



# **Safety of Oral FTC/TDF Pre-exposure Prophylaxis in Men and Trans Women Who Have Sex with Men**

**Sponsored by**

**NIH/NIAID/DAIDS**

**with co-funding by the**

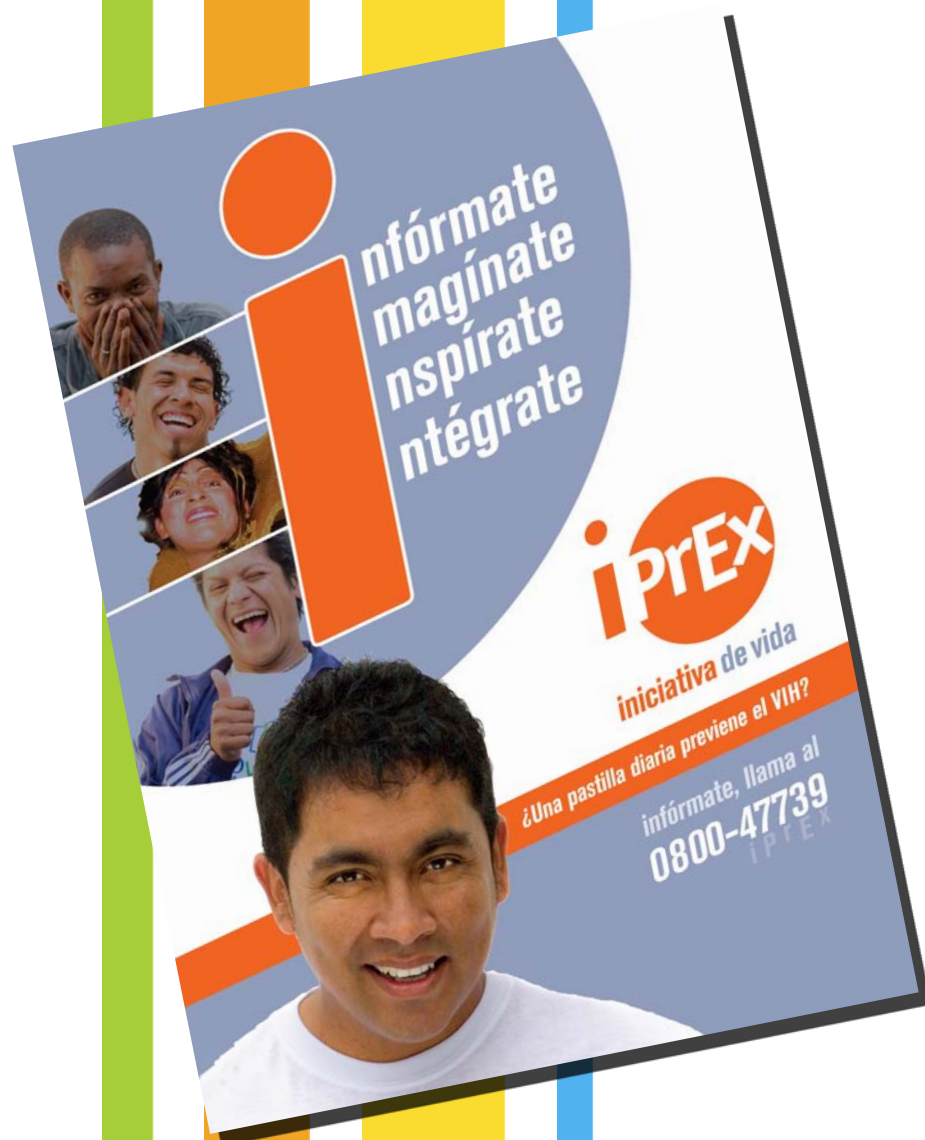
**Bill & Melinda Gates Foundation**

**and drug donated by**

**Gilead Sciences**

# The iPrEx Study

- 2499 MSM and Trans Women
- 11 sites, 6 countries, 4 continents
- Randomized 1:1
- Daily Oral FTC/TDF vs Placebo
- Followed Monthly on Drug for:
  - HIV seroconversion
  - Adverse Events (especially renal & liver)
  - Metabolic Effects (Bone, Fat, Lipids)
  - HBV Flares among HBsAg+
  - Risk Behavior & STIs
  - Adherence
  - If infected
    - *Drug Resistance*
    - *Viral load*
    - *Immune responses & CD4 Count*
  - 2124 person years observed on FTC/TDF



# Adverse events

Adverse Event	TDF/FTC		Placebo		P value
	n (%)	Events	n (%)	Events	
Depression	43 (3%)	46	62 (5%)	63	p=0.07
Grade 3 or Grade 4	151 (12%)	248	164 (13%)	285	p=0.51
Death	1 (<1%)	1	4 (<1%)	4	p=0.18
Serious AE	60 (5%)	76	67 (5%)	87	p=0.57



# Adverse events

Adverse Event	TDF/FTC		Placebo		P value
	n (%)	Events	n (%)	Events	
<b>Creatinine Elevated</b>	25 (2%)	28	14 (1%)	15	p=0.08
<b>Creatinine Elevation Confirmed on Next Visit</b>	5 (0.4%)	7	0	0	p=0.06
<b>Phosphate, Electrolytes, Total Bili, AST, ALT, AlkP, Glucose, Amylase, HCO<sub>3</sub>, Hbg, WBC, Platelets</b>					p>0.15





