

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

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## 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 Patrnrs 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<br>n=199 | PLACEBO<br>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)<br>(median, IQR) | 8 [5-17]         | 8 [6-16]         |
| No. sexual acts (last 4 weeks)<br>(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 |                |                   |               | Table 3. Behavioral characteristics of men with positive HSV-2 serology at enrollment |                |                   |               |
|---|----------------|-------------------|---------------|---|----------------|-------------------|---------------|
|   | HSV-1<br>n=280 | No HSV-1<br>n=116 | p             |   | HSV-2<br>n=155 | No HSV-2<br>n=242 | p             |
| No. sexual partners (last 2 months)<br>(median, IQR)                                  | 10 [5.0;17.3]  | 6.7 [3.3;12.0]    | <b>0.001</b>  | No. sexual partners (last 2 months)<br>(median, IQR)                                  | 10 [6.0;20.0]  | 8.0 [4.0;15.0]    | <b>0.0003</b> |
| No. sexual acts (last 4 weeks)<br>(median, IQR)                                       | 11 [6 ; 20]    | 8 [4 ; 15]        | <b>0.0004</b> | No. sexual acts (last 4 weeks)<br>(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)                              | 21/204 (10%)   | 21/85 (25%)       | <b>0.002</b>  | Condom use in men with receptive anal sex (last 4 weeks)                              | 10/111 (9%)    | 32/180 (18%)      | <b>0.04</b>   |
| STI at enrollment   | 73/280 (26%)   | 36/116 (31%)      | 0.31          | STI at enrollment   | 47/155 (30%)   | 62/242 (26%)      | 0.31          |
| * 4 participants with indeterminated HSV -1 serology                                  |                |                   |               | ** 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

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