

Call with GCAB Scientific Working Group

Dec 3, 2010

Purpose of the call

- To make you are aware of the iPrEx results
- To let you know that HVTN 505 study team is considering what the results mean to 505
- To consider, in a structured way:
 - what do these results mean to you?
 - what do these results mean to your communities?
 - what do you think the results mean for HVTN 505?

iPrEx

Summary of the Study and Results

WHAT IS Pre-Exposure Prophylaxis?



Therapy taken to **prevent** rather than treat an infection or illness

Malaria, TB, Meningitis

Mother to child transmission (MTCTp)

Post-Exposure Prophylaxis (PEP)

Animal studies of HIV **PrEP** show strong protective effect

**iPrEx:
PrEP Initiative**

Sponsored by NIH/NIAID/DAIDS

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And drug donated by

Gilead Sciences



Selected slides, courtesy of Dr Robert Grant

iPrEx (PrEP Initiative)

Fully Enrolled as of December 2009



Number of Participants	2499
Number of Sites	11

PrEP Initiative (iPrEx)

- Men who have sex with men
- Randomized 1:1 FTC/TDF vs Placebo
- Daily oral Truvada (1 pill)
- Followed for:
 - HIV seroconversion
 - Adverse Effects
 - Metabolic Effects
 - HBV exacerbations
 - Risk behavior and STIs (including HSV)
 - Adherence
 - If infected
 - Drug resistance
 - Viral load
 - Immunological responses and CD4 counts

iPrEx: Main Study Question

- Can tenofovir/emtricitabine (FTC/TDF, Truvada), a drug that is already being used to treat people living with HIV infection, also help prevent HIV infection in men who are HIV-negative?
- What is the safety for HIV negative people taking Truvada daily?
- Did people taking the drug change their sexual risk behavior?
- How well were study participants able to take a daily pill?



Comprehensive Prevention Services Given to All

- HIV Testing Monthly
- Pre- and Post-test counseling
- Condoms (15 or more)
- STI testing if any symptoms, monthly
- STI screening for all every 24 weeks
- Partner treatment
- PEP if recently exposed
- HBV vaccine



iPrEX: A few figures

Participants enrolled	2,499
Participant visits	43,248
Visits for HIV Testing and Counseling	39,754
Pages of data generated	650,000
Tablets of study drug dispensed	1,184,400
Syphilis Cases Dx and Rx	1,019
HBV vaccine doses given	4,533
Condoms distributed	585,000

iPrEx Results

Baseline Characteristics of the Participants

Highlights

- Mostly from South America
- High HIV risk: average ~18 partners in the 3 months prior to enrollment
- About half (53%-55%) reported having more than 5 drinks/day

Table 1. Baseline Characteristics of the Subjects.*

Characteristic	FTC-TDF (N=1251)	Placebo (N=1248)	P Value
Age group — no. (%)			0.04
18–24 yr	591 (47)	662 (53)	
25–29 yr	274 (22)	241 (19)	
30–39 yr	249 (20)	224 (18)	
≥40 yr	137 (11)	121 (10)	
Education level — no. (%)			0.26
Less than secondary	279 (22)	244 (20)	
Completed secondary	430 (34)	453 (36)	
Postsecondary	525 (42)	539 (43)	
No answer or missing data	17 (1)	12 (1)	
Race or ethnic group — no. (%) †			0.40
Black	117 (9)	97 (8)	
White	223 (18)	208 (17)	
Mixed race or other	849 (68)	878 (70)	
Asian	62 (5)	65 (5)	
Hispanic	900 (72)	906 (73)	0.72
No. of alcoholic drinks (on days when subject drank in past month) — no. (%)			0.66
0	206 (16)	184 (15)	
1–4 per day	348 (28)	345 (28)	
≥5 per day	666 (53)	687 (55)	
No answer or missing data	31 (2)	32 (3)	
City and country of residence — no. (%)			1.00
Lima, Peru	470 (38)	470 (38)	
Iquitos, Peru	230 (18)	230 (18)	
Guayaquil, Ecuador	150 (12)	150 (12)	
Rio de Janeiro	147 (12)	147 (12)	
São Paulo	39 (3)	37 (3)	
San Francisco	70 (6)	70 (6)	
Boston	43 (3)	44 (4)	
Chiang Mai, Thailand	57 (5)	57 (5)	
Cape Town, South Africa	45 (4)	43 (3)	
Sexual risk factors at screening			
No. of partners in past 12 wk	18±35	18±43	0.51
Unprotected receptive anal intercourse in past 12 wk — no. (%)	732 (59)	753 (60)	0.37
Unprotected anal intercourse with partner with positive or unknown HIV status in past 6 mo — no. (%)	992 (79)	1009 (81)	0.34
Transactional sex in past 6 mo — no. (%)	517 (41)	510 (41)	0.84
Known partner with HIV in past 6 mo — no. (%)	23 (2)	32 (3)	0.22
Sexually transmitted infections diagnosed at screening			
Syphilis seroreactivity — no./total no. (%)	164/1240 (13)	162/1239 (13)	0.95
Serum herpes simplex virus type 2 — no./total no. (%)	458/1241 (37)	430/1243 (35)	0.24
Urine leukocyte esterase positive — no. (%)	23 (2)	22 (2)	1.00
Hepatitis B virus status — no. (%)			0.11
Susceptible	827 (66)	803 (64)	
Immune because of natural infection	247 (20)	222 (18)	
Immune because of previous vaccination	149 (12)	190 (15)	
Current infection with hepatitis B virus	7 (1)	6 (<1)	
Indeterminate	21 (2)	27 (2)	

