Poster 1023

Effect of On Demand Oral PrEP with TDF/FTC on HSV-1/2 Incidence among MSM

ML Chaix[1,2], I Charreau[3], C Delaugerre[1,2], N Mahjoub[2], M Siguier[4], C Capitant[3], C Tremblay[5], F Raffi[6], E Cua[7], G Pialoux[8], L Cotte[9], A Pasquet[10], L Meyer[3,11], JM Molina[1,4] and the ANRS IPERGAY Study Group

[1] INSERM U941, Université Paris Diderot, [2]APHP, Service de Virologie, CHU Saint Louis, Paris, [3]INSERM SC10-US19, Villejuif, France, [4] Service de Maladies Infectieuses, CHU Saint Louis, Paris, France, [5]University of Montreal, Montreal, QC, Canada, [6]CHU de Nantes, Nantes, [7]CHU de Nice, Nice, [8]Tenon Hospital, Paris, [9]CHU de Lyon, Lyon, [10]Centre Hospitalier de Tourcoing, Tourcoing, [11] Université Paris Sud, Paris, France.

Marie-Laure Chaix. MD. PhD
Université Paris Diderot
Paris. France
E-mail: marie-laure.chaix@aphp.fr

Background

The use of topical tenofovir gel for HIV PrEP has been shown to reduce the incidence of HSV-2-infection by 51% in women in the Caprisa 004 Study. Oral tenofovir-based PrEP also reduced HSV-2 acquisition by 28% among heterosexual men and women in the Patrners PrEP study. No reduction of HSV-2 incidence was reported in the Iprex study among MSM with daily TDF/FTC but adherence was low. We wished to assess the impact of on demand TDF/FTC for PrEP on HSV-1/2 incidence in the ANRS IPERGAY PrEP trial among MSM.

Methods

Stored serum samples from participants enrolled in the blinded phase (TDF/FTC or placebo) of the ANRS Ipergay trial were tested at baseline and at their last visit for HSV-1 and HSV-2 antibodies using serological tests (BioPlex 2200 HSV-1 & HSV-2 IgG, Biorad).
We also studied the shedding of HSV-2 in anal swab from HSV-2 seropositive patients. HSV1/HSV2 (HSV1 HSV2 VZV R-gene™ kit Argene) PCR was performed at baseline, M6 and M12.

Table 1. Population characteristics at baseline

	TDF/FTC n=199	PLACEBO n=201
Age (years), (median, IQR)	35.4 [29.2;43.4]	34.2 [28.5;42.0]
Sex (male)	100%	100%
Homosexual	189 (95%)	197 (98%)
Bisexual	10 (5%)	4 (2%)
Circumcision	38 (19%)	41 (20%)
STI* (Sexually Transmitted Infection)	49 (25%)	62 (31%)
No. sexual partners (last 2 months) (median, IQR)	8 [5-17]	8 [6-16]
No. sexual acts (last 4 weeks) (median, IQR)	10 [6-18]	10 [5-15]

* Chlamydia, gonorrhea or syphilis

Results

Of the 400 participants (199 in the TDF/FTC arm and 201 in the placebo arm), **70% (280/396*) were tested HSV-1 seropositive and 39% (155/397**) HSV-2 seropositive at baseline**. Only 18% were seronegative for both HSV-1 and HSV-2.

Table 2. Behavioral characteristics of men with positive HSV-1 serology at enrollment

	HSV-1 n=280	No HSV-1 n=116	p
No. sexual partners (last 2 months) (median, IQR)	10 [5.0;17.3]	6.7 [3.3;12.0]	**0.001**
No. sexual acts (last 4 weeks) (median, IQR)	11 [6 ; 20]	8 [4 ; 15]	**0.0004**
Condom use in men with receptive anal sex (last 4 weeks)	21/204 (10%)	21/85 (25%)	**0.002**
STI at enrollment	73/280 (26%)	36/116 (31%)	0.31

* 4 participants with indeterminated HSV -1 serology

Table 3. Behavioral characteristics of men with positive HSV-2 serology at enrollment

	HSV-2 n=155	No HSV-2 n=242	p
No. sexual partners (last 2 months) (median, IQR)	10 [6.0;20.0]	8.0 [4.0;15.0]	**0.0003**
No. sexual acts (last 4 weeks) (median, IQR)	10 [6.0;18.0]	10 [5.0;16.0]	0. 37
Condom use in men with receptive anal sex (last 4 weeks)	10/111 (9%)	32/180 (18%)	**0.04**
STI at enrollment	47/155 (30%)	62/242 (26%)	0.31

** 3 participants with indeterminated HSV -2 serology

Incidence of HSV-1 and HSV-2 during the follow-up and impact of TDF/FTC

Of the 108 HSV-1-seronegative participants with available samples after enrollment, median follow-up of 10.2 months (IQR: 6.2-20.5), **14 seroconverted for HSV-1**. **Overall HSV-1 incidence was 11.7 per 100 person-years**; 16.2% (95% CI: 7.4%; 30.8%) in the TDF/FTC arm versus 7.8% (95% CI: 2.5%;18.2%) in the placebo arm (p=0.19).

For HSV-2, out of the 218 HSV-2 seronegative participants with samples after enrollment**, 19 seroconverted for HSV-2** after a median follow up of 10.2 months. **Overall incidence of HSV-2 infection was 7.6 per 100 person-years**; 8.1% (95% CI: 4.0%; 14.5%) in the TDF/FTC arm versus 7.0% (95% CI: 3.0%; 13.7%) in the placebo arm (p=0.75).

We found no difference in the proportion of participants acquiring HSV-1 or HSV-2 between TDF/FTC group and Placebo group, even after adjusting for the number of pills taken (< or ≥ 15 pills/month).

HSV-2 shedding

HSV-2 shedding was analyzed in 58 participants with available anal samples (28 in the placebo arm and 30 in the TDF/FTC arm). Only 3 patients had HSV-2 positive PCR, 1 at baseline (4 900 copies/ml), 1 at M12 (115 500 copies/ml) and 1 at M6 (2 816 000 copies/ml) and M12 (595 000 copies/ml), the 2 latter being in the TDF/FTC arm.

Conclusions

The incidence of HSV-1 and HSV-2 was high in these high risk MSM using PrEP.

On demand oral PrEP with TDF/FTC failed to reduce HSV-1/2 incidence in this population.

No case of HIV acquisition was observed in subjects who seroconverted for HSV-1 or HSV-2.

Bibliography

Molina JM et al. NEJM, 2015, 373, 23, 2237-2246.

Abdool Karim SS et al. NEJM, 2015, 373,6, 530-9.

Marcus JL et al. PLOS one , 2014, 9, 3, e91513.

Celum C et al. Ann of Intern Med., 2014, 161, 1.

Looker KJ et al. Lancet, 2017.

Acknowledgments
This trial was funded by the French National Agency for Research on AIDS and Viral Hepatitis (ANRS), and the Bill and Melinda Gates Foundation, and conducted with the support of Gilead Sciences (donation TDF-FTC). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of this poster.