

# Pros and Cons of on demand PrEP

## « Pros »



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## Disclosures

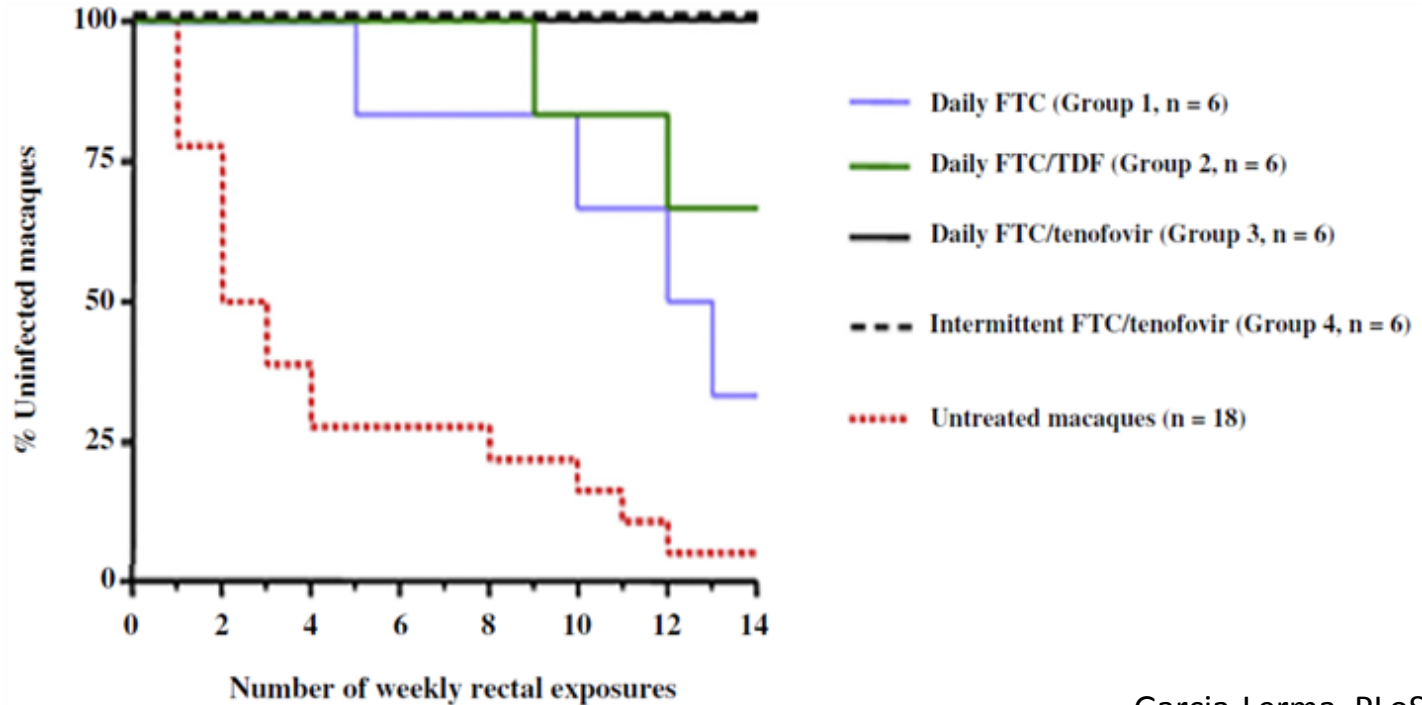
Consulting fees : Mylan, Gilead

Fees for non-CME/CE services : BMS, Gilead, Janssen, MSD

Contracted research : MSD, ViiV Healthcare

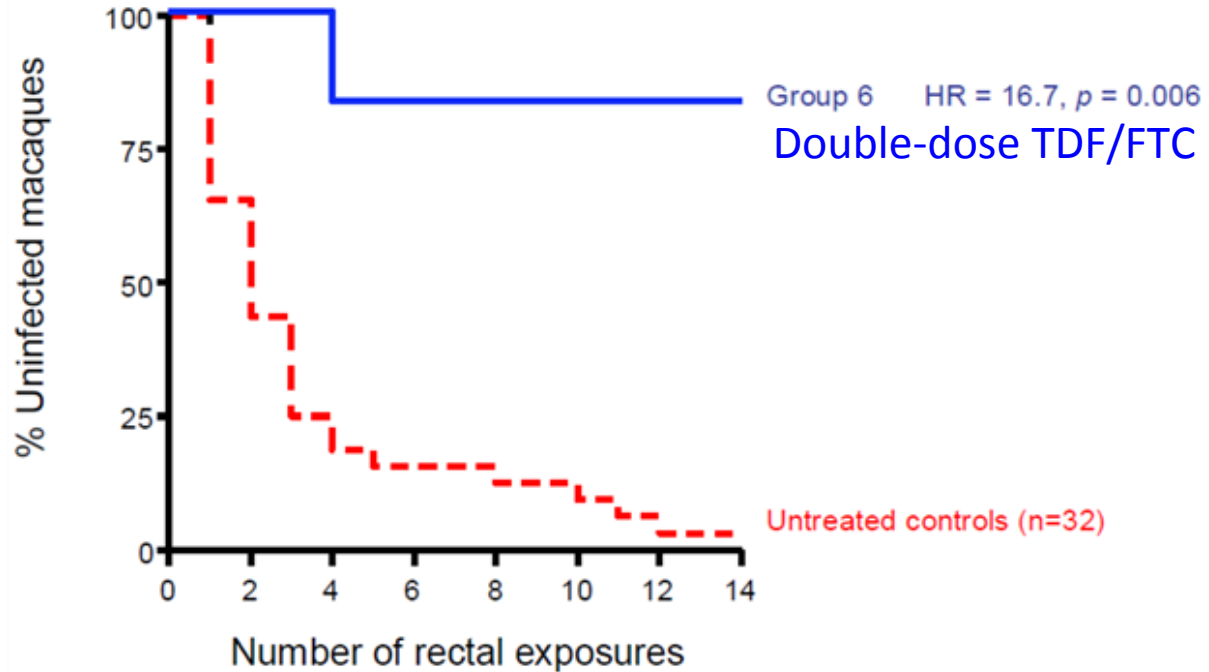
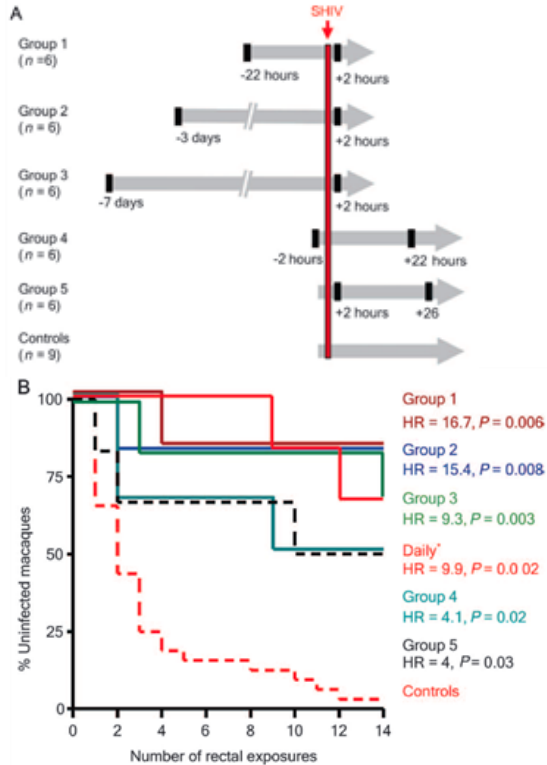