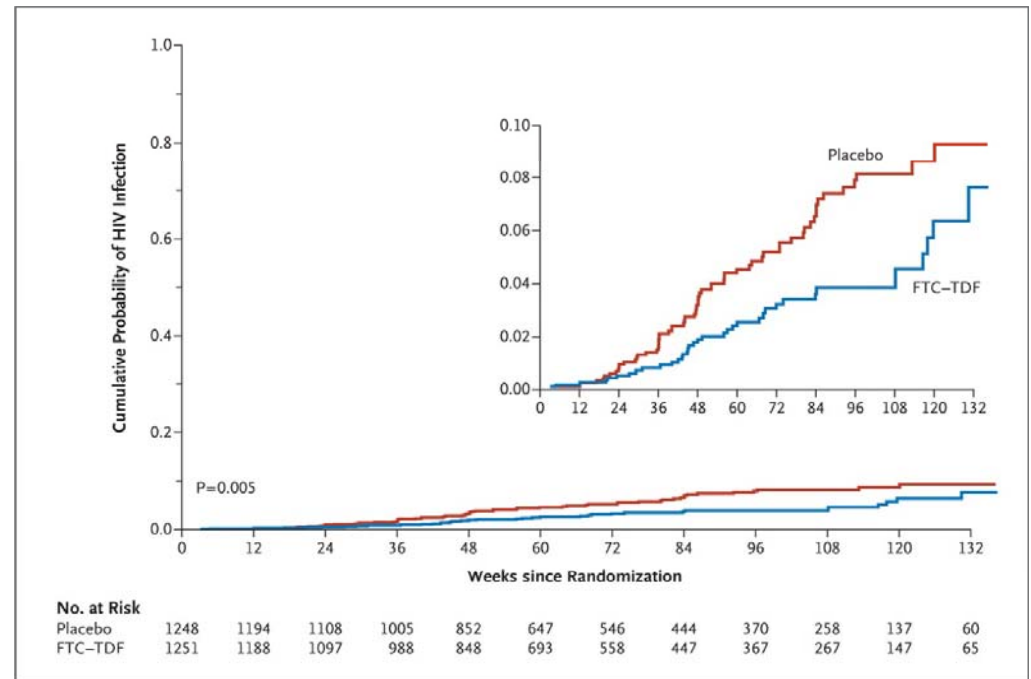
* Plus-minus values are means ±SD. Percentages may not total 100 because of rounding. FTC-TDF denotes emtricitabine and tenofovir disoproxil fumarate.

† Race or ethnic group was self-reported.

Grant RM et al. N Engl J Med 2010. DOI: 10.1056/NEJMoa1011205

What are the results?

- 100 HIV infections among 2,499 participants
 - 36 infections in the study group that received Truvada
 - 64 infections in the group that received placebo
- PrEP group : 44% less likely to become HIV infected than placebo group



**Kaplan–Meier Estimates of Time to HIV Infection
(Modified Intention-to-Treat Population)**

Grant RM et al. N Engl J Med 2010.

What does this mean?

