

Male Tolerance of BufferGel® and PRO 2000/5 Gel IN HIV+ Men

Background

- BufferGel® and PRO 2000/5 Gel are candidate topical microbicides entering Phase III trials to test efficacy in protecting women against HIV.
- BufferGel® is designed to protect against HIV infection by maintaining normally acidic pH of vagina in presence of ejaculate.
- PRO 2000/5 Gel inhibits viral entry.

Background

- Both BufferGel® and PRO 2000/5 Gel have undergone clinical testing in Phase I trials among women and HIV-negative men with favorable safety profiles.
- No data on penile safety in HIV+ men.

Primary Objective and Endpoints

- **Assess toxicity among HIV-infected men**
- **Safety endpoints:**
 - Self-reported urethral pain or burning, and penile itching, rash, or ulceration.
 - Erythema, vesiculation, bullous reaction, & ulceration of penile shaft, foreskin, or glans
 - Erythema or ulceration of urethral meatus
 - Positive urine leukocyte esterase (LE) test ($\geq 1+$).

Secondary Objectives and Endpoints

- **To assess acceptability of BufferGel® and PRO 2000/5 Gel among HIV-infected men**
- **Endpoints:**
 - AEs (other than those listed as primary endpoints) judged related to study products.
 - Perceived positive attributes of study products.
 - Perceived negative attributes of study products.
 - Reported willingness to use study products for sexual intercourse.

Inclusion Criteria

- Age 18 years and older.
- HIV+ and CD4 >200.
- Able to communicate in English.
- Willing to provide informed consent and to provide adequate locator information.
- Willing to abstain – during 3 seven-day product use periods – from sexual intercourse & masturbation (other activities, products that may cause penile irritation)

Exclusion Criteria

- Ever had:
 - History of allergy to any component of study products.
 - History of recurrent or persistent NGU.
 - History of penile contact dermatitis, eczema, severe seborrheic dermatitis

Exclusion Criteria

- In last 6 months:
 - Occurrence of any STD, including genital herpes outbreak.
- In last 30 days:
 - Modification of HIV treatment regimen
 - Participation in any other study of an investigational product