# Adverse events

Adverse Event	TDF/FTC		Placebo		P value
	n (%)	Events	n (%)	Events	
Diarrhea	46 (4%)	49	56 (4%)	61	p=0.36
Headache	56 (4%)	66	41 (3%)	55	p=0.10
Nausea	20 (2%)	22	9 (<1%)	10	p=0.04
Weight Decreased	27 (2%)	34	14 (1%)	19	p=0.04



# Drug Resistance – Clinical Genotyping Assays (TruGene)

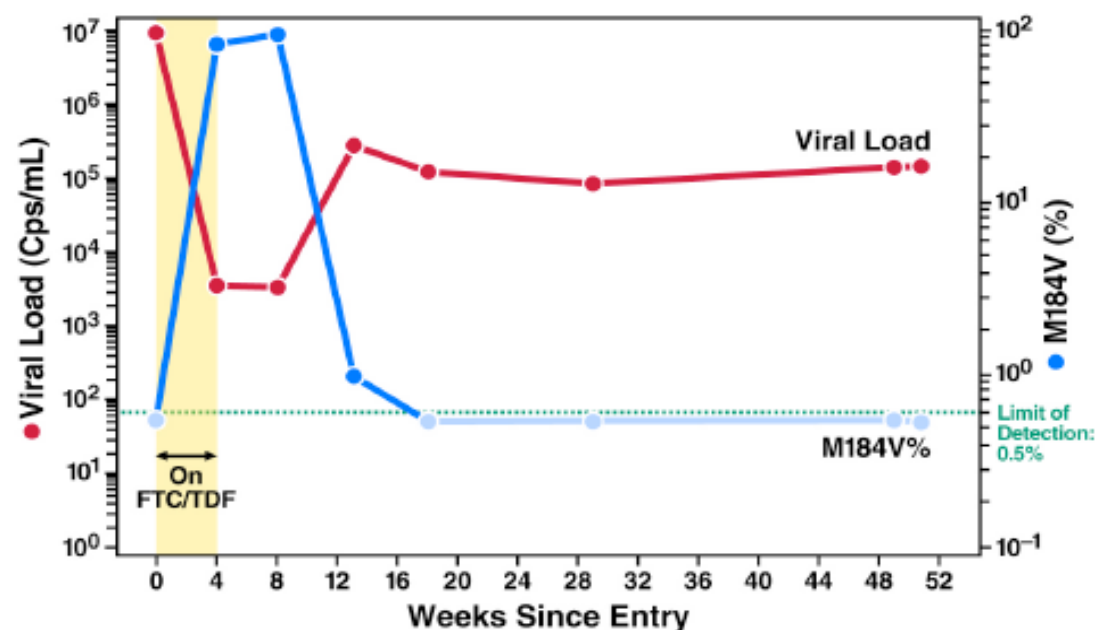
Genotypic Resistance	HIV Status at Enrollment			
	Infected		Uninfected	
	Placebo N=8	FTC/TDF N=2	Placebo N=83	FTC/TDF N=48
<b>65R</b>	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>70E</b>	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>184I</b>	0 (0%)	1 (50%)	0 (0%)	0 (0%)
<b>184V</b>	1 (13%)	1 (50%)	0 (0%)	0 (0%)
<b>TDF Resistance</b>	0 (0%)	0 (0%)	0 (0%)	0 (0%)
<b>FTC Resistance</b>	1 (13%)	2 (100%)	0 (0%)	0 (0%)