# Prevention of Rectal SHIV Transmission in Macaques by Daily or Intermittent Prophylaxis with Emtricitabine and Tenofovir

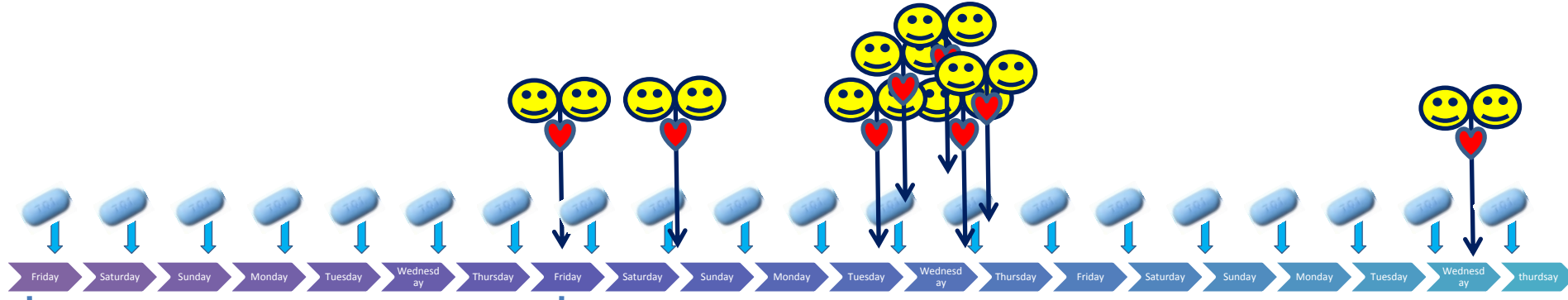




# Intermittent Prophylaxis with Oral Truvada Protects Macaques from Rectal SHIV Infection

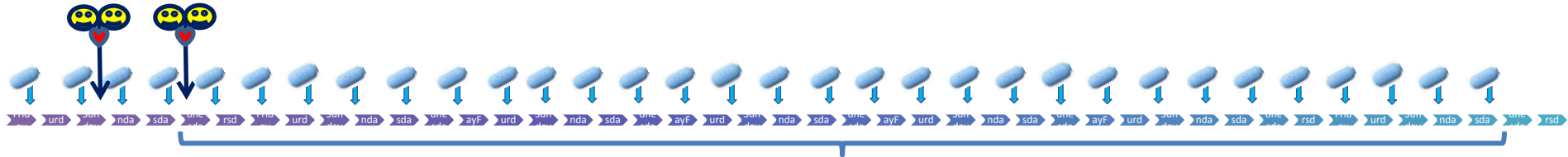