Exclusion Criteria

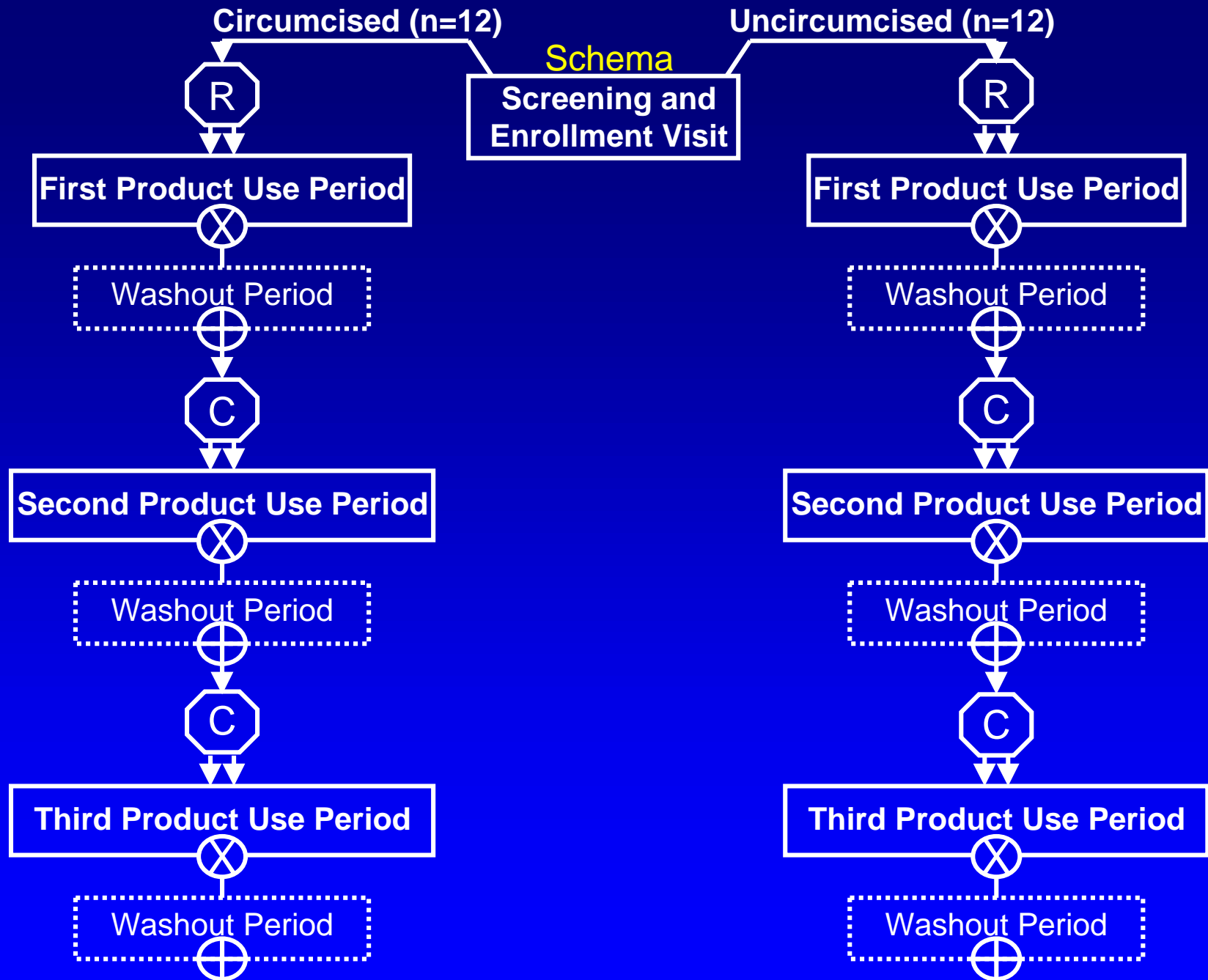
- At screening visit:
 - Penile piercing observed on examination.
 - Current signs or symptoms of an STD.
 - Positive (i.e., >trace) LE test.

Methods

- 24 men HIV+ men (12 circumcised and 12 uncircumcised)
- Blinded cross-over study
- Six possible sequences of nightly application of BufferGel®, PRO 2000/5 Gel, or placebo (KY jelly) for one week.
- One week washout period between products.

Methods

- Participants kept daily study diaries
- Applied product to the penis for 7 nights
- At follow-up visit, participants were interviewed, examined, and first-void urine tested for inflammation by LE.



R = Random assignment to product use sequence; C = crossover to next assigned product
 ⊗ = post-use safety and acceptability assessment; ⊕ = re-screening eligibility assessment

Participant Demographics and CD4 T-Cell Count

	<u>Circumcised</u>	<u>Uncircumcised</u>	<u>Total</u>
• No. Participants enrolled	13	10	23
• Age-- median (range)	38 (26-61)	41 (26-50)	39 (26-61)
• CD4 (cells/μL), median (range)	474 (217-1607)	331 (202-919)	388 (202-1607)
• Race/ethnicity			
– Black or African American	2 (15%)	3 (30%)	5 (22%)
– White	8 (62%)	4 (40%)	12 (52%)
– Other	3 (23%)	3 (30%)	6 (26%)
• Latino or Hispanic origin	2 (15%)	4 (40%)	6 (26%)
• Sex with:			
– Men	10 (77%)	8 (80%)	18 (78%)
– Women	2 (15%)	0	2 (9%)
– Both	1 (8%)	2 (20%)	3 (13%)