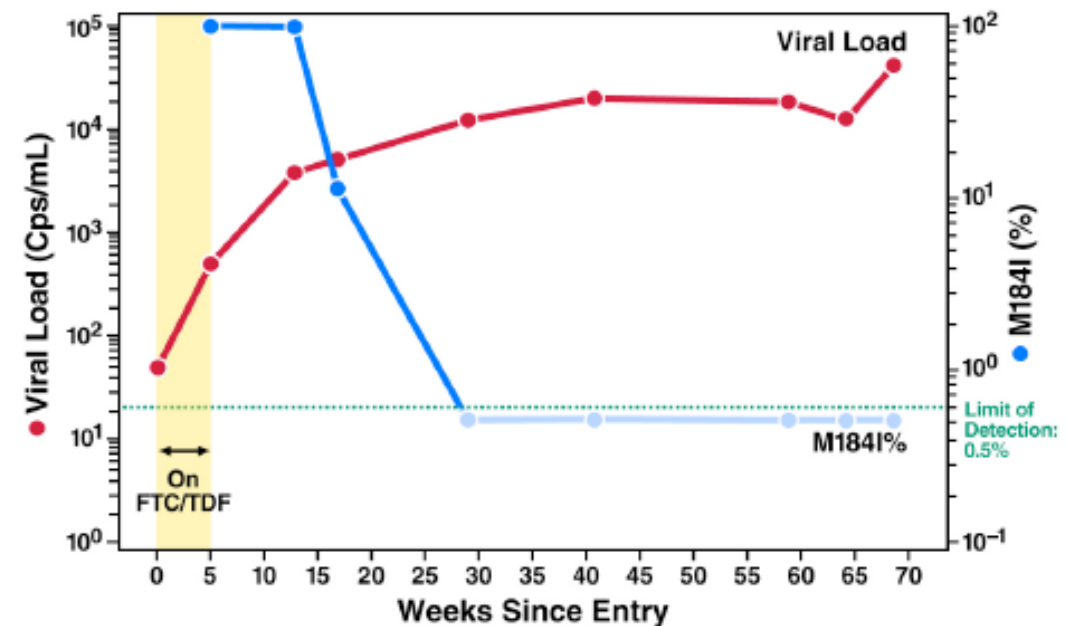
# HIV Resistance – Minor Variant Assays

- Emergent HIV infections (91 samples tested)
  - No drug resistance in participants on FTC/TDF
  - 2 with minor variant drug resistance on placebo (1 to tenofovir, 1 to emtricitabine)
- HIV infections already present at enrollment
  - 2 cases of emtricitabine resistance
  - Resistance dropped to undetectable levels within 6 months after stopping PrEP