# Continuous PrEP



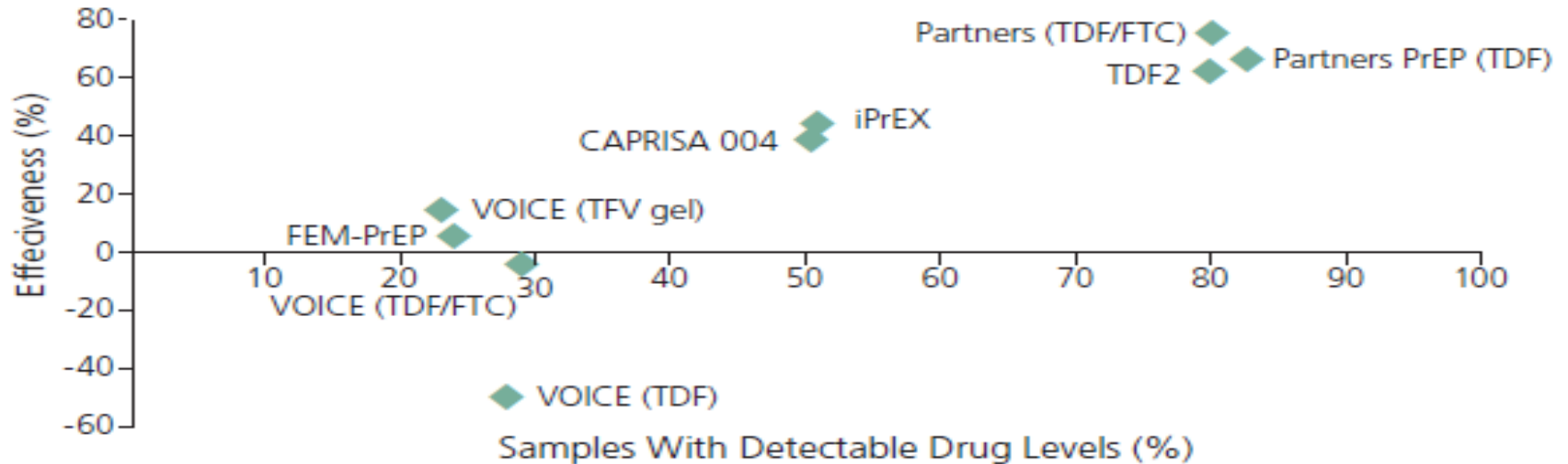
> 7 days to start (♂)...  
... 21 days for ♀ !

1 pill every day whatever your sexual life is...

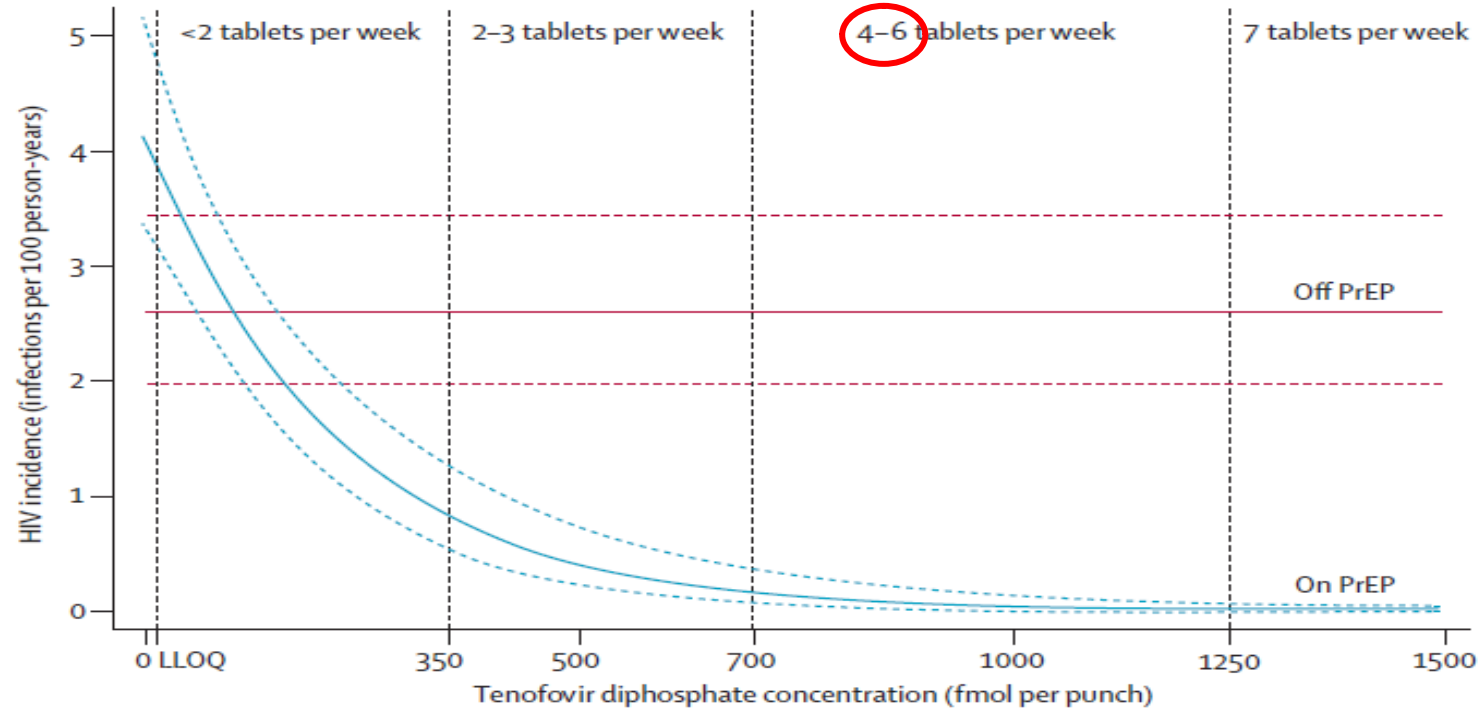


28 days to finish...