Incidence of Adverse Events by Cohorts*

	<u>Circumcised</u>	<u>Uncircumcised</u>	<u>Total</u>
• No. participants who used products	13 (57%)	10 (43%)	23 (100%)
• No participants with ≥ 1 illness/AE	3 (23%)	3 (30%)	6 (26%)
• Conditions reported by participant	2 (15%)	2 (20%)	4 (17%)
– Application site “coldness”		1 (10%)	1 (4%)
– Application site “erythema”		1 (10%)	1 (4%)
– Application site “paresthesia”	2 (15%)		2 (9%)
– Application site “pruritus”	2 (15%)		2 (9%)
• Diagnoses			
– Candida balanitis		1 (10%)	1 (4%)
– Dermatitis	1 (8%)		1 (4%)

*Only Reported Illness/AE that are Definitely, Probably or Possibly Related to Study Products

137-00010-8



137-00010-8



137-00014-5

1/9/02



137-00014-5

1/9/02



137-00014-5

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137-00014-5

1/10/02



137-00014-5

1/10/02



Acceptability of Product A

	<u>Circumcised</u>	<u>Uncircumcised</u>	<u>Total</u>
• Number of participants	12	10	22
• * Liked best about product			
– Sensation	2 (17%)	1 (10%)	3 (14%)
– Lubricating properties	4 (33%)	1 (10%)	5 (23%)
– Nothing	4 (33%)	5 (10%)	9 (41%)
• * Liked least about product			
– Dried too quickly	2 (17%)	2 (20%)	4 (18%)
– Messy		1 (10%)	1 (5%)
– Sensation	2 (17%)		2 (9%)
– Nothing	4 (33%)	4 (40%)	8 (36%)
• Likely to use product	10 (83%)	8 (80%)	18 (82%)
• Object to your partner using product	2 (17%)	1 (10%)	3 (14%)

* 3 most common answers

Acceptability of Product B

	<u>Circumcised</u>	<u>Uncircumcised</u>	<u>Total</u>
• Number of participants	12	10	22
• * Liked best about product			
– Sensation	1 (8%)	3 (30%)	4 (18%)
– Lubricating properties	1 (8%)	2 (20%)	3 (14%)
– Nothing	7 (58%)	3 (30%)	10 (45%)
• * Liked least about product			
– Cold sensation	3 (25%)		3 (14%)
– Dried to quickly	3 (25%)		3 (14%)
– Nothing	2 (17%)	4 (40%)	6 (27%)
– Stickiness		2 (20%)	2 (9%)
– Messy		2 (20%)	2 (9%)
• Likely to use product	10 (83%)	8 (80%)	18 (82%)
• Object to your partner using product	2 (17%)	0	2 (9%)

* 3 most common answers

Acceptability of Product C

	<u>Circumcised</u>	<u>Uncircumcised</u>	<u>Total</u>
• Number of participants	13	10	23
• * Liked best about product			
– Sensation	2 (15%)	3 (30%)	5 (22%)
– Lubricating properties	4 (31%)	2 (20%)	6 (26%)
– Nothing	7 (54%)	3 (30%)	10 (43%)
• * Liked least about product			
– Stickiness	5 (38%)	1 (10%)	6 (26%)
– Sliminess	2 (15%)		2 (9%)
– Nothing	4 (31%)	5 (50%)	9 (39%)
– Messy		2 (20%)	2 (9%)
• Likely to use product	12 (92%)	9 (90%)	21 (91%)
• Object to your partner using product	0	0	0

* 3 most common answers

Lessons Learned

- Preliminary data indicate that BufferGel® and PRO 2000/5 Gel are safe and acceptable among HIV-infected men.
- Likely low sensitivity of urine LE as a screening test for urethral inflammation in microbicide trials
- Lack of objective findings in men with subjective complaints (coldness, pruritis) after applying product

Lessons Learned

- **Difficult to enroll uncircumcised participants**
 - low prevalence of uncircumcised English-speaking HIV+ men in Seattle area.
 - Consider other sites with larger number of uncircumcised men (I.e., Peru).
- **Too stringent exclusion criteria**
 - Occurrence of genital herpes outbreak in past 6 months
 - May be reasonable to enroll lower CD4 (>100)

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