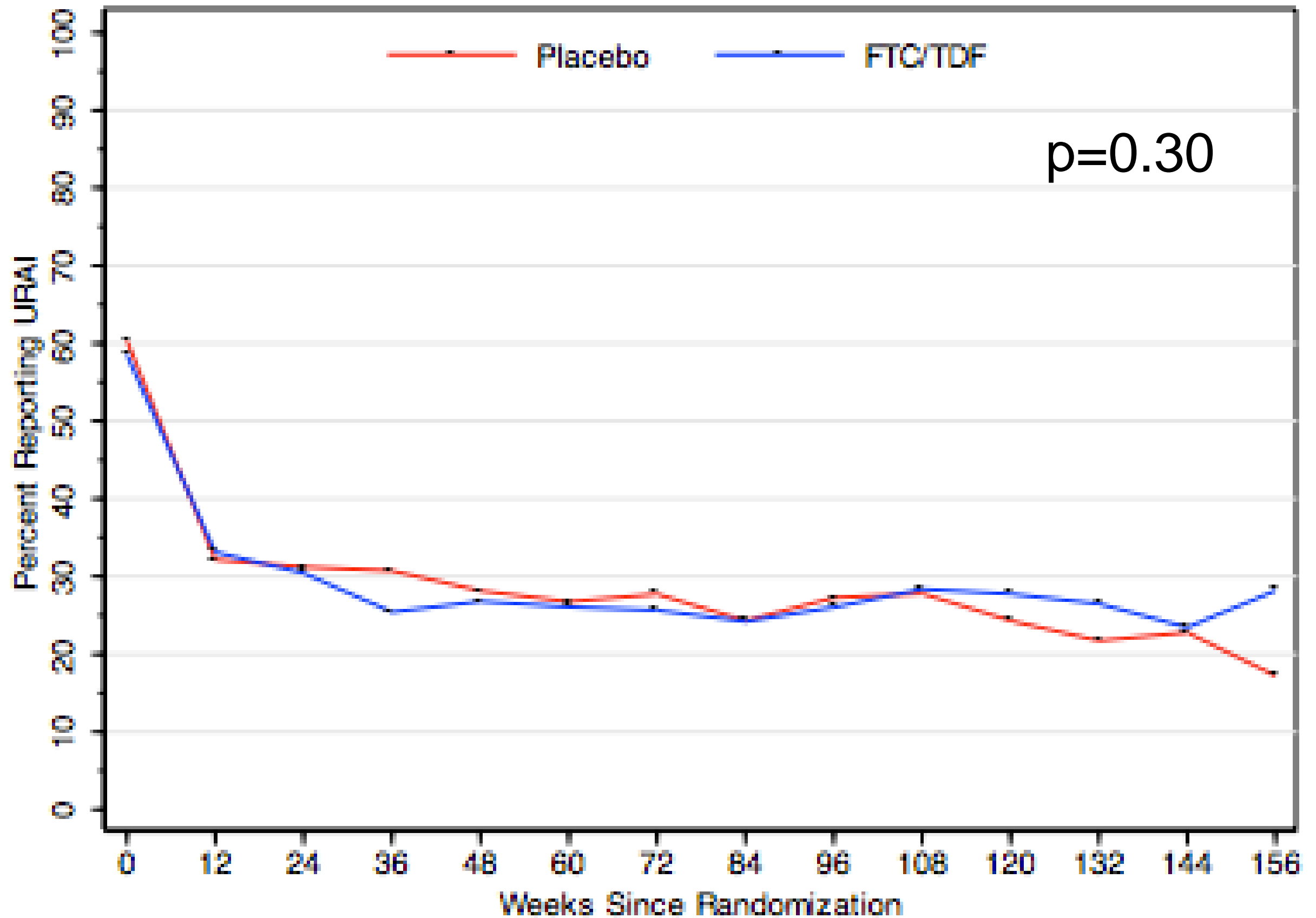
FTC/TDF #1



FTC/TDF #2



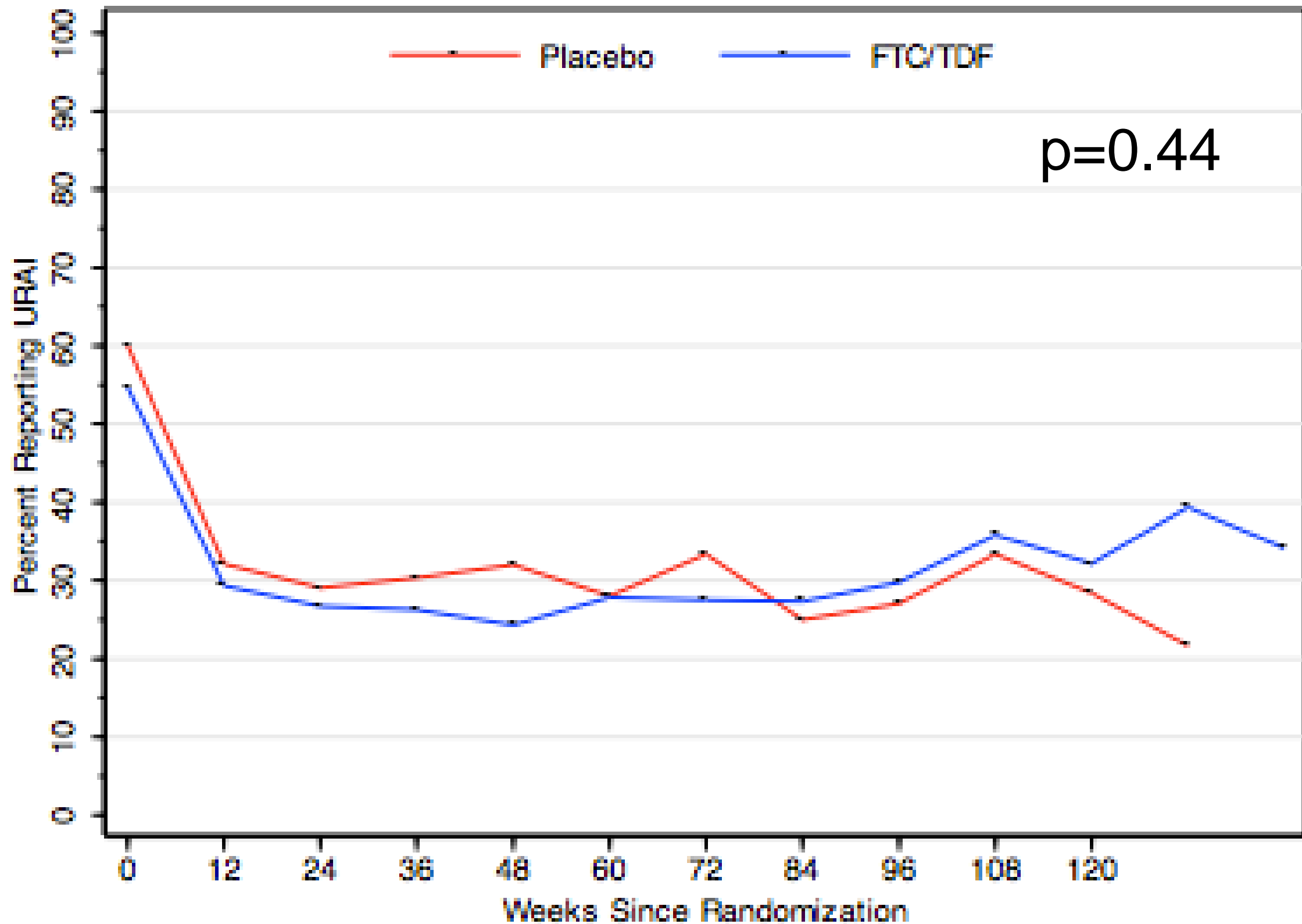
# Unprotected Receptive Anal Intercourse