# PrEP effectiveness and adherence

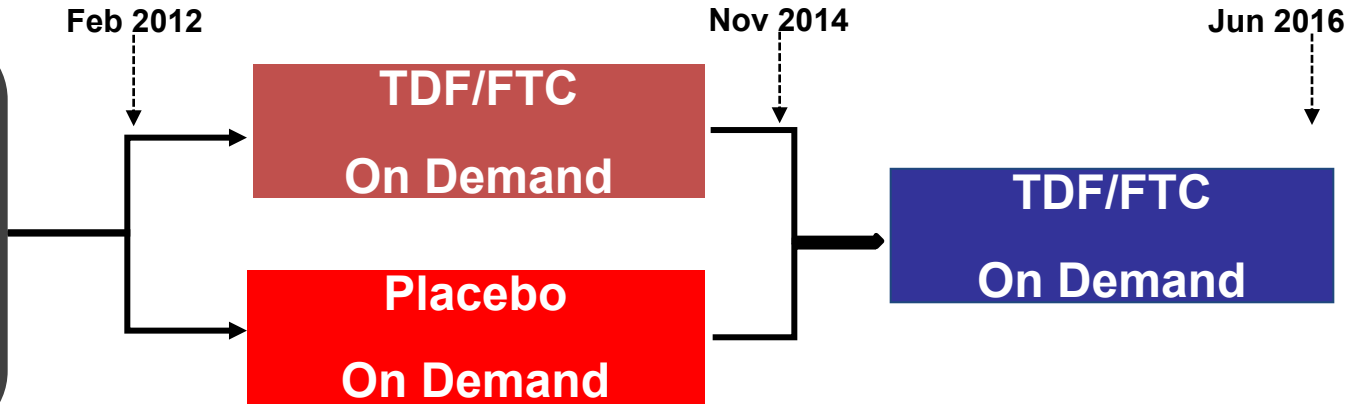


# TDF concentration and HIV incidence : IPrEx OLE



## On-Demand Preexposure Prophylaxis in Men at High Risk for HIV-1 Infection

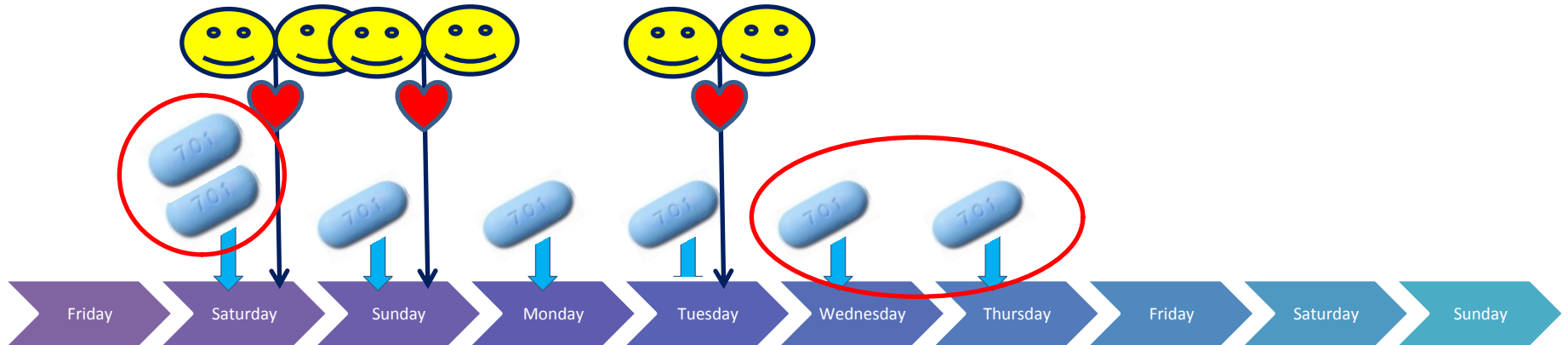
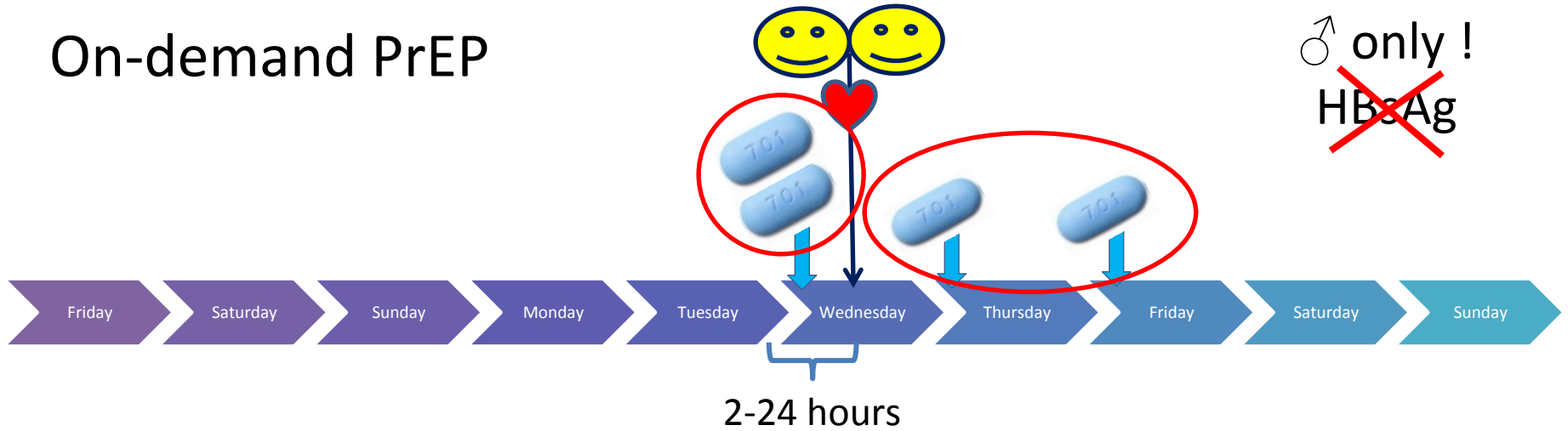
- HIV-negative MSM
- Condomless anal sex with  $\geq 2$  partners in prior 6 months
- Creat. Clearance  $> 60$  mL/mn
- HbS Ag negative

