EPC118

Concordance Between Laboratory Serologic Testing and HIV-1 RNA Testing Among Participants Who Acquired HIV in the DISCOVER Trial

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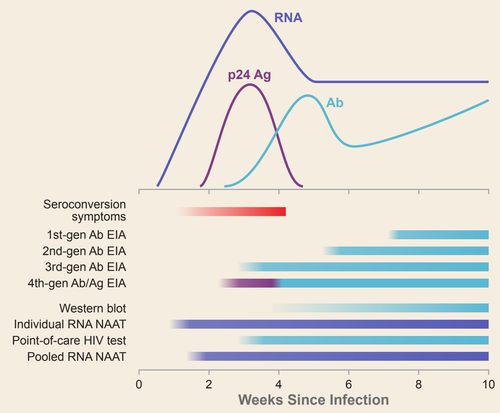
Introduction

Time to Detection[1]



Ab, antibody; Ag, antigen; EIA, enzyme immunoassay; gen, generation; NAAT, nucleic acid amplification test. Adapted from Taylor D, et al.[1]

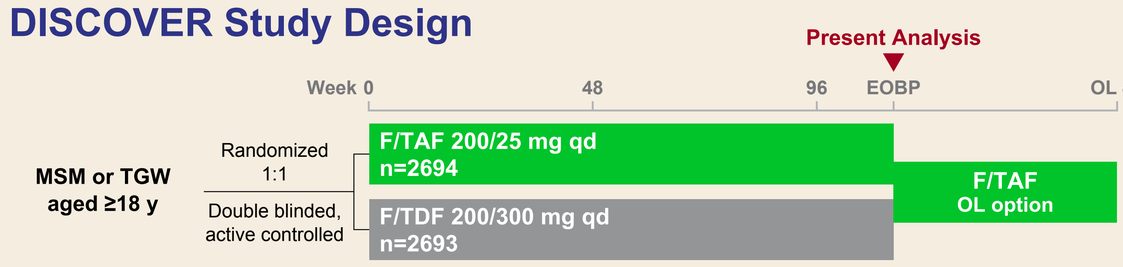
- Among HIV testing modalities, RNA testing has the shortest window period and may become positive before Ab- or Ag-based tests[1]
- Traditionally, HIV testing for people taking pre-exposure prophylaxis (PrEP) has used Ab or Ab/Ag testing
  - Data from HPTN 083 indicate that cabotegravir for PrEP may delay Ab and Ag seroconversion, delaying HIV diagnosis and potentially leading to resistance[2]
  - These findings have prompted recommendations for RNA testing in all people taking PrEP[3]; however, the benefit of RNA testing for daily oral PrEP is uncertain
- DISCOVER (ClinicalTrials.gov NCT02842086) is a large, Phase 3, randomized, controlled trial that demonstrated the noninferiority of emtricitabine/tenofovir alafenamide (F/TAF) to emtricitabine/tenofovir disoproxil fumarate (F/TDF) for PrEP in cisgender men who have sex with men (MSM) and transgender women (TGW)[4]
- A prior analysis of data from the DISCOVER blinded phase showed high correspondence between PrEP adherence and prevention of HIV acquisition[5]

Objectives

- To characterize longitudinal adherence of participants who acquired HIV in the DISCOVER blinded phase
- To assess concordance between rapid point-of-care and laboratory serologic HIV testing and HIV-1 RNA testing among participants who acquired HIV in DISCOVER
- To evaluate evidence of delayed HIV diagnosis in the setting of daily oral PrEP

Methods

DISCOVER Study Design



EOBP, end of blinded phase; OL, open label.

- Study conducted in 94 cities/sites with high HIV incidence in Austria, Canada, Denmark, France, Germany, Ireland, Italy, Netherlands, Spain, UK, and USA
- At EOBP, participants had the option to receive F/TAF in the OL phase

Assessments

	Screening	Day 1 (<30 d after screening)	Week 4	Week 8	Week 12	Week q12wk → 96
Rapid HIV (Ab or Ab/Ag)*	•	•	•	•	•	•
Laboratory HIV test (Ab or Ab/Ag)*	•		•	•	•	•
Plasma samples	•		•	•	•	•
DBS	•		•	•	•	•

*3rd-gen Ab tests used at sites where 4th-gen Ab/Ag tests were not available. DBS, dried blood spot.

