or other intellectual property. Ashley Svenson disclosed the following—Myriad Women’s Health: Employment, Ownership Interest includes stock, stock options, patent or other intellectual property. Dale Muzzey disclosed the following—Myriad Genetics: Employment, Ownership Interest includes stock, stock options, patent or other intellectual property.

Adherence in a Phase 3 Trial of a Multipurpose Vaginal pH-Regulator vs Nonoxynol-9 [2M]
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INTRODUCTION: The multipurpose vaginal pH-regulator (MVP-R) is a water-based, petroleum-free vaginal gel which is acid-buffering and under investigation for prevention of pregnancy and sexually transmitted infections. We assessed treatment adherence in a phase 3 contraceptive trial comparing the MVP-R and nonoxynol-9 (N-9) spermicidal gel.

METHODS: This randomized, open-label, non-inferiority study was conducted at 62 sites in the U.S. and Russia; all sites obtained IRB approval and all subjects provided informed consent. The MVP-R (Amphora®, formerly known as Acidform) and N-9 were provided in pre-filled, single-use applicators. Women were instructed to use 1 applicator immediately before or up to 1 hour before vaginal intercourse, and to reapply product if more than 1 hour elapsed and for additional intercourse within 1 hour. Subjects recorded product use and coital activity on a daily diary.

RESULTS: The 3,324 enrollees included 1,665 MVP-R and 1,659 N-9 subjects. Baseline characteristics were similar between treatment arms; characteristics of the overall Intent-to-Treat population included mean age 27.6±5.6 years, body mass index 27.8±8.9 kg/m² (32.8% obese), 62.0% White, and 76.6% non-Hispanic. The study method was used as the only contraceptive method and used correctly in 85.6% of coital acts (85.9% MVP-R, 85.3% N-9). Overall, 61.5% of all subjects (63.0% MVP-R, 60.1% N-9) were adherent with the proper method use for ≥90% of coital acts. The most common reason for non-adherence was failure to reapply with additional acts of intercourse within 1 hour after application [390/2,935 (13.3%)].

CONCLUSION: Most subjects used these on-demand, women-controlled products as directed. Adherence was similar between the two treatment groups.

Financial Disclosure: Brandi Howard disclosed the following—Evofem Biosciences, Inc.: Employment, Kelly Cutwell disclosed the following—Evofem Biosciences, Inc.: Employment. The other authors did not report any potential conflicts of interest.

Bleeding Patterns With a 1-Year, Segesterone Acetate/Ethinyl Estradiol Contraceptive Vaginal System [3M]
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INTRODUCTION: A segesterone acetate (SA) 0.015 mg/ethinyl estradiol (EE) and 0.013 mg (per day) contraceptive vaginal system (CVS) can be used for up to 1 year. We analyzed bleeding patterns with CVS use and factors associated with unscheduled bleeding/spotting.

METHODS: We pooled results from two multicenter, single-arm, open-label, pivotal, phase 3 studies of the SA/EE CVS conducted in 17 US and 7 international sites. Participants followed a 21/7 day in/out schedule of CVS use for up to 13 cycles, and recorded vaginal bleeding daily in paper diaries. Scheduled and unscheduled bleeding/spotting were summarized by cycle. We used multiple logistic regression to identify factors associated with unscheduled bleeding/spotting. To avoid bias from varying study participation lengths, we analyzed the first 4 cycles of CVS use.

RESULTS: Data from 2070 participants were analyzed. Scheduled bleeding/spotting was documented by 77.9% of women with a mean of 4.6±5.2 scheduled bleeding/spotting days/cycle. Any unscheduled bleeding/spotting ranged from 13.2% to 21.7% of women/cycle; with a mean of 3.4±5.1 days/cycle for those women. Absence of scheduled bleeding/spotting was 5%–8% of women/cycle; absence of any bleeding/spotting (complete amenorrhea) was 2.6%–4.9% of women/cycle. Few women (1.7%) discontinued early due to unacceptable bleeding. Compared with White women, Black/African-American women were more likely to report unscheduled bleeding/spotting (OR 1.49; 95% CI, 1.14-1.94). Body mass index did not influence bleeding patterns.

CONCLUSION: Participants using the SA/EE CVS up to 13 cycles experienced good cycle control. Discontinuations due to unacceptable bleeding were low. Further research into demographic/other differences with reported bleeding is warranted.

Financial Disclosure: Anita Nelson disclosed the following—Agile: Consultant/Advisory Board, Other Research Support includes receipt of drugs, supplies, equipment or other in-kind support; AMG Pharma: Consultant/Advisory Board; Avion: Consultant/Advisory Board, Speaker/Honoraria includes speakers bureau, symposia Carolina Sales Vieira disclosed the following—Bayer: Consultant/Advisory Board, Speaker/Honoraria includes speakers bureau, symposia, and expert witness; Merck: Consultant/Advisory Board, Speaker/Honoraria includes speakers bureau, symposia, and expert witness. Anne Burke disclosed the following—Exelixis: Other Research Support includes receipt of drugs, supplies, equipment or other in-kind support, Principal Investigator. The other authors did not report any potential conflicts of interest.

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