Oral TDF/FTC Provides Early Mucosal Protection In Both On- Demand And Daily Regimen

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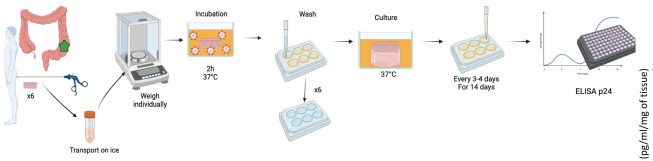
BACKGROUND

- Does PrEP with oral TDF/FTC with either ON-DEMAND or DAILY regimen protects against *ex vivo* infection with HIV of rectal tissue?

Pre-exposure prophylaxis (PrEP) is an effective way of preventing HIV acquisition, demonstrated in large-scale clinical trials in MSM with oral TDF/FTC. The two main dosing regimens are the ON-DEMAND (2-1-1) and DAILY PrEP. We wish to assess whether both PrEP dosing regimens are efficacious to reduce *ex vivo* infection of rectal explants.

METHODS

- We used a validated *ex vivo* challenge model of rectal tissue infection with HIV-1 (BaL, R5 tropism) to assess PrEP efficacy(1).
- Briefly, 6 rectal explants per participant are collected at baseline without PrEP (V1) and after PrEP (V2) either 2 hours after oral intake of two pills of TDF/FTC (ON-DEMAND group) or 7 days after a daily pill of TDF/FTC (DAILY group)
- Rectal explants are infected *ex vivo* with HIV-1 (BaL strain) for 2 hours, washed in PBS and then cultured for 14 days
- HIV antigen p24 is measured at day 3, 7, 10 and 14 in rectal explants supernatants
- Levels of p24 are standardized by the weight of each explant (pg/ml/mg of tissue)



- Overall tissue susceptibility to HIV-1 is estimated by two measures :
- Mean cumulative p24 excretion at day 14 (D14)
- Mean AUC of kinetics of p24 excretion over the 14 days of culture
- Mean D14 cumulative p24 level differences (V2-V1) reflect PrEP efficacy in each participant

- Comparison between V1 and V2 was done using a Wilcoxon test
- Comparison between PrEP dosing regimens was done using a Mann-Whitney test.

One week of daily oral TDF/FTC and two pills of TDF/FTC taken two hours before rectal biopsies similarly reduce *ex vivo* susceptibility to HIV infection

RESULTS

Figure 1: Estimation of the mean differences between with and without PrEP in cumulative p24 values in the *ex vivo* rectal challenge model with each dosing regimen

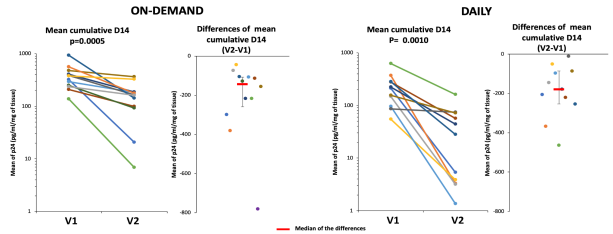
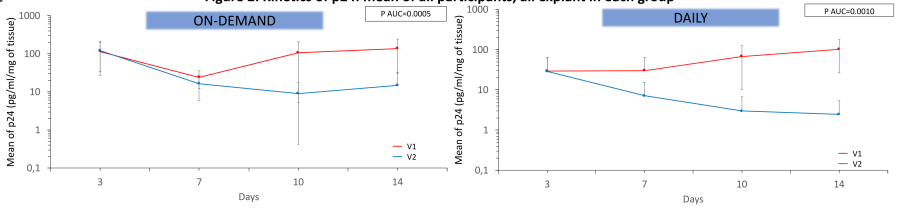


Figure 2: Kinetics of p24: mean of all participants, all explant in each group



- 13 participants were included in the ON-DEMAND group, 12 in the DAILY group. 2 were excluded (one in each group), because of insufficient rectal tissue infection at V1.

Figure 1

- Median AUC of p24 in the ON-DEMAND group were 436 (IQR[370;717]) and 58 (IQR[48; 129]) at V1 and V2, respectively (P=.0005, n=12)
- Median AUC of p24 in the DAILY group were 395 (IQR[213; 630]) and 11 (IQR[5;39]) at V1 and V2, respectively (P=.0010, n=11)

Figure 2

- Median of Mean D14 cumulative p24 difference V2-V1 = -144pg/ml/mg (IQR[-259;-108]) for the ON-DEMAND group (P=.0005, n=12)
- Median of mean D14 cumulative p24 difference V2-V1 = -179pg/ml/mg (IQR[-253;-86]) for the DAILY group (P=.0010, n=11)

- There was no statistical difference in the median cumulative p24 differences between the groups, for a sample of 23 participants analyzed (P=0.93)

CONCLUSIONS

- All participants demonstrated lower *ex vivo* infectability of rectal tissue after exposure to PrEP
- ON-DEMAND PrEP with TDF/FTC reduced *ex vivo* HIV infection of rectal explants taken 2 hours after a leading dose of two pills.
- Similarly, DAILY PrEP with one daily dose of TDF/FTC for seven days reduced *ex vivo* HIV infection in rectal tissue.
- PrEP efficacy in rectal tissue is consistent with results of clinical trials using ON DEMAND or DAILY PrEP.

This study illustrates the potential for using *ex vivo* rectal challenge models to evaluate future PrEP agents or dosing strategies

ADDITIONAL KEY INFORMATION

All participants were included in the ANRS-PREVENIR trial (NCT03113123)

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Reference:
1. McGowan et al. AIDS Res Hum Retrovir 2021