Acute infection with a wild-type HIV-1 virus in a PrEP user with high TDF levels

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Discussion and conclusion

- First case of infection with wild type HIV-1 in a person with documented supposedly protective intracellular levels of TFV-DP.
- Underlying mechanism remains speculative:
  - High repeated HIV exposure and/or mucosal damage?
  - Lower levels of TDF and/or FTC in rectal mucosa?
- Atypical pattern of seroconversion, potentially due to an aberrant immune response under PrEP.
- This underscores the importance of regular HIV testing in PrEP users and being aware of potential atypical patterns of seroconversion.

Objective

We report an individual participating in the Amsterdam PrEP project who was infected with a wild-type HIV-1 with documented high levels of TFV-DP in dried blood spots.

Background

Clinical trials show that pre-exposure prophylaxis (PrEP) with tenofovir/emtricitabine is highly effective against acquisition of HIV-infection. World-wide, only two cases of PrEP failure have been reported under adequate tenofovir-diphosphate (TFV-DP) levels in dried blood spots. Both these individuals were infected with a multi-class resistant virus.

Methods

The Amsterdam Pre-exposure prophylaxis project (AMPrEP) is a demonstration project on the uptake, acceptability and usability of daily and event-driven TDF/FTC, as part of a comprehensive HIV infection prevention program among men who have sex with men (MSM) and transgender persons. The AMPrEP project started in August 2015 at the Public Health Service of Amsterdam, the Netherlands. Participants are tested (including for STI, HIV) 3-monthly.

Case report

- MSM, 50 years old, started daily PrEP
- HIV negative at PrEP start (HIV RNA (Taqscreen) and Ag/Ab (LIASON XL)) and after 1, 3 and 6 months (Ag/Ab)
- After PrEP start: twice rectal *Neisseria gonorrhea* and once rectal *Chlamydia trachomatis* infection
- Reported the use of drugs during sex (amphetamine, cocaine, GHB/GBL, mephedrone and ketamine)
- Reported excellent adherence
- Adequate TDF-DP levels in dried blood spots, 2234 and 2258 fmol/punch, respectively, at six and 8 months after start of PrEP
- Eight months after PrEP start: symptoms of fever and dysuria → HIV diagnostics: Ab positive; Ag and HIV RNA negative (see Figure 1 for details)

•No HIV-DNA was detected in bulk peripheral blood mononuclear cells and no HIV-DNA and RNA (cDNA) from three sigmoid biopsies at the moment of seroconversion → no acute HIV infection diagnosed

•→ PrEP was interrupted, HIV RNA tested at regular intervals (Fig 1), and became detectable after 3 weeks

•No HIV-1 mutations in reverse transcriptase or protease associated with resistance against TDF, FTC, or other antiretroviral agents (routine sequencing)

•Started tenofovir/emtricitabine 1 tab OD, boosted darunavir 800mg/100mg OD and dolutegravir 50mg TD, resulting in an undetectable load after one month

Table 1: Sexual risk behaviour of PrEP user who seroconverted for HIV with high TDF-DP levels in dried blood spots

	Month 1	Month2	Month 3	Month 4	Month 5	Month 6 ★	Month 7	Month 8 ★
Anal sex partners[a]	75	56	56	50	38	49	66	12
Days he reported CAS[a]	21/31	12/30	13/31	15/31	15/29	19/31	17/30	3/20
Median [IQR] number of sex partners per day with CAS[a]	3 [1-7.5]	4.5 [2.25-8.5]	4 [1.5-6]	4 [1-5]	2 [1-5]	3 [1-4]	5 [2-6]	5 [1-5]
CAS partners[b]	90		51			Not reported		
CAS episodes[b]	100		100			Not reported		

a Per month, data collected via daily diary via application for mobile phone
b In 12-week periods, collected through computer-assisted self-reported questionnaires
CAS: condomless anal sex

★ Time point dried blood spots were collected

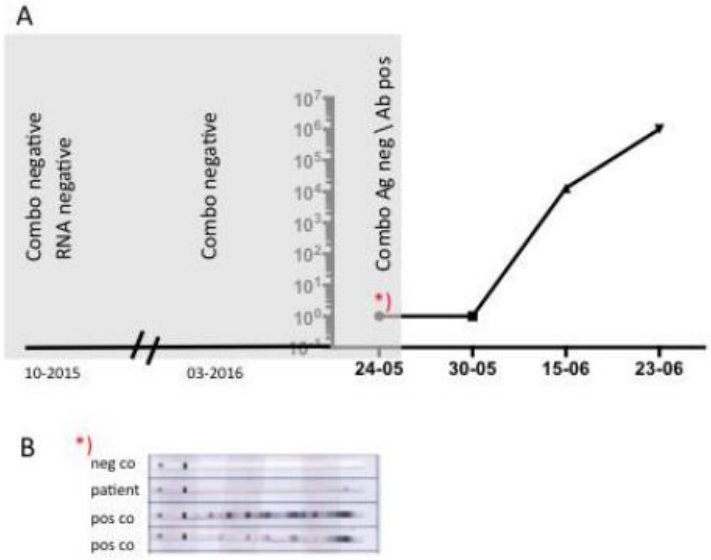

Figure 1: A: Use of PrEP and timing of HIV tests (X-axis), and plasma HIV RNA (copies/mL) (Y-axis) B: Western blot performed at seroconversion (indicated by asterisk).