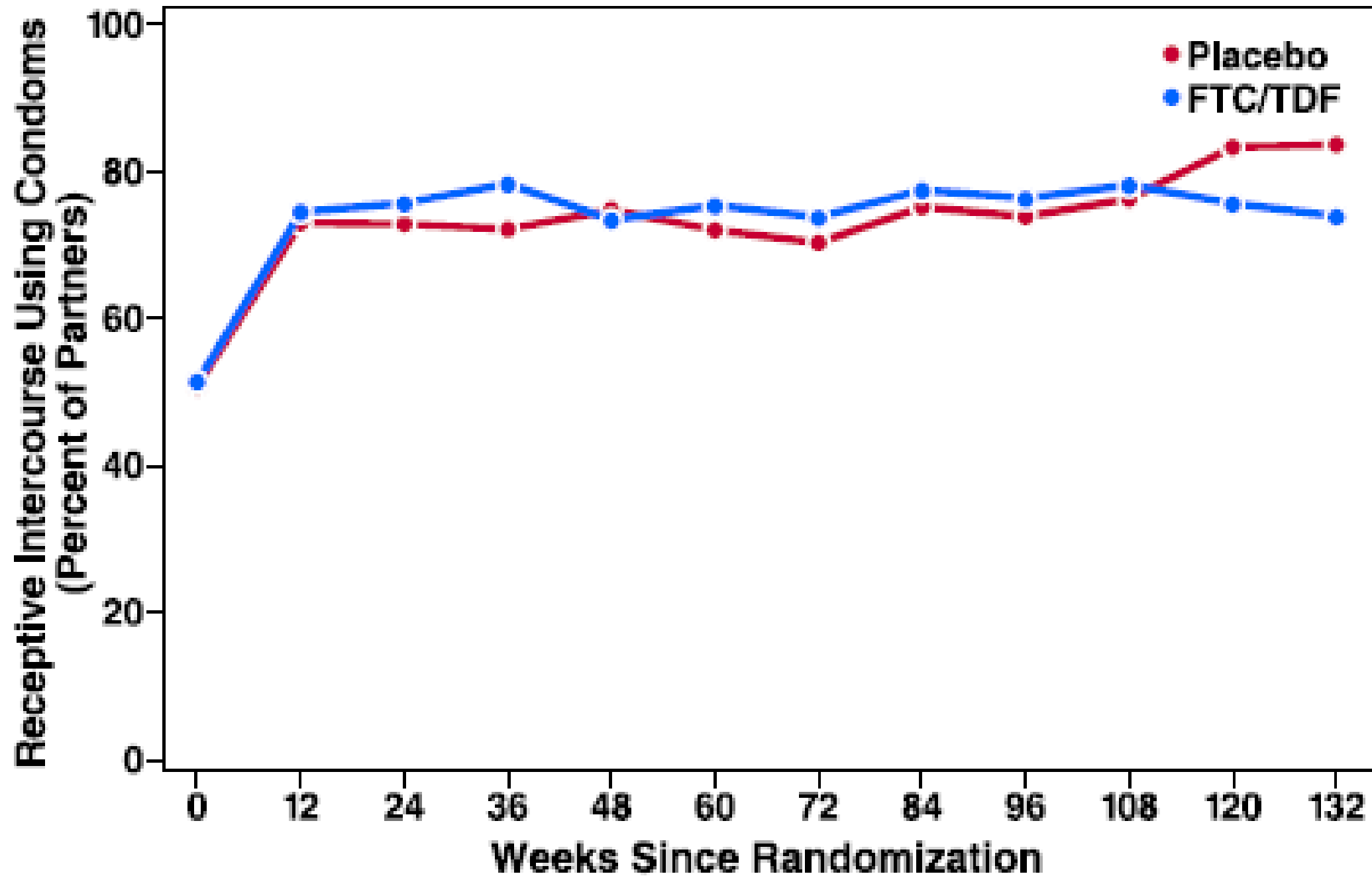


# Unprotected Receptive Anal Intercourse

Those who believed they were taking FTC/TDF



# Condom Use



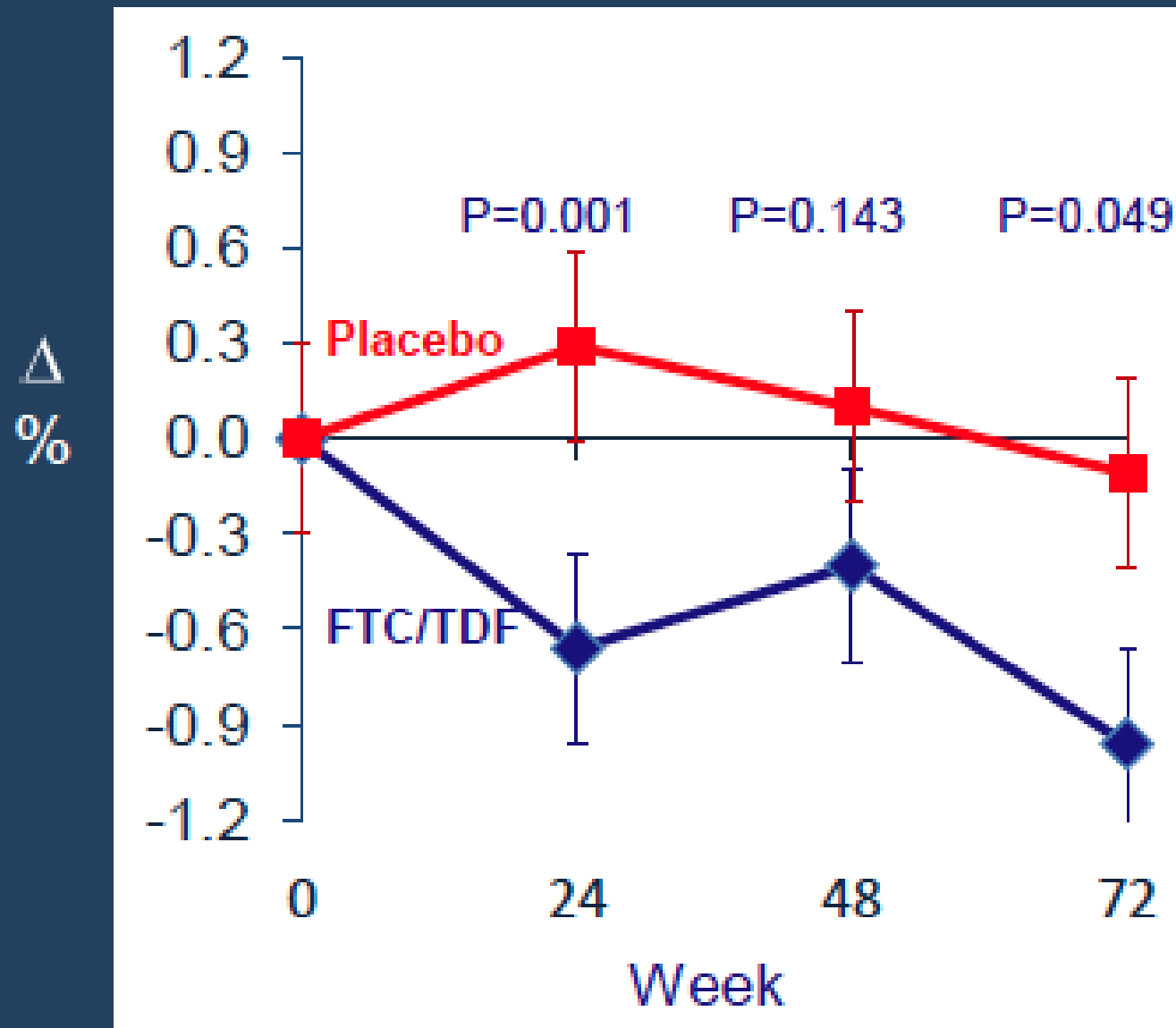
# Acute HIV Infections

	Tests with RNA	Ab-,RNA+	Prevalence	Fold Change (95% CI)
