

March 23, 2016

Dear New York City and New York State PrEP Providers,

Last month, the first reported case of a breakthrough HIV infection in a patient consistently taking oral tenofovir disoproxil fumarate and emtricitabine (TDF/FTC, or Truvada®) as pre-exposure prophylaxis (PrEP) to prevent HIV was [reported](#) at the 2016 Conference on Retroviruses and Opportunistic Infections (CROI) in Boston [\[1\]](#). The patient was infected with a strain of HIV resistant to both TDF and FTC. While such viruses are extremely rare, the case demonstrates that PrEP, like other preventive medications and behavioral interventions, does not provide 100% protection against HIV infection. Nevertheless, the body of scientific and clinical data previously presented about the efficacy of PrEP confirms the critical role of this intervention in reducing new HIV infections in New York City (NYC), and New York State (NYS).

As such, the New York City and New York State Departments of Health (DOH) continue to fully support the use of TDF/FTC as PrEP for individuals at risk of HIV infection. The rare event reported at this conference provides an opportunity to revisit NYSDOH AIDS Institute guidance for PrEP and to clarify the importance of communicating with patients about PrEP and the risk of HIV and other sexually transmitted infections (STIs).

We urge providers to adhere to [CDC](#) and [NYSDOH AIDS Institute](#) PrEP guidance with their patients on PrEP by:

1. Testing for HIV every three months using a laboratory-based, ideally 4th generation, HIV test;
2. Assessing for signs of acute HIV infection at every visit;
3. Having a low threshold for testing for acute HIV and other STIs; and
4. Encouraging patients on PrEP (or on HIV treatment) to use condoms as often as possible.

#### **THE CASE REPORTED AT CROI 2016**

A 43-year-old man in Toronto, Canada, was diagnosed with acute HIV infection after taking PrEP for 24 months, during which time he tested negative for HIV 7 times. Patient self-report, pharmacy data and laboratory analysis indicated the patient had long-term adherence to PrEP and a high concentration of TDF/FTC in his blood at the time of seroconversion. The patient was diagnosed with acute HIV infection when visiting an emergency room with severe abdominal pain and a high fever; he reported receptive anal sex without condoms with multiple male partners in the 2 to 6 weeks before diagnosis. Subsequent viral sequencing determined that the patient was infected with a strain of HIV-1 that demonstrated genotypic evidence of high-level resistance to emtricitabine and low-level resistance to tenofovir disoproxil fumarate, the two antiretroviral (ART) drugs in PrEP. The transmitted virus also demonstrated resistance to integrase inhibitors, medications used in first-line HIV treatment and post-exposure prophylaxis (PEP) regimens. The patient immediately began HIV treatment and achieved an undetectable viral load by taking a combination of dolutegravir (Tivicay®), darunavir/cobicistat (Prezcobix®) and rilpivirine (Edurant®).

## CLINICAL CONSIDERATIONS

This case indicates that PrEP, even when taken consistently, may not provide full protection against multi- drug resistant viruses. But this finding does not diminish the role of PrEP in preventing the vast majority of HIV transmissions. Among over 9,000 people taking PrEP in clinical trials, none were infected with HIV resistant to both TDF and FTC [2]. Furthermore, major clinical providers of PrEP have reported zero cases of new HIV infection in patients consistently taking PrEP in observational studies of real-world cohorts [3,4].

PrEP, like vaccines and many other preventive medications or interventions, does not provide 100% protection. Clinical trials have established that PrEP can reduce the risk of HIV infection by over 90% if taken correctly [5]; one modeling study estimates that PrEP may be over 99% effective if taken every day [6]. Use of condoms during sex reduces the risk of infection ever further. Given this exceptional efficacy, PrEP continues to be a key tool in the HIV prevention toolkit to end the epidemic of HIV in NYC and NYS.

Thus, this case highlights the importance of following [CDC](#) and [New York State guidance](#) when providing antiretroviral therapy for prevention or treatment.

1. Test patients on PrEP for HIV at least every three months.
  - a. A lab-based HIV test, ideally 4th generation antibody/antigen combination assay, is recommended given the test's higher sensitivity and ability to identify infections earlier than standard rapid HIV tests (whether oral fluid- or whole blood-based).
  - b. Promptly initiate newly infected patients on appropriate treatment to both: (1) avoid the development of virus resistant to TDF and FTC; and (2) achieve viral suppression.
2. Routinely assess patients' risk of HIV exposure for signs and symptoms of acute HIV infection.
  - a. Test for acute infection in symptomatic patients using an HIV-1 RNA assay in conjunction with a 4th generation screening test (see [NYS acute infection guidelines](#)).
  - b. Encourage patients to report any symptoms or signs of acute infection, such as fever, rash, pharyngitis, myalgia, and malaise (similar to influenza or mononucleosis illness).
3. Encourage patients on PrEP (or HIV treatment) to use these strategies as part of a combination approach to preventing HIV infection or transmission.
  - a. Consider PrEP as part of a package of interventions for those at risk. FTC/TDF received U.S. FDA approval as PrEP in combination with condom use, adherence counseling, risk-reduction education, and regular testing for STIs.
  - b. Encourage your patients to use condoms as often as possible.
  - c. Counsel patients, including those who do not consistently use condoms, that PrEP is over 90% effective in preventing HIV when taken as prescribed, and that condoms both prevent other STIs and provide additional protection against HIV. Encourage patients to use all the tools in the HIV prevention toolkit that best fit their lives.
  - d. Treating HIV infection to suppress viral loads in people living with HIV may reduce HIV transmission by 93% [7]. Support people with HIV to stay in HIV care and encourage them to adhere to antiretroviral therapy (ART) for their personal health and to help prevent transmission of HIV to their partners.
  - e. Remind patients on PrEP and HIV treatment that condoms provide additional protection against the transmission of HIV and other STIs. Encourage patients to use all the tools in the HIV prevention toolkit that best fit their lives.

## Summary

This case illustrates that, in rare instances, breakthrough HIV infection can occur in patients despite adherence to daily oral PrEP. But the case also provides a reminder about the importance of adherence to clinical guidance for prescribing PrEP and to clinical guidelines for treating HIV infection, and of

providing thorough, thoughtful, evidence-based counseling for patients regardless of HIV status.

The New York City and New York State Health Departments encourage clinicians to continue to support patients who are using or considering PrEP, and to address any concerns they may have. An expanding set of tools enable us to prevent or to successfully treat HIV. With your help, we can help New Yorkers #PlaySure and end the epidemic of HIV.

Sincerely,



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NYC Department of Health and Mental Hygiene



Dan O'Connell  
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1. [Knox, et al. CROI 2016. Abstract 169aLB.](#)
  2. [CDC, PrEP for the Prevention of HIV, Clinical Guidelines, 2014, tables 3 and 6.](#)
  3. [Volk et al. \*Clin Infect Dis.\* 2015, 61\(10\):1601-3.](#)
  4. [McCormack et al. \*Lancet\* 2016, 387\(10013\):53-60.](#)
  5. [Anderson et al. \*Sci Transl Med.\* 2012, 4\(151\).](#)
  6. [Grant et al. \*Lancet Infect Dis.\* 2014, \(9\):820-9.](#)
  7. [Cohen et al. IAS 2015, program number MOAC0106LB.](#)