

Safety of a lambda carrageenan microbicide (Carraguard™) in South Africa

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What is Carraguard™?

- Population Council's lead candidate microbicide (PC-515)
- Derived from seaweed (carrageenan)
- Carrageenans used widely food, cosmetics, pharmaceuticals
- Inexpensive, available in bulk, and temperature stable
- *lambda*-carrageenan (80% to 95%) plus *kappa*-carrageenan
- Sulfated polymer – high molecular weight
- No effect on sperm motility



**Phase II:
South Africa**

Endpoints

- Primary endpoints:
 - Safety: local irritation and self-reported complaints
 - Acceptability
 - Feasibility of study implementation
- Secondary endpoint
 - Preliminary effectiveness: HIV, chlamydia, gonorrhea, trichomoniasis, syphilis

Study design

- Randomized
- Placebo-controlled
- Double-blinded trial with two arms:
 - Carraguard™ (PC-515) gel
 - Matching placebo (methyl-cellulose) gel
- HIV-prevention package (condoms, counseling, STI dx and tx) given to all women
- Gel use 3 times per week and no more than 1hr before sex

Sites and collaborators

- Population Council
- Gugulethu, Cape Town. University of Cape Town
- Ga-Rankuwa, near Pretoria. Medical Univ of Southern Africa
- Medical Research Council (SA)
- Family Health International

Study population

- 400 women (200 each in Gugulethu and Ga-Rankuwa) attending family planning or general health clinics.
- Women were followed at Day 14 and Monthly for 6-12 months (average duration of follow-up 9 months).

Participant characteristics

- Most women at each site had sex in past year: vaginal (95%), anal (3%) and oral (10%)
- Nearly half at each site had husband or steady partner
- Of women married or having a stable partner:
 - in Ga-Rankuwa
 - 15% of women also had other partners
 - 15% of women said their partners had other partners
 - and in Gugulethu
 - 8% of women also had other partners
 - 20% of women said their partners had other partners

RTI prevalence at Phase II screening

Site	HIV	Syphilis	Gonorrhoea	Chlamydia	Trich	Bacterial vaginosis	Candida
Gugulethu (n=408)	23%	13%	9%	15%	10%	50%	5%
Ga-Rankuwa (n=407)	19%	8%	5%	7%	12%	43%	8%
TOTAL (n=815)	21%	10%	7%	11%	11%	46%	6%

**Preliminary findings of primary
endpoints: Safety, acceptability, and
feasibility**

Data management and cleaning ongoing...

- Verifying all outcome variables
- Coding infections as incident
- Determining precise denominators (person-time of follow-up)
- Taking adherence with gel and condom use into account
- Unblinding at end of analysis process

Safety (1) Signs

Clinical finding	Group A n=189	Group B n=201
Abnormalities on vulva/labia ever found during follow up	14.8%	13.4%
Abnormalities on vagina ever found during follow up	5.8%	6.0%
Abnormalities on cervix ever found during follow up	10.1%	13.9%

Safety (2) Signs

Clinical finding	Group A n=189	Group B n=201
Pain on bimanual exam ever found during follow up	3.7%	5.5%
Cx motion tenderness ever found during follow up	0.5%	1.0%
Adnexal masses ever found during follow up	0.0%	0.5%

Safety (3) Symptoms

Reported symptom	Group A n=189	Group B n=201
Ever had genital itching, burning or pain	28.9%	32.8%
Study gel ever caused any itching, burning or pain	6.9%	4.5%
Partner ever experienced any symptom with study gel	6.9%	2.5%

Safety (4) Symptoms

Reported symptom	Group A n=189	Group B n=201
Ever had vaginal discharge (mod/profuse)	62.3%	62.2%
Ever had frequent urination during follow up	0.6%	0.0%
Ever had bleeding between periods	0.0%	0.0%

