Changes in Kidney Function Among MSM Initiating On-Demand TDF/FTC for HIV Pre-Exposure Prophylaxis G. Liegeon¹, G. Antoni², G. Pialoux³, L. Cotte⁴, C. Tremblay⁵, C. Capitant², E. Cua⁶, F. Raffi⁷, E. Senneville⁸, P. Charbonneau¹, S. Le Mestre⁹, V. Doré⁹, L. Meyer², JM. Molina¹ for the ANRS IPERGAY Study Group ipergay ANRS

Characteristics at baseline

Age ≤40 years (n=247)

Age >40 years (n=142)

Hypertension (n=15)

n= number of patients

No Hypertension (n=374)

 $eGFR > 90ml/min/1.73m^{2}(n=333)$ 633

 $eGFR \le 90 ml/min/1.73 m^2 (n=56) 104$

PARIS DIDEROT

¹Hôpital Saint-Louis, Paris, France ¹NSERM, Villejuif, France ³Hôpital Tenon, Paris, France ¹CHU de Lyon, Lyon, France ¹CHU de Nontréal, QC, Canada ⁶CHU de Nice, Nice, France ¹CHU de Nantes, Nantes, France ¹CHU de Nontréal, QC, Canada ⁶CHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ⁶CHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ఄGHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ఄGHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ゥCHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ゥCHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ゥCHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France ゥCHU de Nontréal, QC, Canada ゥCHU de Nice, Nice, France ゥCHU de Nantes, Nantes, France

⁸Centre hospitalier Gustave Dron, Tourcoing, France ⁹Agence Recherche Nord&Sud Sida-HIV Hépatites, Paris, France

Abstract 0960



Introduction

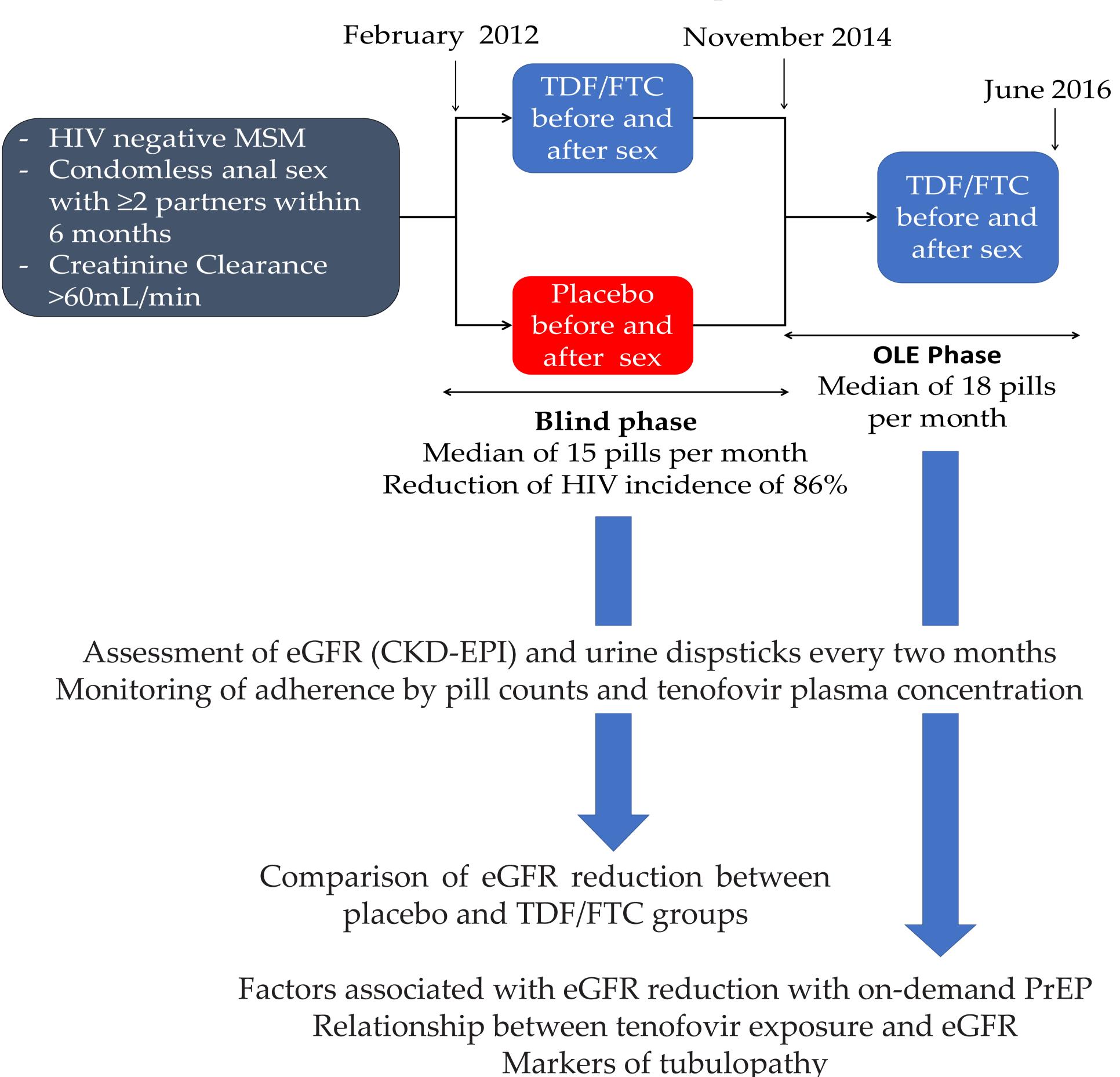
Instituts I Inserm
SC10
Institut national de la santé et de la recherche médicale

