Safety and Acceptability of Daily and Coitally Dependent Use of 1% Tenofovir Over Six Months of Use

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HPTN 059: Safety and Acceptability Study of the Vaginal Microbicide 1% Tenofovir Gel

Primary objective –

- To assess the local and systemic safety of tenofovir 1% gel for vaginal use in HIV-uninfected women versus a placebo gel over 24 weeks of daily and coitally dependent use

Secondary objective –

- Acceptability and adherence to, two regimens of tenofovir or study gel use in women

Timeline and Retention

- **Pregnancies per 100 woman-years of follow-up: 2**
- **Retention 96% at 6 months**

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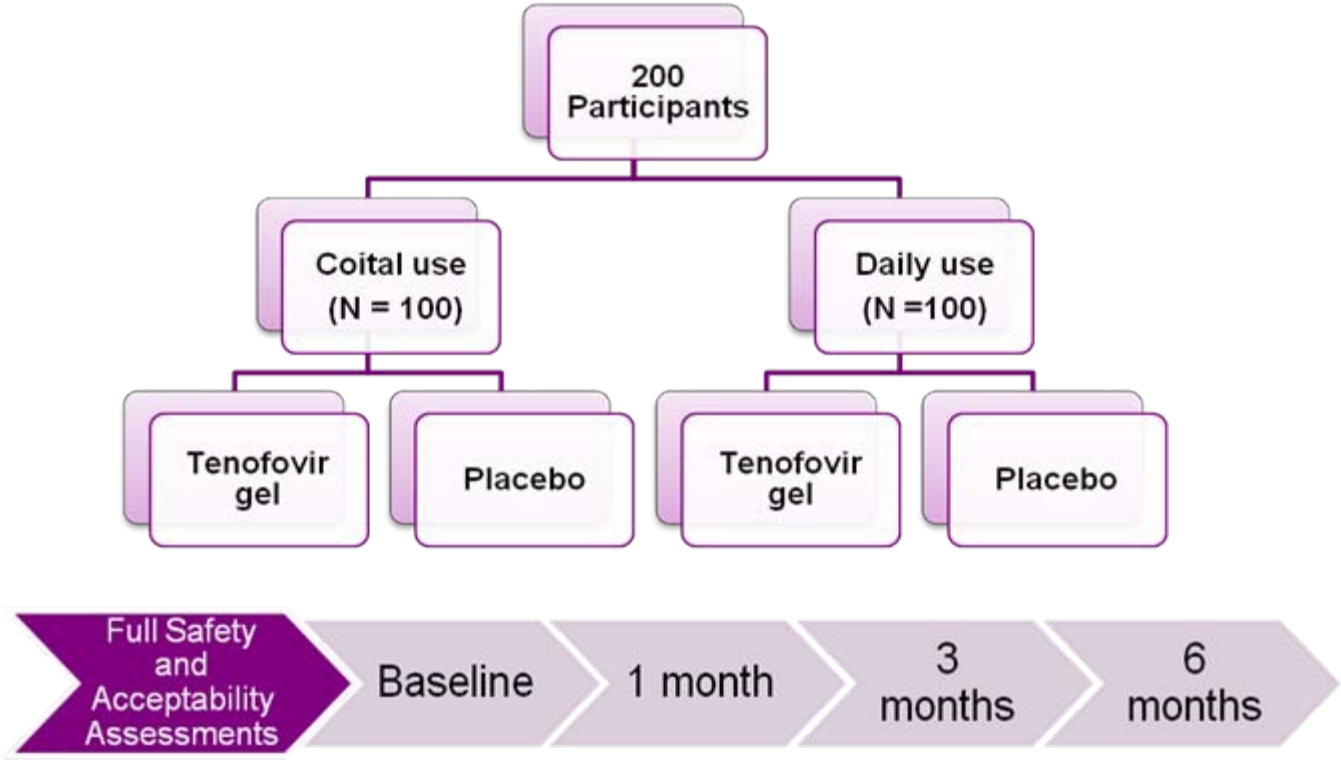
Study Design