- The rate of HIV infection was 44% lower in men who were receiving Truvada as PrEP
- highly unlikely these results are due to chance
 - Statistically significant: 95% confidence interval (95% CI) was 15% - 63%
 - Meaning: it can be determined with 95% confidence that the true efficacy in this trial falls somewhere between 15 and 63%
- NOTE: *very important* to
 - take medication
 - be monitored for HIV infection
 - receive comprehensive evaluations for any side effects

Was PrEP more effective when people took the pill more consistently?

- Adherence was measured in different ways:
 - asking the participants monthly how many pills they took,
 - counting number of pills given to participants each month, counting the number of pills participants brought back each month
 - *None of the measures of adherence are perfect and all have limitations*
- Participants who reported taking the drug more often experienced more protection
 - Study participants who reported taking Truvada on 50% or more of days had 50% fewer HIV infections (95% CI 18-70%; P=0.006)
 - Those who reported using PrEP on 90% or more of the days had 73% fewer HIV infections (95% CI 41-88%; P=0.001)

Was PrEP more effective when people took the pill more consistently?

- Blood levels of study drug were compared in a small group who became HIV-infected and a small group that didn't
 - Among those given Truvada, study drug was detected in :
 - Less than 10% of people who became HIV infected
 - About half of those who remained HIV-negative
 - Participants who had drug detected in their blood were more likely to be protected from HIV than those who didn't
- Next step: drug level testing in many more samples
- **Further studies required to understand how to help people take the pills more consistently, and to what extent doing so will increase protection against HIV**

Were there any side effects or risks to taking the medication?

- Overall, generally safe and well tolerated
 - **No differences in serious side effects** between the group who received Truvada and group who received placebo
- **Mild side effects**
 - 9% of individuals who received PrEP reported **nausea** in the first month of the study, compared to 5% of those who received placebo
 - **unintentional weight loss** of more than 5% was reported in 2.2% of people receiving PrEP compared with 1.1% of placebo users (P=0.04)
 - There were a few mild abnormalities in **kidney function**
 - 2% in the group receiving Truvada vs. 1.1% in the placebo group experienced increase in creatinine (a marker of kidney function)
 - None of the abnormalities were permanent (they resolved after the medication was stopped)

Did taking PrEP lead to drug resistance in this study?

- Two cases of resistance to emtricitabine component of Truvada
 - In 2 people who took Truvada and were infected at enrollment, but too recently to be detected by HIV antibody tests at enrollment
 - Stored blood specimens from their enrollment visit were found to have HIV present by viral load testing
- **For anyone using PrEP, to minimize the chance of resistance, *very important* to**
 - ensure regular HIV testing,
 - conduct health screening for viral symptoms prior to starting PrEP, &
 - stop PrEP immediately if a person becomes HIV infected

What are some remaining questions not answered by the study

- Is PrEP is safe and effective in other populations?
- Safety and potential protective effect of alternative dosing regimens, (e.g., intermittent PrEP):
 - How often does the pill have to be taken? Either before and after sex, or on a regular schedule several times a week
 - Additional studies planned
- What's the cost-benefit of a PrEP program?
- If beneficial, how best to implement a PrEP program?
- What is the potential public health impact of providing broad access to PrEP for HIV prevention ?

iPrEx: Take home points

- Truvada taken once a day decreased the risk of HIV infection by 44% among MSM
 - taken consistently in combination with condom use, risk reduction counseling and STD care and monthly HIV testing
 - medications taken on an ongoing basis, *not* tied to specific behavior or possible exposure
- PrEP may be an additional tool for HIV prevention for MSM and transgender women
 - in combination with standard HIV prevention tools such as HIV testing and counseling, provision of condoms and lube, and STI testing and treatment
 - should be coordinated under the care of a health professional

We would like to hear from you

What do iPrEx results mean to you and your communities?

- How applicable are these results to you personally and to your community or those represented by your organization?
 - What do you think it means for MSM and transwomen in the United States?
- Based on these results, how likely would you be to consider taking PrEP (or how likely by others in your community/social network)?
- And if you were to take it, would you take it intermittently (only when you are about to have sex) or every day?
 - Do you think that PrEP is for everyone? Why or why not?
- What do you think it means to other HIV prevention studies that are going on – like the vaccine study HVTN 505, which as you know is conducted among MSM and transgender women in the US at risk for HIV infection?

Thank you

- Any questions?
- We value your input!