Daily pre-exposure prophylaxis (PrEP) with tenofovir disoproxil fumarate and emtricitabine (TDF/FTC) is associated with a small but statistically significant decrease in estimated glomerular filtration rate^{1,2} (eGFR).

We assessed the renal safety of on-demand TDF/FTC based PrEP in HIV uninfected men.

Material and Methods

The ANRS-Ipergay Study: A Double-Blinded Randomized Placebo Controlled Trial of On-demand TDF/FTC Based PrEP with Open-Label Extension Phase^{3,4}



Results

Table 1. Characteristics of participants included in the study.

	Bli	All						
Characteristics at baseline	TDF/FTC (N=199)	Placebo (N=201)	<i>P</i> value	participants on TDF/FTC ^a (N=389)				
Median age - year (IQR)	35 (29-43)	34 (28-42)	0.56	35 (29-43)				
White race - no (%)	188 (95)	178 (89)	0.04	356 (92)				
Use of recreational drugs ^b - no. (%)	86 (44)	92 (48)	0.51	160 (43)				
Medical history								
Diabetes - no (%)	1 (0.5)	2 (1)	1	3 (1)				
Hypertension - no (%)	8 (4)	6 (3)	0.58	15 (4)				
Dyslipidemia - no (%)	0 (0)	4 (2)	0.13	2 (1)				
Use of NSAID - no (%)	7 (3.5)	4 (2)	0.35	19 (5)				
Weight (kg) - median (IQR)	71 (65-80)	72 (65-80)	0.56	72 (66-80)				
$eGFR^{c}$ (mL/minute/1.73m ²) - median (IQR)	106 (97-115)	108 (96-115)	0.44	106 (97-115)				
eGFR >90mL/min/1.73m ² - no (%)	173 (87%)	169 (84%)	0.42	333 (86%)				
eGFR < 90mL/min/1.73m ² - no (%)	26 (13%)	32 (16%)		56 (14%)				

a All the patients who initiated TDF/FTC: 199 participants from the TDF/FTC arm, 161 from the placebo arm and 29 new participants including in the OLE phase. b Recreational drugs that were reported in the past 12 months included ecstasy, crack cocaine, cocaine, crystal. speed, and γ -hydroxybutyric acid or γ -butyrolactone. c Estimated glomerular filtration rate calculated by the Chronic Kidney Disease Epidemiology Collaboration equation. IQR interquartile range; TDF tenofovir disoproxil fumarate; FTC emtricitabine; NSAID non-steroidal

relationship between higher tenofovir exposure and lower eGFR.