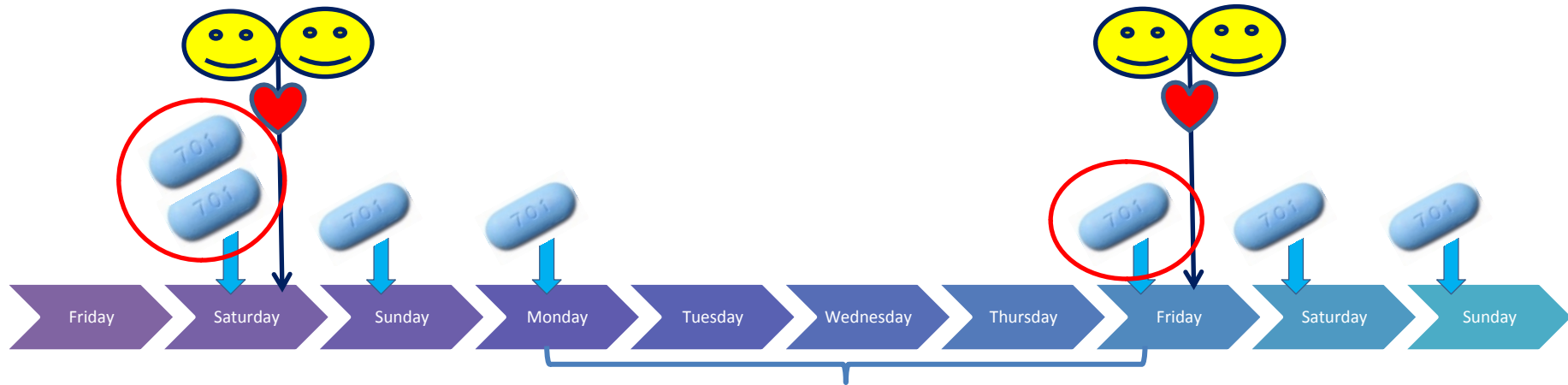




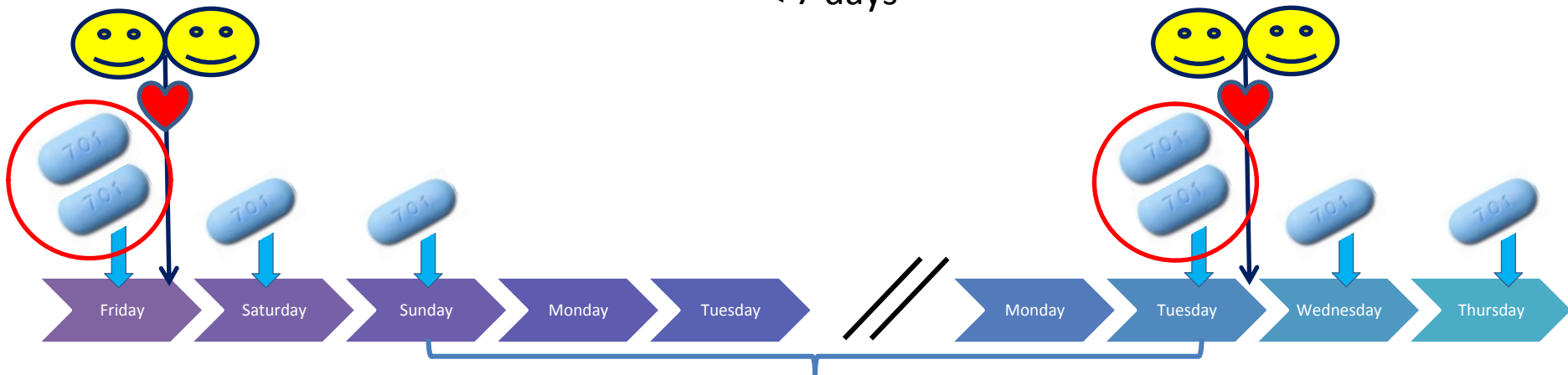
# On-demand PrEP

♂ only!  
~~HBsAg~~





< 7 days

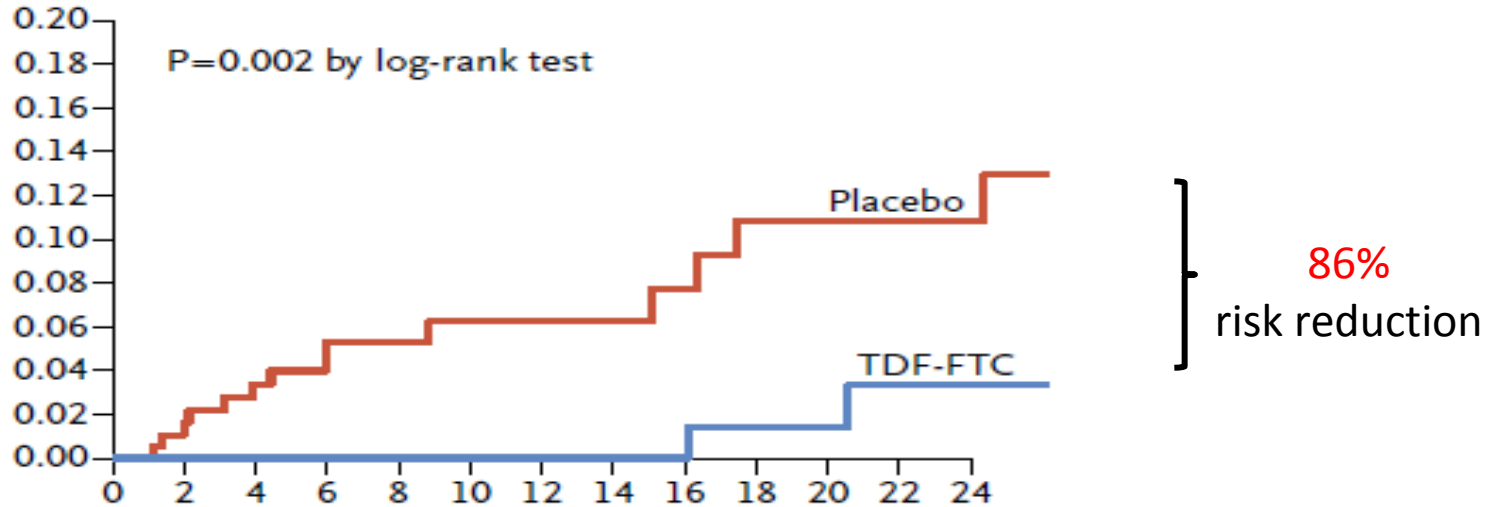


≥ 7 days

# Baseline Characteristics

Characteristics (Median, IQR) or (n, %)	TDF/FTC n = 199	Placebo n = 201
Male	199 (100%)	201 (100%)
Age (years)	35 (29-43)	34 (29-42)
White	188 (94)	178 (89)
Post-secondary education	146 (73)	149 (74)
Not in couple	144 (72)	149 (74)
History of PEP use	56 (28)	73 (37)
>5 alcohol drinks / day	49 (25)	42 (21)
Use of psychoactive drugs*	<u>85 (43)</u>	<u>92 (46)</u>
Circumcised	38 (19)	41 (20)
STI at screening (NG, CT, TP) **	49 (25)	62 (31)
Nb sexual acts in prior 4 weeks	<u>10 (6-18)</u>	<u>10 (5-15)</u>
Nb sexual partners in prior 2 months	<u>8 (5-17)</u>	<u>8 (5-16)</u>

# Effectiveness of on-demand PrEP



- 2 HIV-1 infections in the TDF/FTC arm @ M16 and M20
  - Both subjects were non adherent (60/60 and 58/60 pills return at time of infection)
  - No drug detected in plasma (TDF < 0.1 ng/ml and FTC < 0.4 ng/ml)