- Tenofovir diphosphate (TFV-DP) concentrations were measured from stored DBS from all visits to assess longitudinal adherence with PrEP
- HIV-1 RNA was evaluated in all participants with a positive rapid or laboratory HIV test during follow-up using samples collected from the corresponding visit (n=24)
- HIV-1 RNA was assessed retrospectively in the visits prior to HIV diagnosis among participants with available banked plasma samples (n=16)

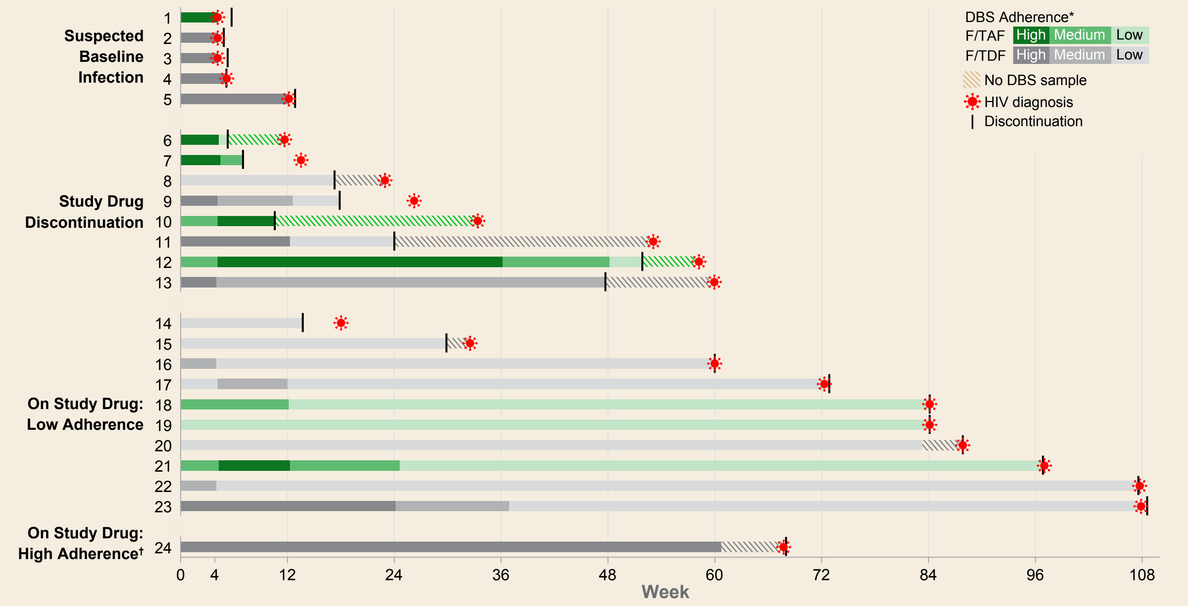
Results

Baseline Demographics and Clinical Characteristics

	Acquired HIV: n=24	Did Not Acquire HIV: n=5311
Median age, y (Q1, Q3)	27 (23, 33)	34 (28, 43)
Race, n (%)		
White	16 (67)	4463 (84)
Black/mixed Black	6 (25)	453 (9)
Asian, Pacific Islander, or Native Hawaiian	1 (4)	268 (5)
Other (non-Black)	1 (4)	38 (1)
Hispanic/Latinx ethnicity, n (%)	6 (25)	1295 (24)
Cisgender MSM, n (%)	24 (100)	5238 (99)
Region, n (%)		
USA	16 (67)	3161 (60)
EU	5 (21)	1802 (34)
Canada	3 (13)	348 (7)
Self-reported HIV risk factors, n (%)		
≥2 receptive condomless sex partners in last 12 wk	19 (79)	3140 (61)
Binge drinking*	3 (13)	1208 (23)
Recreational drug use in past 12 wk	17 (71)	3522 (67)
Taking PrEP at baseline	1 (4)	895 (17)

*≥6 drinks on ≥1 occasion at least monthly. Q, quartile.

Summary of Adherence Data: Participants Who Acquired HIV



*High ≥4, medium 2–3, and low <2 doses/wk; TFV-DP levels: F/TAF high ≥900, medium ≥450–<900, and low <450 fmol/punches; F/TDF high ≥700, medium ≥350–<700, and low <350 fmol/punch; †Returned pill counts indicated suboptimal adherence preceding diagnosis.