Slope difference in eGFR per year

 $(mL/min/1.73m^2)(\pm SE)$

 $0.56 (\pm 0.39)$

1.29 (±0.99)

Multivariate P

 $0.46 (\pm 0.59) \quad 0.44$

 $0.49 (\pm 0.41) \quad 0.24$

 $1.25 (\pm 1.00)$ 0.22

The slope of eGFR decline was not statistically different between TDF/FTC and placebo group. Significant reductions of eGFR were

There was a dose-response

reversible (of the 45 participants with eGFR <70mL/min/1.73m², 22 participants had just one episode).

Table 4. Relationship between recent TDF/FTC exposure and eGFR in all participants initiating TDF/FTC in the study.

		Estimation of the effect on eGFR (ml/min/1.73m²) (±SE)								
	PY	Univariate modela	P	Adjusted analysis ^b	P					
Number of pills per month in the last two months ^c										
15 pills (n=1941)	255	Reference								
15 pills (n=2279)	370	- 1.38 (±0.30)	< 0.001	- 0.88 (±0.30)	< 0.01					
enofovir plasma concentration at the time of eGFR assessment ^c										
2 ng/mL (n=1714)	231	Reference								
$-2 \text{ to } \le 10 \text{ ng/mL (n=327)}$	50	- 1.27 (±0.50)		- 0.98 (±0.49)						
$10 \text{ to } \le 40 \text{ ng/mL (n=512)}$	80	- 1.42 (±0.42)		- 1.28 (±0.42)						
· 40 ng/mL (n=2231)	351	- 2.06 (±0.30)	<0.001 ^d	- 1.82 (±0.30)	<0.001 ^d					
	1 1 1 1		10 1		1.70					

a For univariate analysis, we used a linear mixed effects model. b linear mixed model adjusted on time, age > 40 years, hypertension and baseline eGFR <90mL/min/1.73m². c Time-dependant variables. d Global *P* value. n = number of visit; SE standard error; PY persons years; eGFR estimated glomerular filtration rate.

Table 2. Reduction of eGFR and severe adverse events during the study.

	Bli	All		
	TDF/FTC (n=201)	Placebo (n=199)	<i>P</i> value	participants on TDF/FTC (N=389)
Median of follow-up - months (IQR)	9.4 (5.1-20.6)	9.4 (5.1-20.6)		19.2 (18-26.9)
Mean slope of eGFR decline per year ^a (mL/min/1.73m ²)	- 1.53	- 0.88	0.27	- 1.20
At least one eGFR <70mL/min/1,73m ² - n	20	9	0.04^{b}	45
At least one eGFR <60mL/min/1,73m ² - n	4	3	0.74^{b}	14
Treatment discontinuation for kidney adverse event - n (%)	0	0		3° (1%)

a The slope of eGFR decline was modelized using a linear mixed effects model. b Log-rank test. c Two participants had grade 1 kidney adverse events (with a decline in eGFR to 58 mL/min/1.73m² and 49 mL/min/1.73m²) and one participant had grade 2 (with a decline to 39 $mL/min/1.73m^{2}$).