  - No drug resistance mutation detected

# Adverse Events / lab. abnormalities

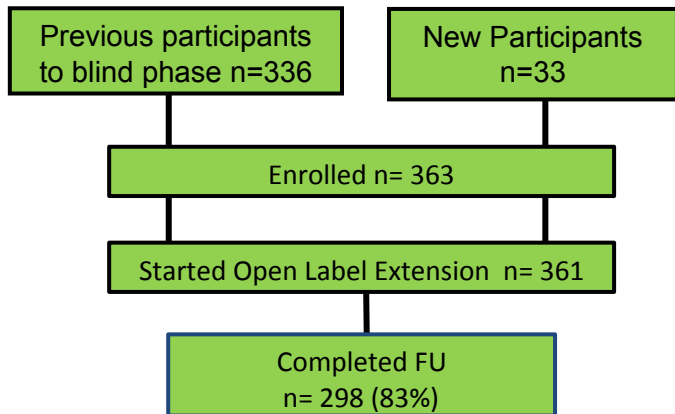
Adverse effects	TDF/FTC n=199	Placebo n=201	P value
Any AE	186 (93%)	181 (90%)	0.21
Any Serious AE	20 (10%)	17 (8%)	0.58
Any Grade 3 or 4 AE	19 (10%)	15 (7%)	0.45
Treatment D/C due to AE	1* (1%)	0	
GI AEs	28 (14%)	10 (5%)	0.002
Grade 1 Creatinine	35 (18%)**	20 (10%)	0.03
Proteinuria ≥ 2+	11 (6%)	9 (4%)	0.63
Glycosuria ≥ 2+	1 (1%)	0	0.5
All Grades ALAT	33 (17%)	26 (13%)	0.30
Grade 3 or 4 ALAT	1 (1%)	4 (4%***)	0.36

\* deep venous thrombosis with suspected DDI with dabigatran

\*\* 2 Participants in the TDF/FTC arm had a transient creatinine clearance < 60 ml/mn

\*\*\* Acute HCV infection in 3 and syphilis in one

# Open Label Extension phase



**97%** relative reduction vs. placebo

Treatment	Follow-Up Pts-years	HIV Incidence / 100 PY (95% CI)
Placebo	212	6.60 (3.60-11.1)
TDF/FTC (double-blind)	219	0.91 (0.11-3.30)
TDF/FTC (open-label)	515	0.19 (0.01-1.08)

# Adherence

Face to face interviews : « Have you used PrEP since last visit »