Enrollment	2,499	10	0.4%	Ref
Follow-up: Placebo	11,322	12	0.1%	-3.8 (-1.5 to -9.5)
Follow-up: FTC/TDF	11,407	7	0.06%	-6.5 (-2.2 to -20.2)

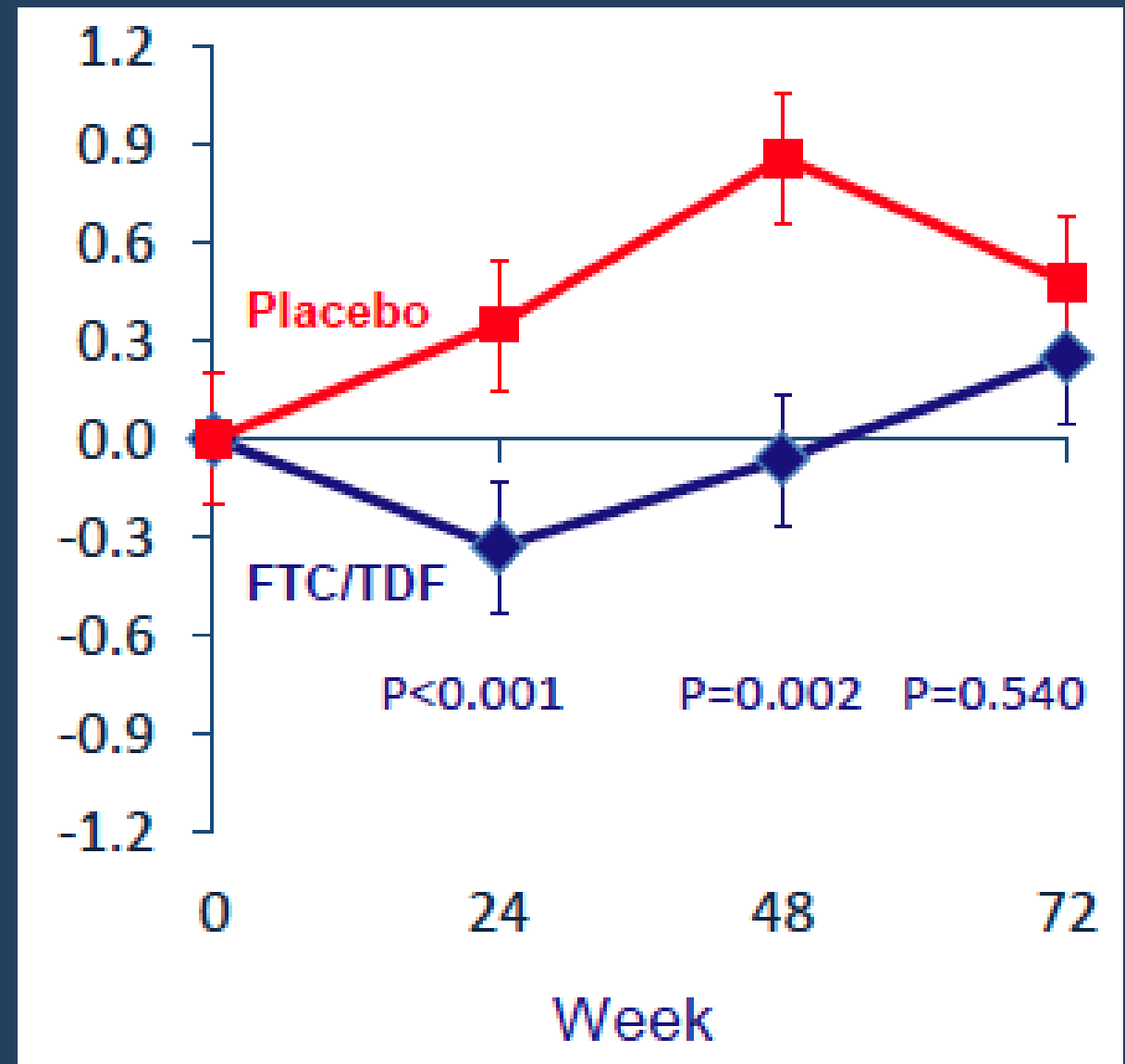
p=0.004 for Placebo  
p=0.002 for FTC/TDF