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Study Population

	India	US
	N=100	N=100
Age (mean, range)	33 (24-46)	31(18-49)
Married	99%	28%
Own income	60%	73%
Education	21% >10	63% >12 yr
Race/ethnicity		
Black	0	58%
White	0	23%
Asian	100%	1%
Mean monthly income	4376 R	$1503

Behavior at Enrollment by Arm

	Coitally Dependent		Daily Use	
	Tenofovir	Placebo	Tenofovir	Placebo
	N=50	N=51	N=49	N=50
Vaginal sex, past 7 d	2.5	1.9	1.9	2.2
% sex, past 7 d	86%	82%	78%	82%
No condom, past 7 d	65%	60%	53%	66%
Douche before sex	14%	12%	8%	6%
Douche after sex	38%	39%	37%	34%
Water with soap in vagina past month	22%	22%	24%	22%

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Behavior at Enrollment by Arm

	Coitally Dependent		Daily Use	
	Tenofovir	Placebo	Tenofovir	Placebo
	N=50	N=51	N=49	N=50
Ever anal sex	24%	25%	33%	28%
Anal sex, past 7 d	2%	0%	4%	2%
Hormonal contraception	40%	37%	41%	34%

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Safety Laboratory Results

- Hemoglobin/hematocrit
- WBC count
- WBC differential
- Platelets
- Alkaline phosphatase
- AST (SGOT)/ALT (SGPT)
- GGT
- Bilirubin
- Creatinine
- BUN

- No difference between
  - active and placebo
  - coital vs. daily
  - baseline, 4, 12, 24 wks

Incidence of Genital Symptoms During Follow-up of 198 Women

	Daily Use		Coital Use	
	Tenofovir	Placebo	Tenofovir	Placebo
Itching	33%	35%	18%	27%
Burning	25%	14%	22%	16%
Bleeding*	13%	4%	22%	6%
Odor	6%	10%	8%	2%
Pain with sex	4%	8%	2%	2%

No statistically significant differences

*Bleeding was lighter or normal bleeding occurring between menses.

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Incidence of AEs by Treatment Arm at 6 Months of Follow-up

	Daily Use		Coital Use	
	Tenofovir	Placebo	Tenofovir	Placebo
≥ 1 AE	57%	69%	47%	42%
Candidiasis	18%	22%	18%	13%
Discharge	2%	8%	2%	2%
Burning	18%	10%	13%	4%
Abd. Pain	2%	4%	7%	1%
Dysuria	7%	6%	0%	2%
Cx Friability	2%	0%	0%	6%
No statistically significant differences, only AEs thought to be definitely, probably, or possibly related (all severities)				

STI/RTI During Follow-up

- No acquisitions of HIV, gonorrhea, or hepatitis B
- One acquisition of HSV-2
- No increase in BV by Nugent score

		Tenofovir gel group	Placebo gel group
ENR	24 WKS		
NL	NL	61%	57%
NL	BV	20%	10%
BV	NL	6%	12%
BV	BV	16%	12%

Condom and Gel Use: Coitally Dependent Arm

	All	NY	AL	Pune
	N=101	N=24	N=27	N=50
At least one sex act last month	100%	100%	100%	100%
Sex acts with condom past month	88%	91%	90%	86%
Sex acts with gel past month	86%	83%	78%	93%
Gel use within 2 hr	80%	78%	78%	82%

