

Safety of the Duet[®] used continuously or pre-coitally in Zimbabwean women

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Abstract

Background: The Duet® is a single-size diaphragm-like cervical barrier designed to deliver a microbicide on both its cervical and vaginal sides, and is under investigation as a potential HIV prevention method for women. This is the first study to evaluate the safety of the device used either pre-coitally or continuously (removed once daily, washed and re-inserted) for 14 days in African women.

Methods: We enrolled 103 healthy, non-pregnant, sexually-active Zimbabwean women aged 18-40 from December 2008 through April 2009, using a randomized crossover study design. HIV status was not an exclusion criteria. Forty women were assigned to use the Duet with BufferGel® continuously for 14 days, followed by a 14 day washout period, and 14 days of pre-coital use; forty assigned to the reverse regimen order; and 20 assigned to observation only (no Duet use). At all visits women had a pelvic exam, and were assessed for Bacterial Vaginosis (BV) by BVBLUE® assay. Adverse events were measured by self-report and clinical observation at interim and follow-up visits.

Results: Most participants (97%) completed the study as scheduled, and no serious AEs were reported. There was one discontinuation because of symptomatic genital infections. 87 AEs were reported among 56 participants: including 31 that were gynaecologically-related and classified as “probably not”(8), “possibly” (12); or “probably” (11) related to the study products. 3 gynaecological AEs were reported in the observation arm. Eighteen related AEs were reported during the continuous-use regimen, and 12 during the pre-coital use regimen. There were 22 women positive for BV at enrollment, 13 women with baseline infection had recurrent BV at follow-up, and four “incident” BV cases diagnosed during the FU period.

Conclusions: Duet appears safe for use either continuously or pre-coitally for 14 days and should be further studied for delivery of vaginal gels.

Background

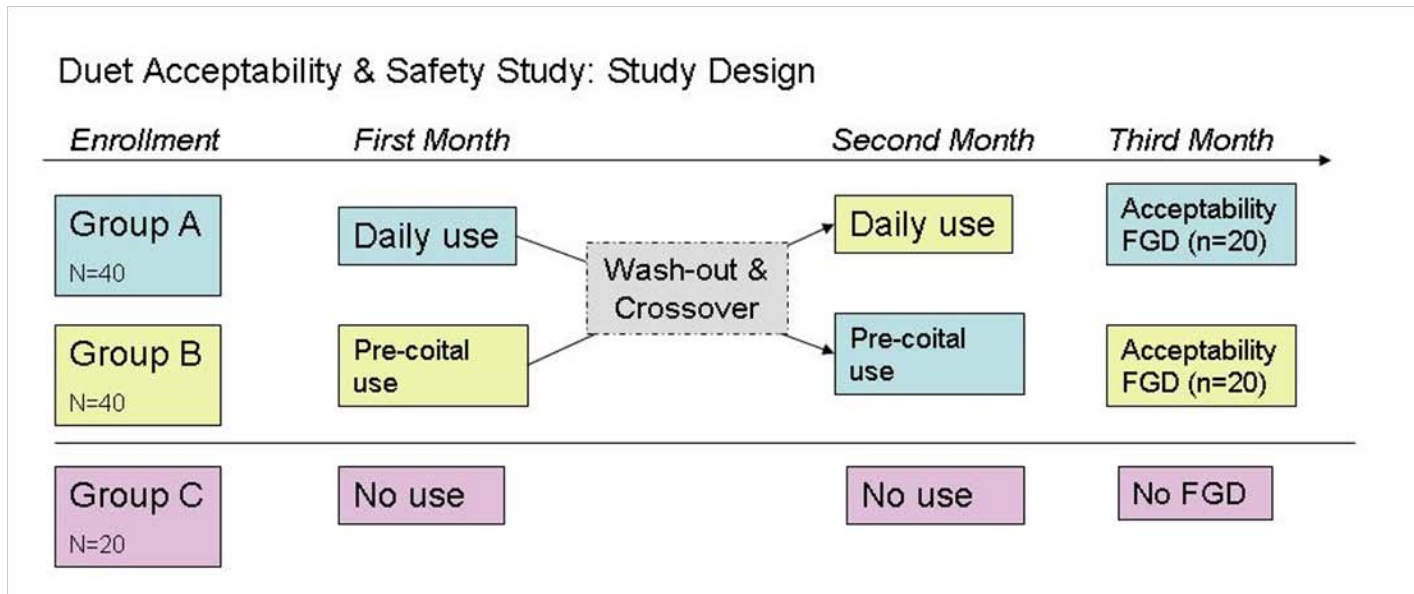
- Duet[®] is a diaphragm-like cervical barrier that delivers microbicide gel on both its cervical and vaginal side, and is being investigated as a potential female-initiated HIV prevention method.
- A phase I safety and acceptability study of the Duet in the US and Dominican Republic concluded that further product development was warranted (Ballagh et. al., *Contraception*, 2008)
- This is the first study
 - Of the safety and acceptability of Duet in African women
 - To assess continuous use (for 14 days) of the device

Study Objectives

Assess the safety of the Duet for use among African women, when used continuously for 14 days and pre-coitally for 14 days.

