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Introduction

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}



Changes in Kidney Function Among MSM Initiating On-Demand TDF/FTC for HIV Pre-Exposure Prophylaxis

Results

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Table 1. Characteristics of participants included in the study.

Blind phase Placebo TDF/FTC Characteristics at baseline (N=201) value (N=199) Median age - year (IQR) 34 (28-42) 0.56 35 (29-43) White race - no (%) 178 (89) 188 (95) Use of recreational drugs^b - no. (%) 86 (44) 92 (48) Medical history 2 (1) Diabetes - no (%) 1(0.5)6 (3) 0.58 Hypertension - no (%) 8 (4) Dyslipidemia - no (%) 0(0)Use of NSAID - no (%) 7 (3.5) 4 (2) 71 (65-80) 72 (65-80) 0.56 Weight (kg) - median (IQR) eGFR^c (mL/minute/1.73m²) - median (IQR) 106 (97-115) 108 (96-115) 0.44 106 (97-115) eGFR >90mL/min/1.73m² - no (%) 173 (87%) 169 (84%) 0.42 333 (86%) $eGFR < 90 mL/min/1.73 m^2 - no$ (%) 26 (13%) 32 (16%)

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 v-hvdroxybutyric acid or v-butyrolactone. c Estimated glomerular filtration rate calculated by the Chronic Kidney Disease Epidemiology Collaboration equation. IQR interguartile range; TDF tenofovir disoproxil fumarate; FTC emtricitabine; NSAID non-steroidal anti-inflammatory drugs

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

	Bli	All		
	TDF/FTC (n=201)	Placebo (n=199)	P 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/1.73m²)	- 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 ^c (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.

	Slope difference in eGFR per year (mL/min/1.73m²)(±SE)					
Characteristics at baseline	PY	eGFR at baseline	Univariate	Р	Multivariate	Р
		$(mL/min/1,73m^2)$	model ^a	value	model ^a	value
$eGFR > 90ml/min/1.73m^{2}(n=333)$	633	108	0 66 (±0 57)	0.25	0.46 (±0.59)	0.44
$eGFR \le 90ml/min/1.73m^2$ (n=56)	104	84	0.66 (±0.57)	0.23	$0.40(\pm 0.39)$	0.44
Age ≤40 years (n=247)	448	110	0.56 (±0.39)	0.16	0.49 (±0.41)	0.24
Age >40 years (n=142)	290	94	$0.30(\pm 0.39)$	0.10	$0.49(\pm 0.41)$	0.24
No Hypertension (n=374)	709	105	1.29 (±0.99)	0.20	$1.25(\pm 1.00)$	0.22
Hypertension (n=15)	28	94	$1.29(\pm 0.99)$	0.20	1.25 (±1.00)	0.22

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









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

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		Estimation of the effect on eGFR (ml/min/1.73m ²) (±SE)						
	PY	Univariate model ^a	Р	Adjusted analysis ^b	P			
s per month in the last two months ^c								
1)	255	Reference						
'9)	370	- 1.38 (±0.30)	< 0.001	- 0.88 (±0.30)	< 0.01			
na concentration at the time of eGFR assessment ^c								
'14)	231	Reference						
L (n=327)	50	- 1.27 (±0.50)		- 0.98 (±0.49)				
nL (n=512)	80	- 1.42 (±0.42)		- 1.28 (±0.42)				
231)	351	- 2.06 (±0.30)	< 0.001 ^d	- 1.82 (±0.30)	< 0.001 ^d			

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.