- 24 participants acquired HIV through EOBP (8 with F/TAF and 16 with F/TDF):
  - 5 had suspected unrecognized baseline infection
  - 8 discontinued drug ≥30 d before diagnosis
  - 10 had DBS consistent with low adherence preceding diagnosis
  - 1 had prior DBS consistent with high adherence, but no DBS sample at diagnosis; returned pill counts indicated suboptimal adherence preceding diagnosis

Discordant HIV Test Results in Participants Who Acquired HIV

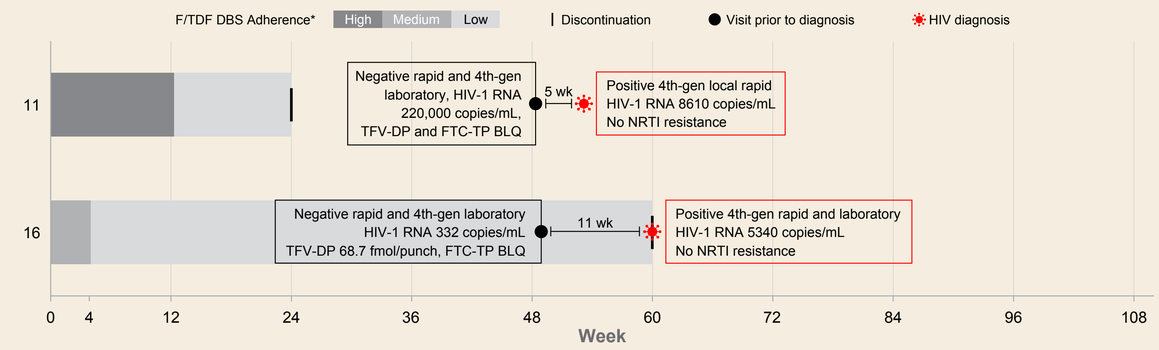
Discordance between HIV tests | Concordance between HIV tests

	Participant	HIV Rapid Test	Laboratory HIV Test (HIV test type)	HIV-1 RNA: Qualitative	HIV-1 RNA Copies/mL
Suspected Baseline Infection	1	Negative	Positive (4th-gen Ab/Ag)	RNA detected	<20
	3	Negative	Positive (4th-gen Ab/Ag)	Not completed	114,000
Study Drug Discontinuation	12	Negative	Positive (4th-gen Ab/Ag)	RNA detected	199,000*
	13	Negative	Positive (4th-gen Ab/Ag)	Not completed	6,320,000
On Study Drug: Low Adherence	17	Negative	Positive (4th-gen Ab/Ag)	Not completed	3,630,000
	20	Negative	Positive (4th-gen Ab/Ag)	Not completed	567
	23	Negative	Positive (4th-gen Ab/Ag)	Not completed	7170

*Completed 13 d after rapid and qualitative HIV-1 RNA test.

- 7 participants had a negative rapid HIV test the same day laboratory HIV testing was reactive
- There were no discordant results between laboratory HIV testing and HIV-1 RNA tests at the time of HIV diagnosis

Retrospective HIV-1 RNA Testing



*High ≥4, medium 2–3, and low <2 doses/wk; TFV-DP levels: high ≥700, medium ≥350–<700, and low <350 fmol/punch. BLQ, below limit of quantification; FTC-TP, emtricitabine-triphosphate; NRTI, nucleos(t)ide reverse transcriptase inhibitor.

- 2 of 16 participants had detectable HIV-1 RNA in the visit prior to HIV diagnosis
  - 1 discontinued PrEP >5 mo before HIV diagnosis
  - 1 discontinued PrEP 8–10 d prior to a suspected exposure event; DBS drug concentrations were consistent with average adherence of ~1 dose/2 wk over the preceding 8 wk
  - Neither had NRTI-resistance mutations
- In all other participants with available samples (n=14), no HIV-1 RNA was detected in retrospective testing of banked plasma from prior visits

Conclusions

- Nearly all HIV diagnoses occurred in the context of unrecognized baseline infection, PrEP discontinuation, or low adherence
- There was no discordance between 4th-gen Ab/Ag and HIV-1 RNA viral load testing at the time of HIV diagnosis; however, several participants had false-negative rapid test results
- 2 participants had detectable HIV-1 RNA prior to Ab-/Ag-based diagnosis; however, the absent or minimal PrEP dosing in these participants and the absence of resistance development argues against delayed diagnosis attributable to PrEP use
- Analysis of seroconversions in DISCOVER over 11,000 person-years of follow-up suggests that 4th-gen Ab/Ag testing alone is appropriate and sufficient for assessing HIV status in people using daily F/TDF or F/TAF for PrEP

References: **1.** Taylor D, et al. Int J STD AIDS 2015;26:215-24; **2.** Marzinke MA, et al. J Infect Dis 2021;224:1581-92; **3.** US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States—2021 Update: a Clinical Practice Guideline; **4.** Mayer KH, et al. Lancet 2020;396:239-54; **5.** Doblecki-Lewis S, et al. CROI 2020, poster 3815.

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