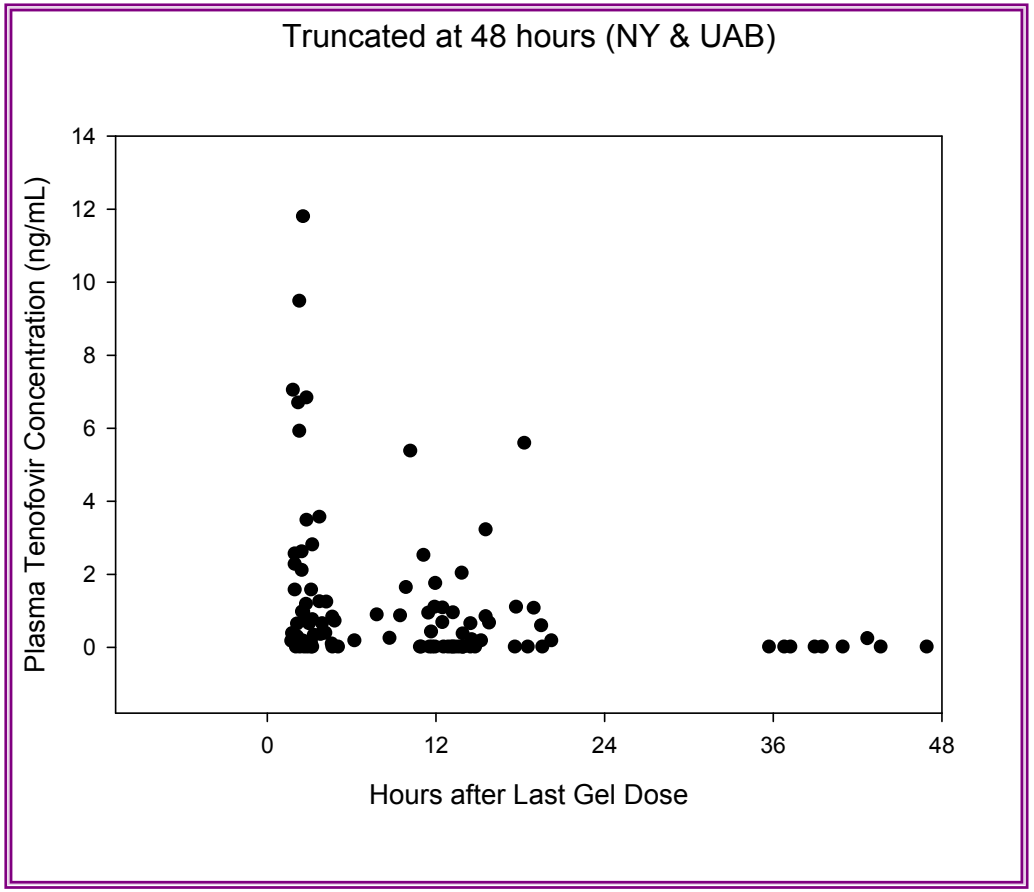
Coitally Dependent Gel Use Past Month

		Gel Used	
		+	-
Condom used	+	232 (81%)	19 (7%)
	-	19 (19%)	16 (6%)