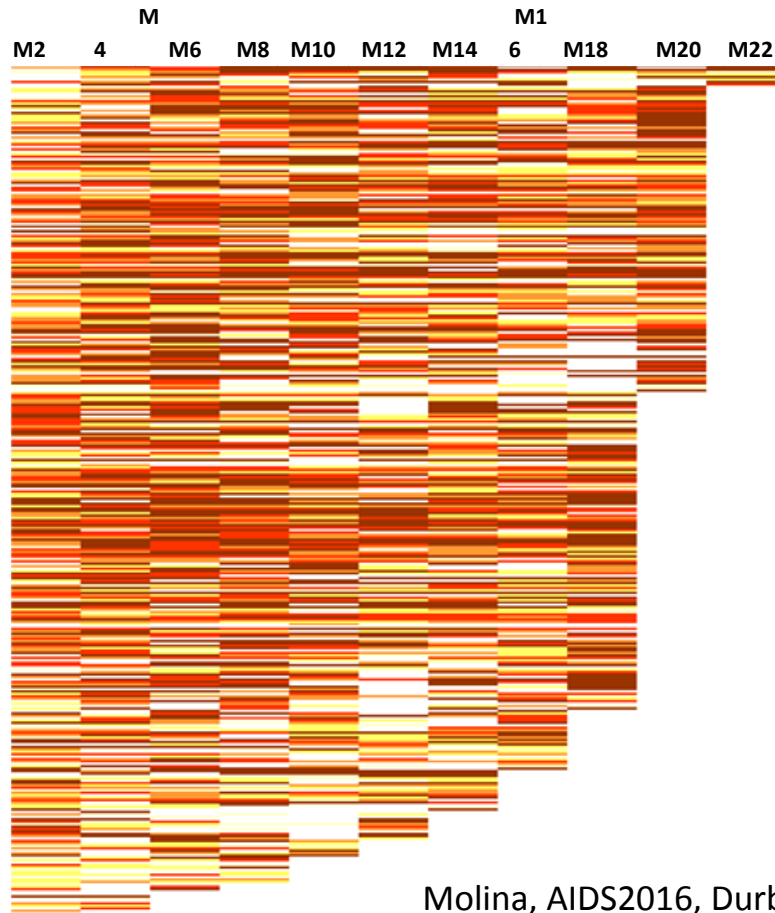
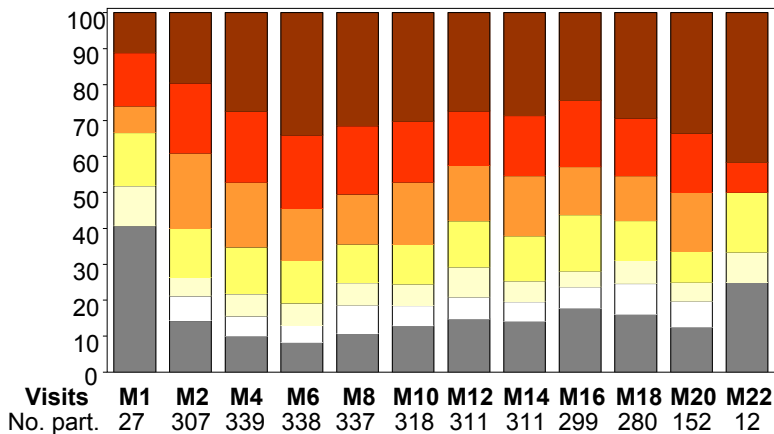
- For each sexual intercourse: 76%
- Often: 11%
- From time to time: 4%
- No: 9%

Questionnaires : PrEP use at the last sexual intercourse

% PrEP (min-max)	Double-Blinded % (min-max)	Open-Label % (min-max)	P-Value
Correct*	42 (35-51)	50 (46-53)	0.007
Sub-Optimal	29 (20-38)	24 (16-31)	
No PrEP	29 (22-39)	26 (21-35)	

\*At least one pill before and one pill after

# Pattern of pill use (OLE phase)

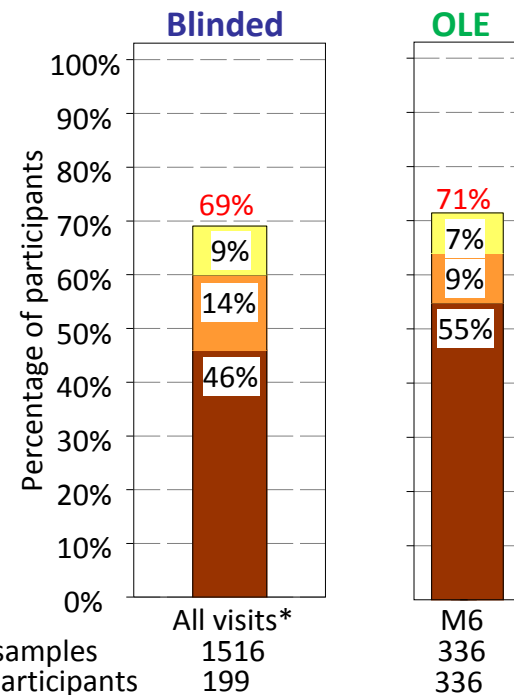
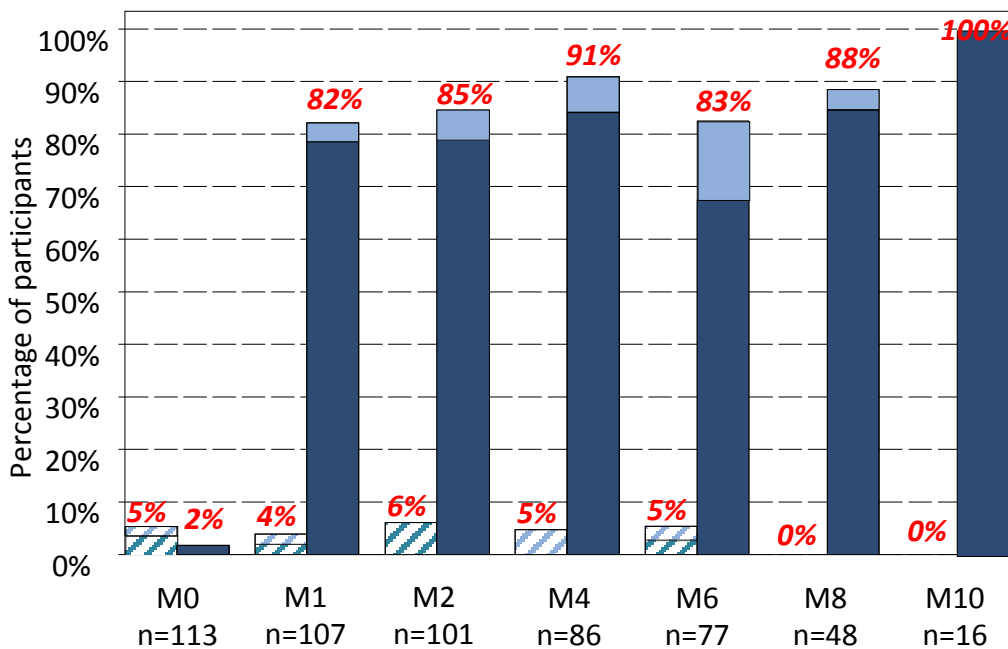




