

Howard Brown Breakthrough HIV-1 Infection in Setting of Cabotegravir for PrEP Health Aniruddha Hazra^{1,2}, Connor Quinby¹, Catherine Creticos¹

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BACKGROUND

- Long-acting cabotegravir (CAB-LA) is highly effective as HIV PrEP and superior to daily oral F/TDF in sexually active adults
- Despite its superior efficacy, PrEP failures associated with CAB-LA have been described in clinical trials
- We report a 28-year-old gender diverse patient assigned male at birth whose HIV-1 infection was detected 91 days after transitioning from F/TAF to CAB-LA despite on-time dosing

METHODS

- Electronic medical records were reviewed to assess patient history and CAB-LA administration
- Plasma 4th generation HIV-1/2 Ag/Ab combination immunoassay and HIV-1 RNA quantitative PCR were performed at each injection visit
- Plasma CAB concentration was performed by a

CASE DESCRIPTION

- Patient on daily F/TAF for PrEP 10 months prior, reporting one missed dose per week
- History of controlled hypothyroidism and self-reported hypogonadism with illicit use of IM testosterone and significantly elevated total testosterone levels
- Sexually active with cisgender men
- condomless oral and anal sex
- primary partner & 20-30 unique partners monthly
- recently engaging in anal fisting intercourse
- diagnosed with syphilis and mpox in past 6 months
- Primary partner was living with HIV resistant to NRTIs (65R, 118I) and INSTIs (92G) with undetectable HIV-1 RNA for over 24 months on DRV/c + DTG
- Uncomplicated administration of 600mg of CAB-LA into left gluteal medius on day 0, 27, and 91
- Flu-like illness with + SARS-COV-2 PCR on day 76; completed course of nirmatrelvir-ritonavir (NMV/r)

RESULTS

- HIV 1/2 Ag/Ab non-reactive and HIV-1 RNA PCR not detected on Day 0 and 27 injections
- At 3rd injection on Day 91
- HIV 1/2 Ag/Ab non-reactive
- HIV-1 RNA PCR test detected at 1.48 log10 c/mL
- Repeat testing on day 100
- HIV 1/2 Ag/Ab reactive
- HIV-1 Ab detected on differentiation assay
- HIV-1 RNA PCR detected at 1.30 log10 c/mL
- unable to perform standard HIV-1 sequencing
- HIV-1 DNA qualitative PCR below LLOQ and HIV-1 proviral DNA resistance unable to be performed
- Plasma CAB concentration on Day 128 (Day 37 from most recent injection) 1180 ng/mL
- Fully suppressive ART regimen (DRV/c + DTG) chosen based on primary partner's regimen and historical genotypes

CONCLUSIONS

- Patient's history and testing suggests HIV infection despite on-time and appropriate CAB-LA injections and detectable CAB concentration
- To our knowledge, this is the first case of CAB-LA PrEP failure outside the setting of a clinical trial
- Highlights diagnostic and management challenges that may occur with CAB-LA PrEP failures
- Reinforces need to better understand HIV-1 reservoirs in such breakthrough infections (ACTG A5321)

ACKNOWLEDGMENTS

- Ebony Warren, MA; Howard Brown Health
- Mark Marzinke, PhD; Johns Hopkins University
- Raphael Landovitz, MD, MSc; UCLA Health
- Toyin Nwafor, MD, Heidi Swygard, MD, MPH, Sonia Patel, PharmD; ViiV Healthcare

Rectal GC/CT NAAT : neg

TSH/FT4: **8.48 mIU/L**; 1.6 ng/dL

Total testosterone: 421 ng/dL

HIV-1 Infection Detected research laboratory DRV/c + DTG NMV/r F/TAF CAB-LA Injection #1 F/TAF CAB-LA Injection #2 CAB-LA Injection #3 **Day 91** Day 128 Day -56 Day 27 **Day 76** Day 100 Day 112 Day 0 HIV Ag/Ab: non-reactive HIV Ag/Ab: non-reactive HIV Ag/Ab: reactive HIV Ag/Ab: non-reactive SARS-CoV-2 PCR: detected HIV-1 RNA: not detected HIV-1 Ab: detected HIV-1 RNA: not detected HIV-1 RNA: not detected HIV-1 RNA: 1.30 log10 c/mL Plasma CAB level: 1180 ng/mL HIV genotype: TNP Real world case of CAB-LA PrEP HIV Ag/Ab: non-reactive BMI: 30.55 kg/m^2 HIV Ag/Ab: non-reactive HIV-1 RNA: not detected HIV-1 RNA: **1.48 log10 c/mL** HIV Ag/Ab: non-reactive HIV-1 DNA qual PCR: not detected Mpox PCR (penis): detected RPR: non-reactive failure despite on-time dosing and HIV-1 proviral DNA resistance: TNP TSH/FT4: 5.49 mIU/L; 2.0 ng/dL Oral GC/CT NAAT: neg RPR: non-reactive Urine GC/CT NAAT : neg Total testosterone: 9318 ng/dL Oral GC/CT NAAT : neg Rectal GC/CT NAAT: neg Urine GC/CT NAAT : neg appropriate laboratory monitoring.