Adherence to Product: Daily Use

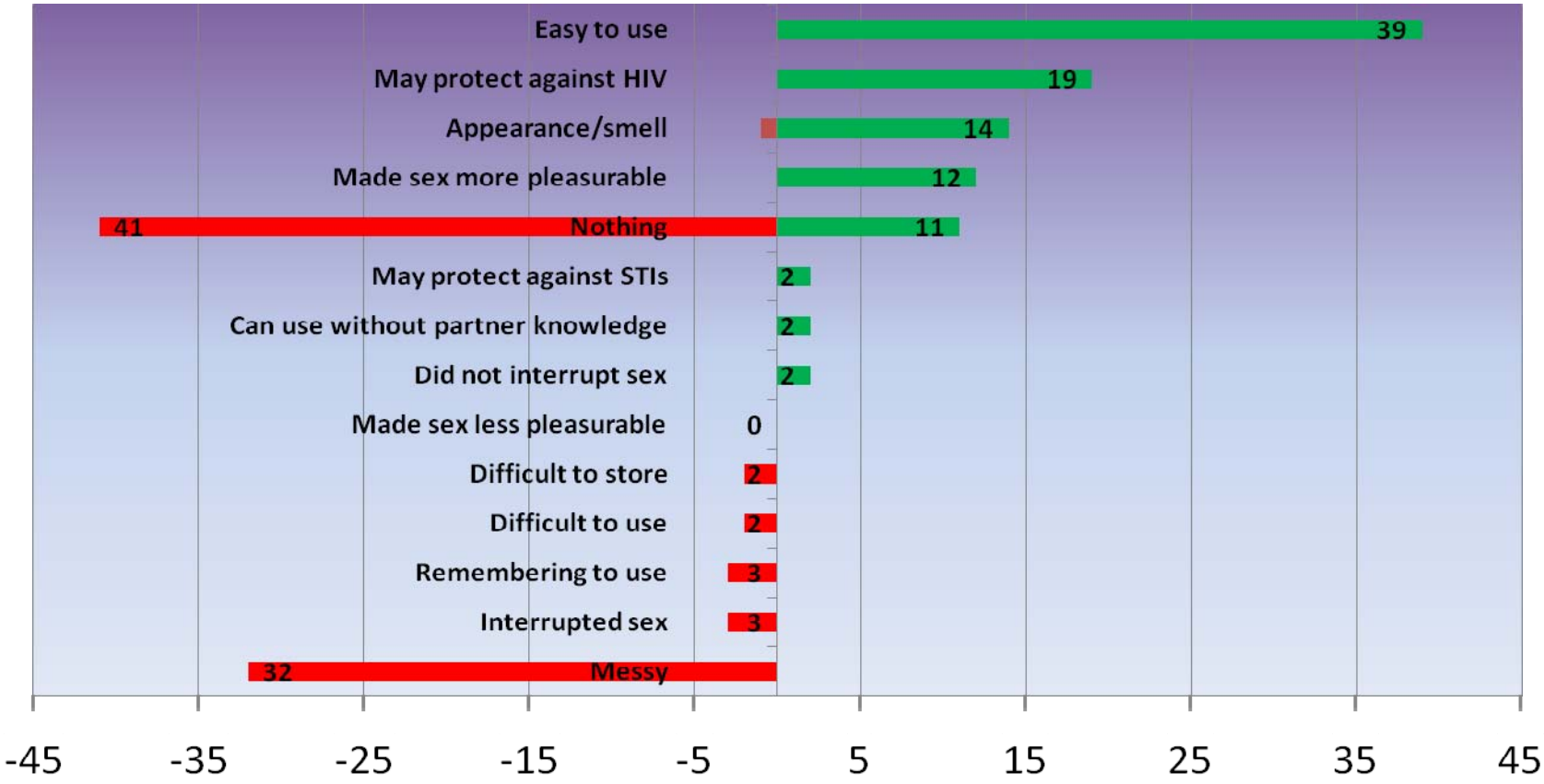
	All	NY	AL	Pune
	N=97			
Used gel every day past week	27%	26%	46%	18%
Mean study gel used/d	.83	.85	.87	.80
Inserted ≥6X	75%	69%	82%	72%
If missed dose, why not used?				
Forgot	23%	44%	40%	5%
Menses	41%	33%	0%	65%

Plasma Tenofovir vs. Last Gel Use



Category	% Detectable
0 – 24 hours	70
0 – 12 hours	79
12 – 24 hours	53
>24 hours	12
	60%
Coitally dependent	43
Daily	60
	51%

Gel Acceptability at Study Exit



Social Harms During Follow-up

	Coitally Dependent	Daily
Problem from being in study		
Spouse/partner	6%	11%
People at home	2%	2%
Friends	2%	1%

All 12 respondents, noted that the social harms were emotional, not financial or physical.

Minor arguments with husband regarding gel and condom use.

Boyfriend was angry and claimed participant was HIV+.

Mother scolded her for being in study.

But Would They Use It Again? Study Exit Assessment

"Would you want to use the gel if it is found to help prevent people from getting HIV?"

Yes	**Tenofovir**	**Placebo**	**P**
Overall	92%	94%	.72
Coitally Dependent	92%	88%	.48
Daily Use	91%	100%	.07
Yes	**Coitally**	**Daily**	**P**
	90%	96%	.14

HPTN-059 Lessons Learned

- **Safety:** Daily or coitally dependent 1% tenofovir gel no different from placebo
- **Adherence:** Coitally dependent adherence within 2 hours of sex: 80%; 83% of daily doses reported used
- **PK:** 79% of women reporting gel use in past 12 hours had low but detectable plasma tenofovir supporting self reported adherence data
- **Acceptability:** Daily and coital use highly acceptable to women and they would use it if found to be effective at preventing HIV

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