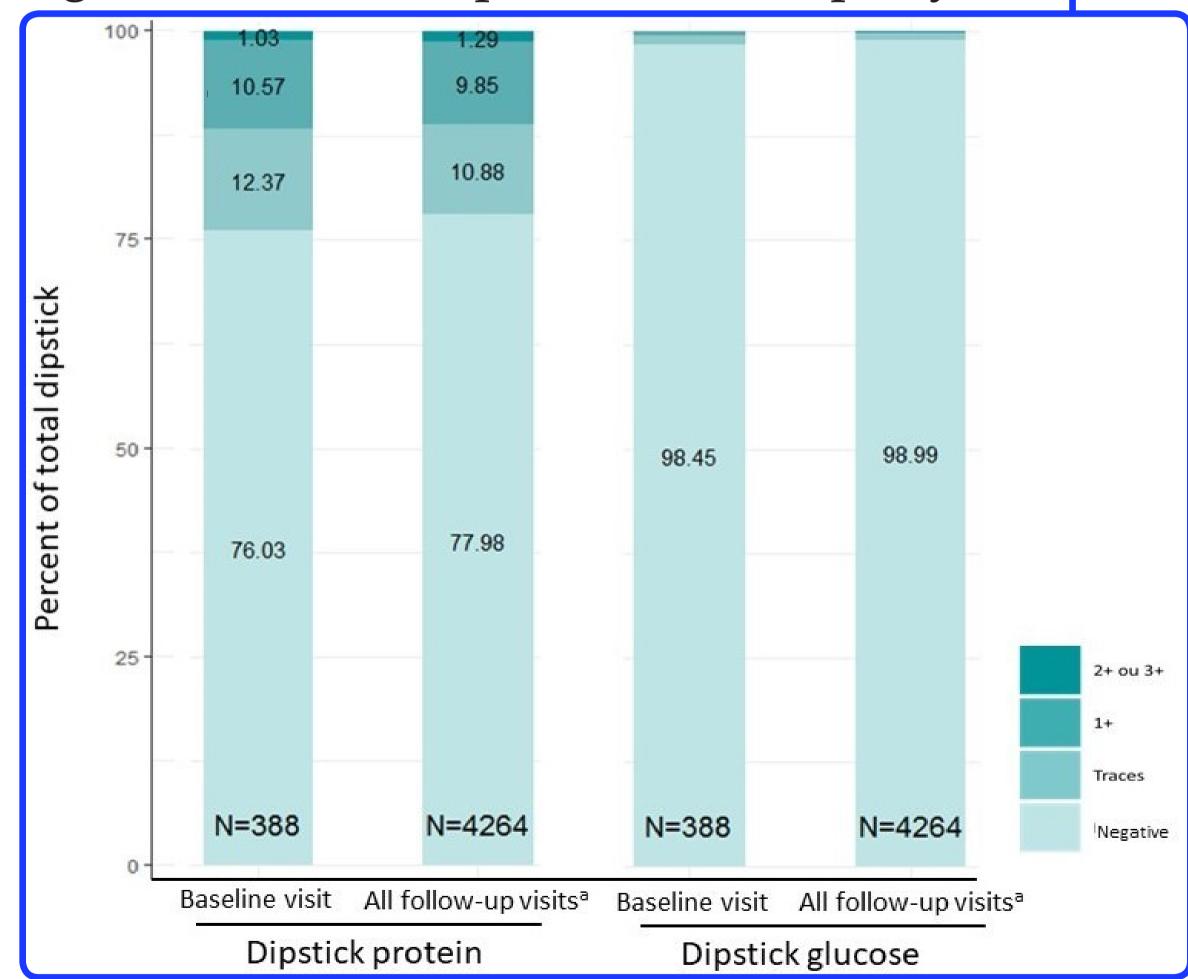
Table 3. Reduction of eGFR among participants at-risk of renal dysfunction in the study.

FR at baseline

a For univariate and multivariate analysis, we used a linear mixed effects model. SE standard error; PY persons years; eGFR estimated glomerular filtration rate;

108

Figure 1. Markers of proximal tubulopathy.



a median of follow-up of 19.2 months (IQR 18.0 to 26.9). N= number of dipsticks urine. Proportion of study visits with protein and glucose in urine dipsticks at baseline and during the

follow-up (median of 19.2 months) in all participants initiating TDF/FTC.

The slope of eGFR reduction was not significantly greater in participants with age >40 years, eGFR<90m/min/1.73m² or hypertension.

Absence of markers of tubulopathy on urine dipsticks

Conclusion

The renal safety of on-demand TDF/FTC based PrEP was good, including in participants with eGFR<90mL/ min/1.73m², age >40 years or hypertension. There was a dose reponse relationship between tenofovir exposure and lower eGFR.

The overall reduction and intermittent exposure to TDF/FTC may explain the good renal safety of on-demand PrEP.

Acknowledgments

This trial was funded by the French National Agency for Research on AIDS and Viral Hepatitis (ANRS), the CTN (Canadian Trial Network), the "Fonds Pierre Bergé pour la prevention", the SIDACTION and the Bill and Melinda Gates Foundation. It was conducted with the support of Gilead Sciences (donation TDF-FTC). The funders had no role in study design, data collection, analysis and publication.

Solomon and al. AIDS. 2014.

?] Mugwanya and al. JAMA Intern Med. 2015. [3] Molina J-M and al. N Engl J Med. 2015.

[4] Molina J-M and al. Lancet HIV. 2017.

Geoffroy LIEGEON Department of Infectious Diseases APHP - Saint Louis Hospital 1 avenue Claude Vellefaux, 75010 PARIS FRANCE Mail: geoffroy.liegeon@phpt.org