4.00	0 or missing
	]1 - 4]
	]4 - 11]
	]11 - 18]
	]18 - 25]
	]25 - 30]



Median Nb pills/month:  
18 (IQR: 11-25)

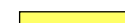




# Detection of TFV in Plasma



Placebo  
 Quantifiable  
 Detectable

TDF/FTC  
 Quantifiable  
 Detectable

 ]1-10] ng/mL  
 ]10-40] ng/mL  
 > 40 ng/mL

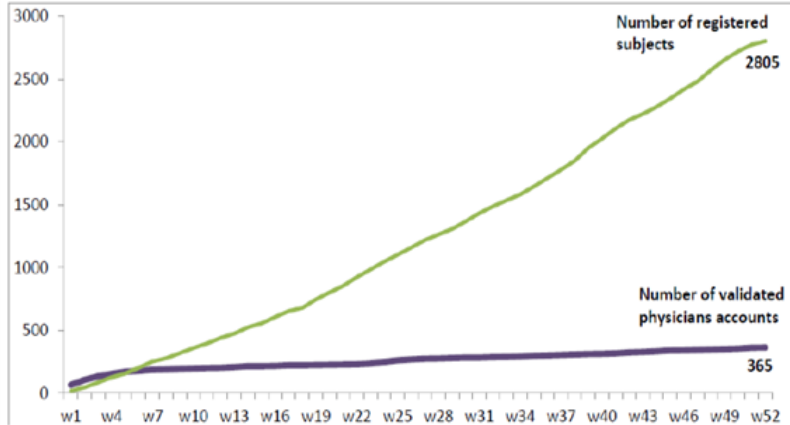
# Ipergay economic results

n= 199 participants on TDF/FTC (mean)	Average utilization	Cost per participant (€)
Counseling & pre PrEP workup	1	748
On demand TDF-FTC (tablets per month)	15.62	3,129
HIV ELISA tests	8.6	126
HIV Plasma viral loads	0.3	16
Consultations (protocol-driven)	8.2	205
Serum creatinine & ALAT (protocol driven)	16	31
Total cost of STIs (mostly chlamydia)		793
Total per participant		4,812

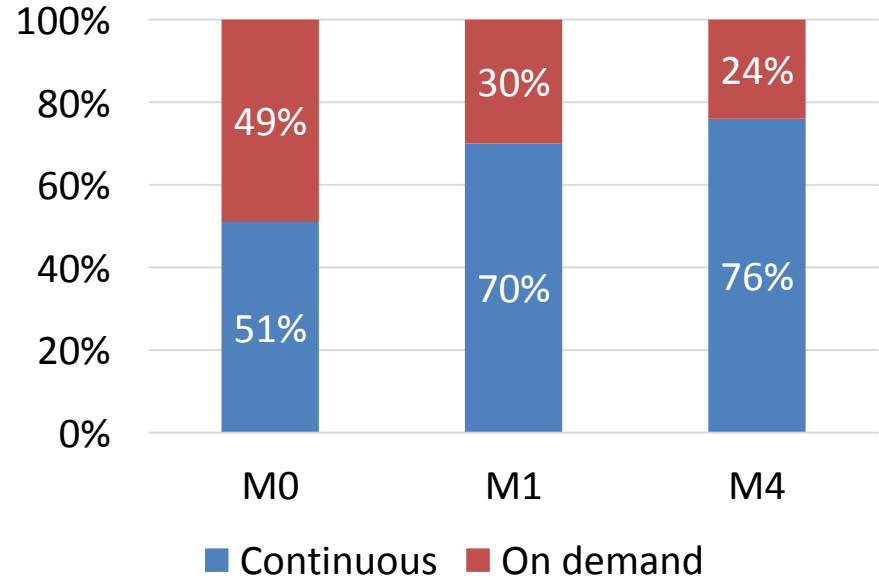
\* TDF/FTC : 65% of costs (**77%** if STI costs excluded; 87% for continuous PrEP)

# French temporary market authorization for TDF/FTC PrEP

Figure 2: Number of validated physician's accounts and registered subjects by week



- 2805 patients / 2016
- 97.9% ♂, 0.3% transgender ♀
- Continuous 41.4%
- **On demand 58.1%**



Evolution of PrEP regimen (n=132)



## More On-Demand PrEP results in Paris in July !



On-Demand PrEP with TDF/FTC remains highly effective among MSM with infrequent sexual intercourse: A sub-study of the ANRS IPERGAY trial



One-year experience with Pre-Exposure Prophylaxis (PrEP) Implementation in France with TDF/FTC

# Continuous vs on demand PrEP

	Continuous PrEP	On demand PrEP
RCT efficacy	✓	✓
Real life efficacy	✓	✓
Patients	♂ and ♀	♂ only, no HBsAg
Clinical safety	✓	✓
Kidney safety	✓	✓
BMD safety	✓	ND
Resistance	✓	✓
Adherence	✓	✓
Cost reduction	-	9-15 % ? *
% concerned	-	25-40 % ?
Individualized treatment	✗	✓ ✓ ✓

\* 11-17 % if STIs cost excluded



# Acknowledgments



- The Participants
- The Study Staff and Peer-Counselors
- The Trial Scientific Committee
- The DSMB
- The Community Advisory Board
- The ANRS Staff
- INSERM SC10-US19



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BILL & MELINDA  
GATES foundation

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PIERRE BERGÉ



GILEAD