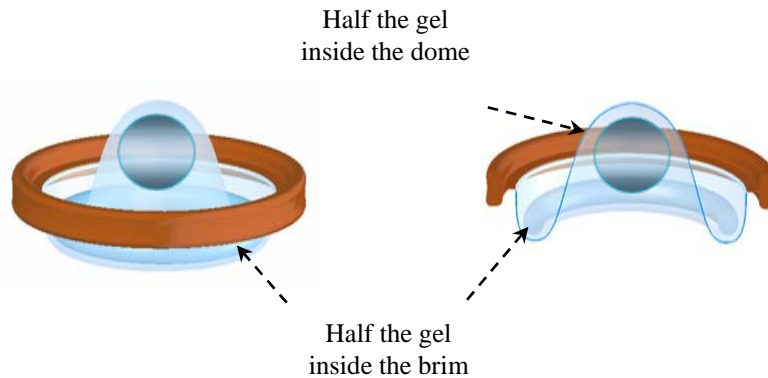
Study Design

- Open-label, randomized cross-over design with 2 intervention arms and 1 observation arm



Study Products: Duet

Duet is shaped like a hat, holds gel inside its dome and brim, and is inserted and removed like a diaphragm



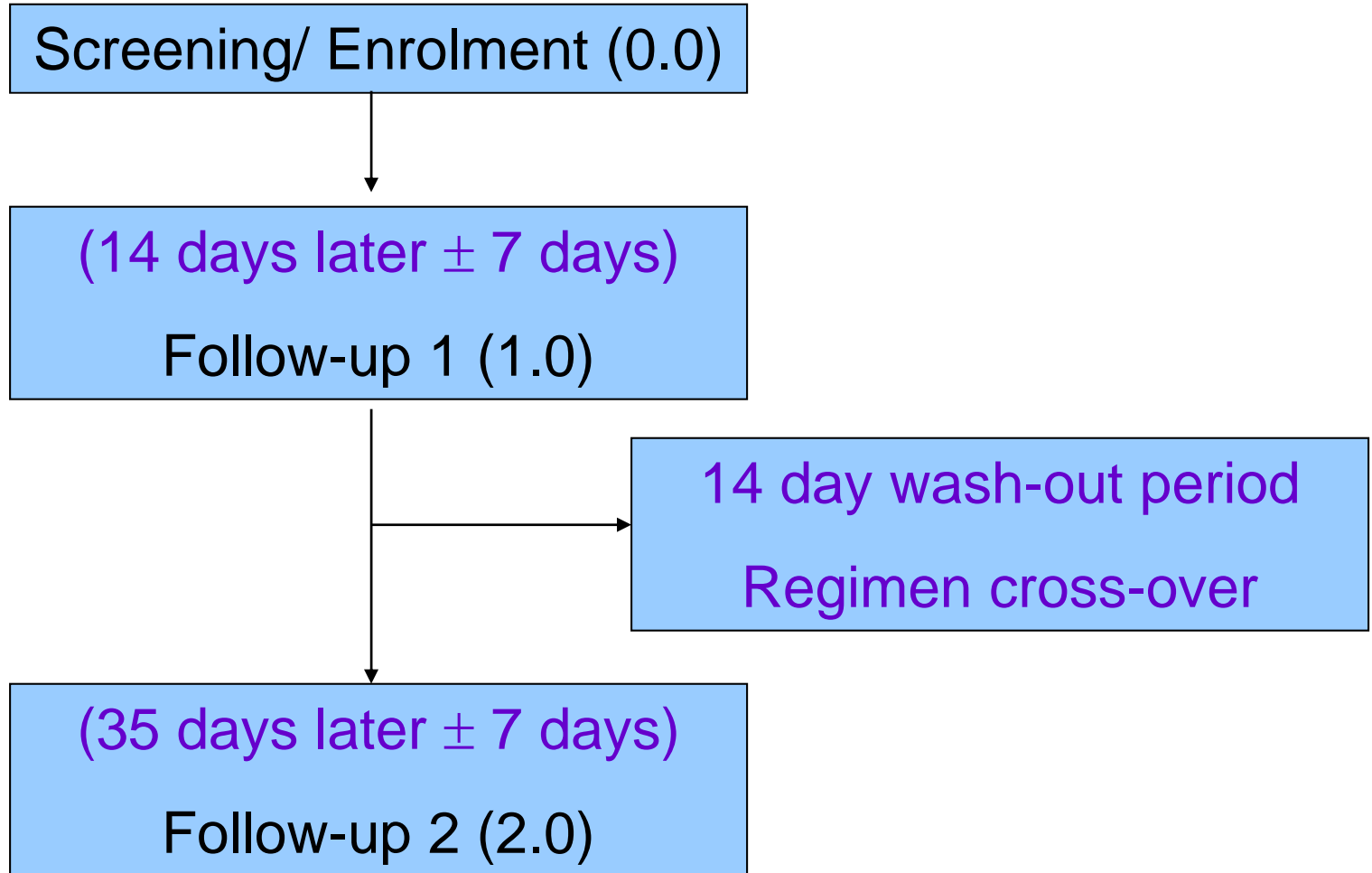
Participants were provided with BufferGel in individual sachets to load onto the device