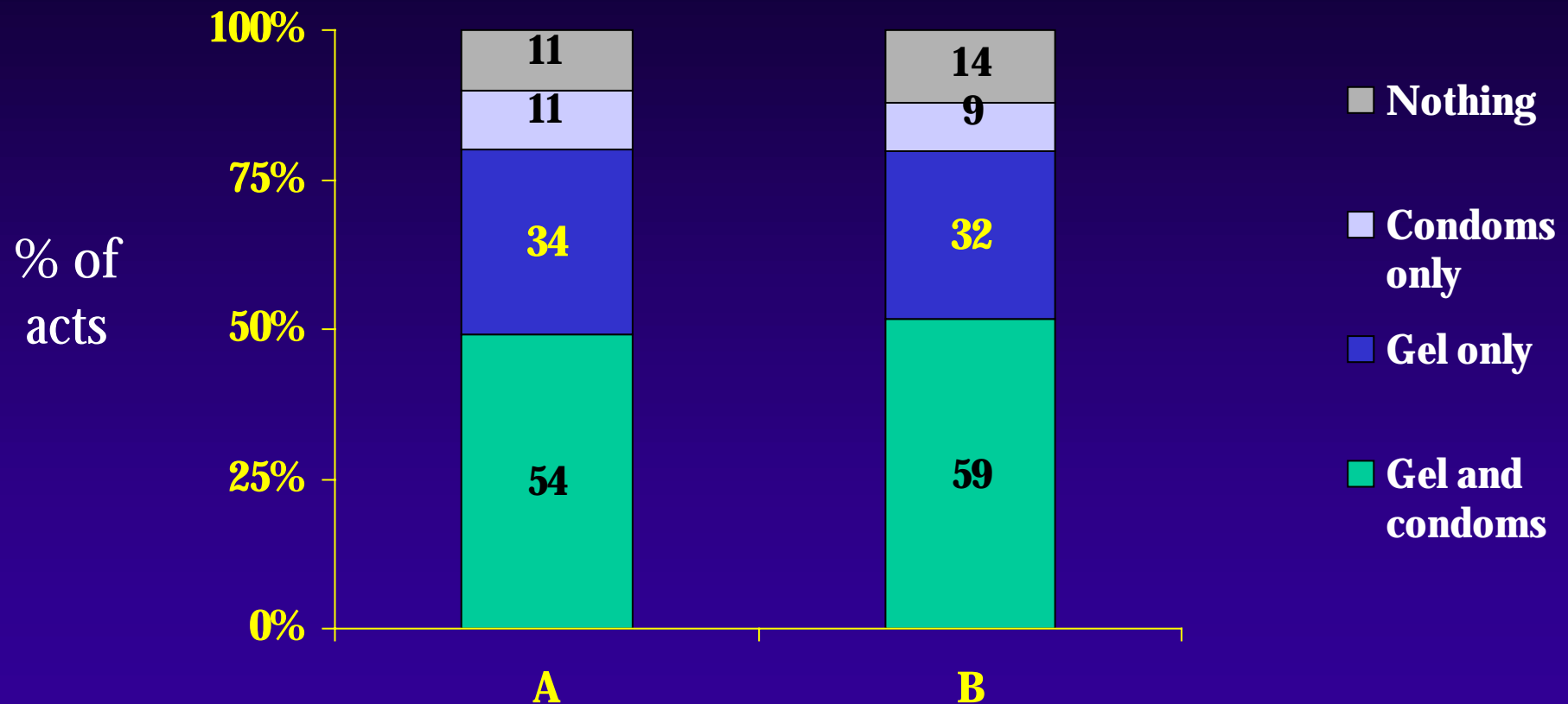
Acceptability

- Women in both groups overwhelmingly found the gel and the applicator to be acceptable
- Preliminary data indicates acceptability remained high over time
- (Poster: Blanchard *et al*)

Feasibility of Study Implementation

- Screened 902 women to enroll 400 (200 per site); approximately 44% of women screened enrolled
- Women were in the trial 9 mo. on average
- Lost to follow up: 12 in Cape Town, 2 at Medunsa
- Vast majority of women had vaginal sex during the study (>90%)
- Few women had anal sex (mean of 0 acts per group during follow up)

Product use during sex



Adherence

	Group A	Group B
9 or > gel uses per month > 75% of time	78.8% (152)	75.3% (152)
Gel use during sex > 75% acts	65.7% (117)	60.2% (115)

**Preliminary findings of secondary
endpoint: Preliminary effectiveness**

Preliminary effectiveness: Number of infected women, by study arm

	A	B
HIV		
- 16 seroconversions	8	8
Chlamydia		
- 41 women	23	18
Gonorrhea		
- 67 women	32	35
Syphilis		
- 36 women	18	18

Preliminary effectiveness

- Power inadequate, particularly for HIV infections
- In animal models, Carraguard very effective against viral STIs, but contradictory results for bacterial STIs
- Study did not have no-gel arm
- To get complete picture, need to analyze:
 - Denominators (person-time of follow-up)
 - Covariates (including adherence to gel and condom use; some infected women had not used gel)
 - Timing of seroconversions (some women seroconverted early)

Conclusions

- Carraguard is likely safe
- Both gels are acceptable
- Implementing this trial in non sex-worker populations was feasible
- Preliminary effectiveness: Need Phase III trial
- **In conclusion:**

We are proceeding with Phase III