

SAVVY Trials

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SAVVY (C31G)

Two Phase III trials of 1% SAVVY gel

- 2,142 HIV antibody-negative participants in each country
- 1:1 ratio SAVVY : placebo
- 12 months recruitment; 12 months of product use for each participant
- Manufactured by Biosyn Inc.
- Funded by USAID

SAVVY Key Eligibility Criteria

- Non-reactive OMT antibody rapid test
- 18 to 35 years old
- **≥3 sexual acts per week**
- **>1 sexual partner in the last 3 months**
- Not be pregnant or desire pregnancy
- No other vaginal products
- Not be an injection drug user
- No gynecological abnormality

SAVVY Statistical Summary

- 80% power to detect a 50% reduction in the HIV infection rate
- Assumptions:
 - HIV incidence $\geq 5/100$ w-y in placebo group
 - $>80\%$ retention at 12 months
 - Observe 66 incident infections

SAVVY Timeline

	Ghana	Nigeria
1 st pt enrolled	Mar 2004	Oct 2004
Interim analysis	Jun 2005	Apr 2006
Last pt enrolled	July 2005	May 2006
Last FU visit	Feb 2006	Dec 2006

Screening and Enrollment

	Ghana	Nigeria
Screened	3490	3334
Enrolled	2142	2153
Screened but not enrolled:	39%	35%
• Did not return for enrollment	17%	20%
• OraQuick reactive	9%	13%
• Pregnant	7%	3%

Baseline Contraceptive Use (%)

	Ghana		Nigeria Pooled
	SAVVY	Placebo	
Condom	46	48	71
None	39	37	6
Oral	11	12	8
Injectable	2	2	0.7
IUD	0.5	0.5	0.7
Other	0.4	0.4	14

Self-reported Sexual Behavior (median)

Number of partners	Ghana	Nigeria
Screening (past 3 months)	3	4
FU (past month)	3	4
Vaginal sex (past week)		
Screening	4	5
FU	6	9
Anal sex (ever)	12%	8%

Mean percentage use for vaginal sex in last 7 days

Ghana

Nigeria

Condom (with or w/o gel)

89%

87%

Gel (with or w/o condoms)

75%

79%

Gel *when condom NOT used*

43%

62%

Pregnancy

	Ghana		Nigeria
	SAVVY	Placebo	Pooled
Probability @ 12 months	43	44	32
Time off product	10%		6%

Pregnancy (cont.)

	Theoretical Probabilities			Ghana	Nigeria
	1	2	3		
Days unprotected					
Condom use	90%	90%	85%	89%	87%
Acts per cycle	10	20	20	24	32
Pregnancy probability	30%	51%	66%	43%	32%

HIV Outcomes

	Ghana		Nigeria
	SAVVY	Placebo	Pooled
N (%)	8 (1.0)	9 (1.1)	33 (1.9)

Ghana Adverse Events

SOC	SAVVY %	Placebo %	Rate Ratio
Reproductive system	10.4	7.9	1.33 (0.99, 1.80)
Gastrointestinal	7.1	7.5	0.93 (0.67, 1.30)
Pregnancy	0.7	1.2	0.57 (0.19, 1.57)
Renal and urinary	1.2	1.7	0.69 (0.30, 1.53)

Ghana Adverse Events

Reproductive AEs	SAVVY %	Placebo %
Genital pruritus female	2.6	2.0
Vaginal candidiasis	2.7	2.8
Vaginal discharge	1.6	1.1
Vaginitis bacterial	1.9	1.4
Vulvovaginitis	1.1	0.5

Ghana Serious Adverse Events

- 22 SAEs (15 SAVVY; 7 placebo)
 - One (gonorrhea) considered related to study gel (participant received placebo)
- Most common: hospitalization due to malaria, diarrhea and car accidents
- 2 deaths
 - sickle cell crisis (SAVVY)
 - viral hepatitis (placebo)
- No product discontinuations due to a medical reason

Nigeria Adverse Events

- Reproductive disorders (13.5% of women)
- Infections (20.3%)
- Gastrointestinal (6.8%)
- Respiratory (5.3%)
- Skin/subcutaneous tissue (3.2%)

Nigeria Adverse Events

- Reproductive Tract AEs (% of women)
 - Genital itching (3.9%)
 - Bacterial vaginitis (3.7%)
 - Candidiasis (3.1%)
 - Vaginal discharge (1.4%)

Nigeria Serious Adverse Events

- 21 SAEs (none considered related to study gel)
 - Most common: hospitalizations for typhoid and appendicitis
- 2 discontinuations due to a medical reason
 - Dermatitis; vaginal itching

DMC Meetings and Conclusions

- **Ghana:** Given the HIV low incidence, the DMC concluded that was not feasible obtain the required number of endpoints in Ghana.
- **Nigeria:** The DMC concluded that the trial was unlikely to provide convincing evidence that SAVVY protects against HIV.

Summary

- **There is no evidence to suggest that SAVVY is harmful to women based on the unblinded data from Ghana.**
- **We cannot make any conclusion about product effectiveness using this protocol in the Ghana cohort.**
- **Nigeria trial was stopped for futility, and a final evaluation of effectiveness/safety in will be forthcoming.**