# PERCENT CHANGES FROM BASELINE IN BMD BY RANDOMIZATION GROUP

## SPINE (L1-L4)



## TOTAL HIP



Placebo	247	199	124	59
FTC/TDF	256	203	124	59

Placebo	247	199	124	59
FTC/TDF	256	202	125	59

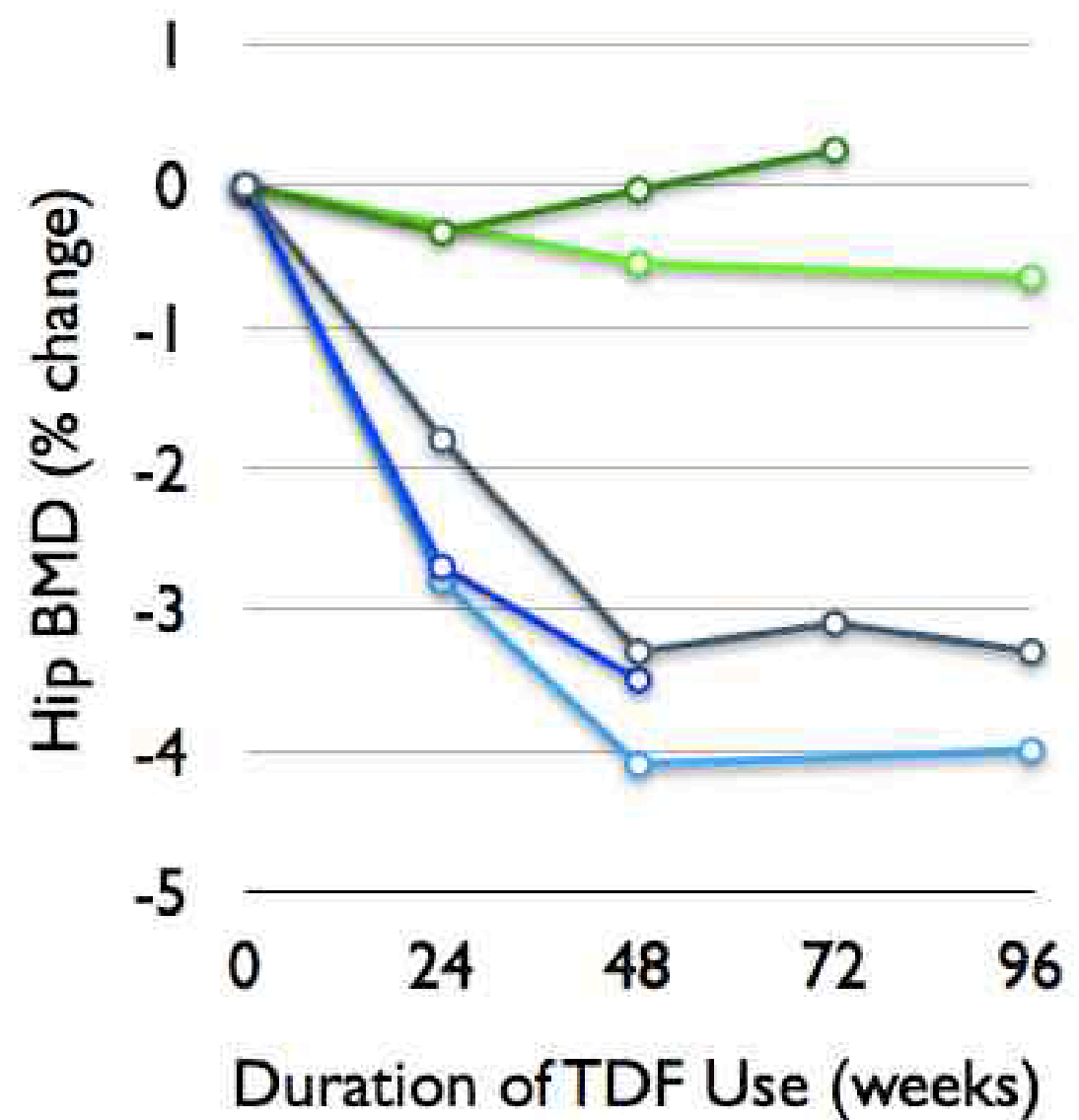
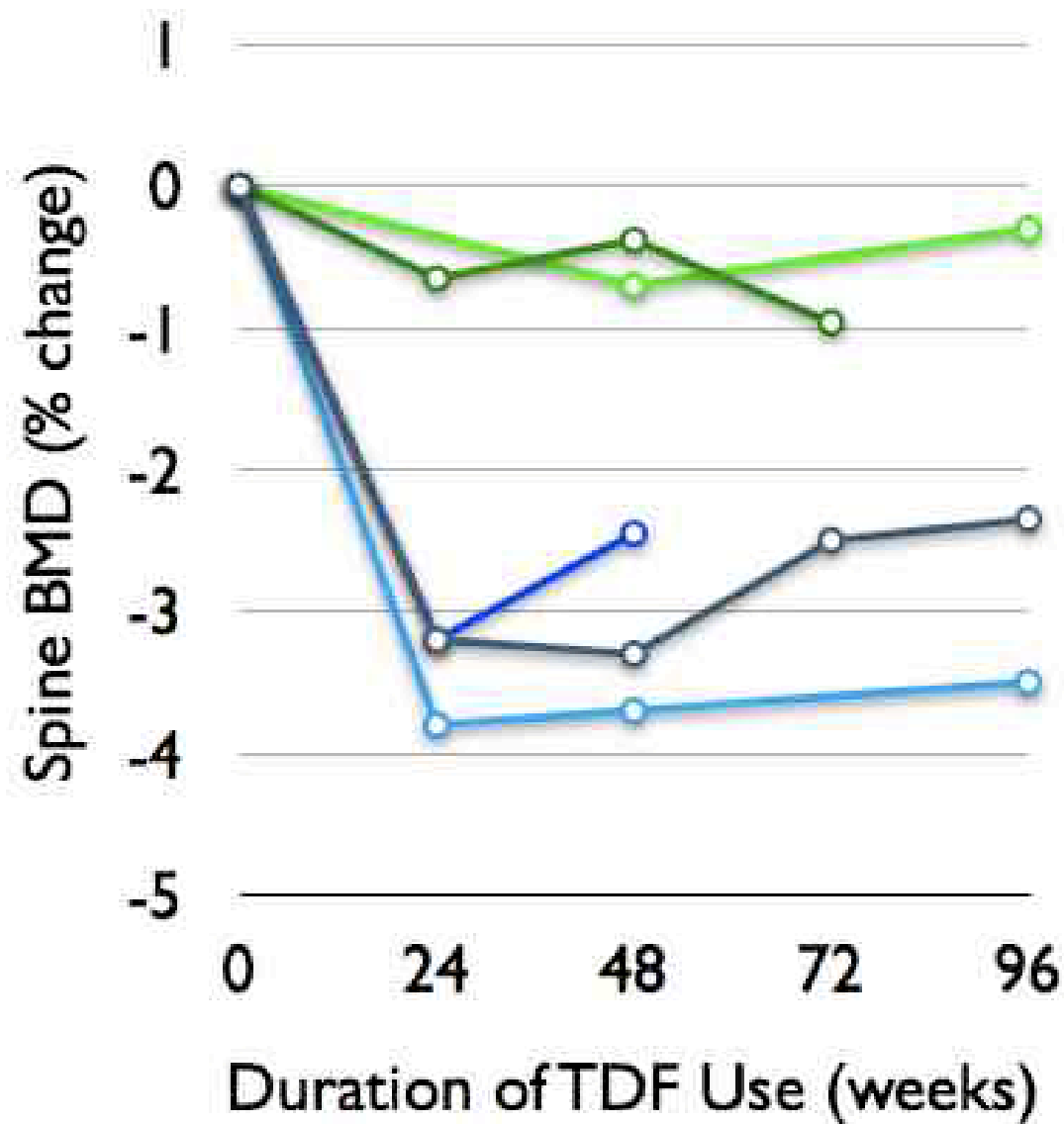
Mean, SE and P-values by linear mixed model