Study sample: n = 103

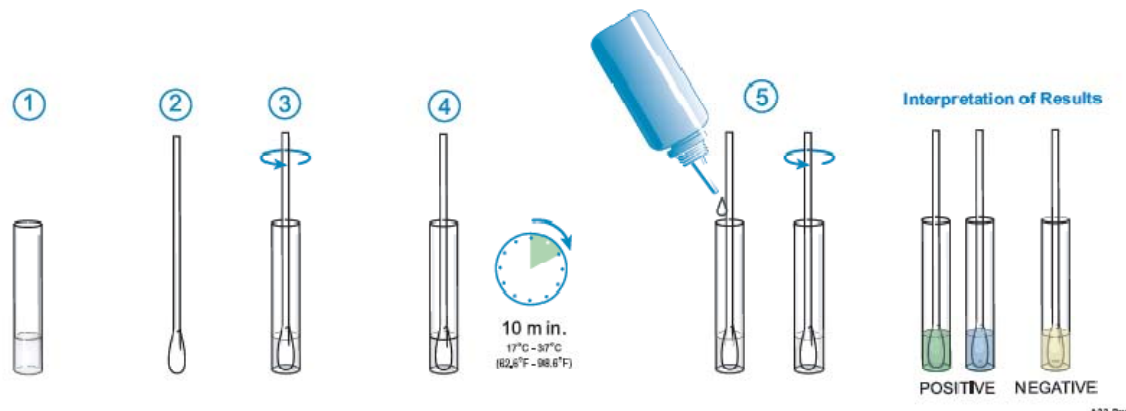
- Main Inclusion criteria:
 - Women aged 18 – 40
 - Sexually-active (=>1 times/week in past 3 months)
 - Non-pregnant and on effective contraception
 - Asymptomatic for genital infections
- HIV status was not an eligibility criteria

Visit Schedule



Methods

- Adverse events:
 - assessed by participant self-report and clinician exam at follow up visits
- BV:
 - assessed by BVBLUE® side-room assay



- Results tabulated in SAS

Results

- 103 women enrolled
 - 100 (97%) completed study as scheduled;
 - 1 woman discontinued for unresolved symptomatic genital infection
- No SAEs reported
- 90 AEs reported among 57 individuals
 - 68% classified as “mild”
 - 32% classified as “moderate”
- 21 women BV-positive at enrollment
 - only treated if symptomatic
- 19 BV positive results during follow-up period
 - 13 in women positive at baseline
 - 6 in women negative at baseline

Gynaecological AE's by regimen and relatedness

| <i>Regimen</i> | <i>Gynae-related</i> | <i>Relatedness to Duet</i> | | |
|----------------|----------------------|----------------------------|-----------------|---------------------|
| | | <i>Probably</i> | <i>Possibly</i> | <i>Probably not</i> |
| Continuous use | 18 | 5 | 9 | 4 |
| Coital use | 13 | 5 | 4 | 4 |
| No use | 4 | NA | NA | NA |
| Total | 35 | 10 | 13 | 8 |

BV positive cases, by group and time period

| Time period | Group | | | Total |
|-------------|---------------------------------|---------------------------------|--------------|-------|
| | A Continuous > Pre-coital | B Pre-coital > Continuous | C Control | |
| Baseline* | 12 | 6 | 3 | 21 |
| | | | | |
| FU1 | 5 | 4 | 2 | 11 |
| FU2 | 5 | 0 | 3 | 8 |

**Only treated if symptomatic*

BV positive cases, by regimen

| REGIMEN | No. Cases |
|--------------|-----------|
| Continuous | 5 |
| Pre-coital | 9 |
| No Use | 5 |
| <i>Total</i> | 19 |

Conclusion

Duet appears safe for use either daily or pre-coitally for 14 days and should be further studied for delivery of vaginal gels.

Qualitative and quantitative analysis of the acceptability of the Duet is forthcoming.