# NO DIFFERENCE IN FRACTURE RATES IN iPrEx (data for entire study)

	<b>FTC/TDF (N=1251)</b>	<b>Placebo (N=1248)</b>	<b>P-value</b>
Number of participants (%)	15 (1.2%)	11 (0.8%)	0.41
Number of events	16	12	

*P-value by log-rank test; Grant NEJM 2010*

# Change in Bone Mineral Density During TDF-Based Treatment and PrEP



- GS903
- Assert
- A5224s
- iPrEx
- CDC PREPare





Gladstone Institute  
of Virology and  
Immunology

Robert Grant  
Vanessa McMahan  
Pedro Goicochea  
K Rivet Amico

Patricia Defechereux  
Robert Hance  
Jeanny Lee  
Jeff McConnell



David Glidden  
Furong Wang  
Kathy Mulligan



Juan Guanira  
Maria Esther Ramirez  
Carmela Ganoza



Javier Lama  
Lorena Vargas



Suwat Chariyalertsak



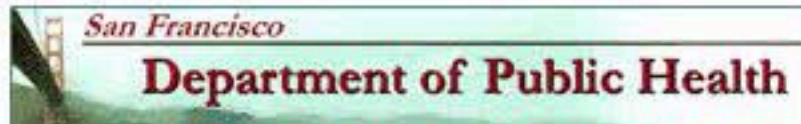
Ken Mayer



Orlando Montoya  
Telmo Fernández



Martin Casapia



Susan Buchbinder     Albert Liu



Esper Kallás



Mauro Schechter



Valdilea Veloso

Desmond Tutu HIV Foundation  
Masibambane Ngezandla



Linda-Gail Bekker



Peter Anderson  
Lane Bushman



Brian Postle



Howard Jaffe     Jim Rooney

BILL & MELINDA  
GATES foundation

Stephen Becker



National Institute  
of Allergy and  
Infectious Diseases

David Burns

Grace Chow  
Ana Martinez



The iPrEX Study: Safety, Efficacy, Behavior, and Biology