HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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VIROLOGIC AND IMMUNOLOGIC MONITORING AND RESISTANCE ASSAYS

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JUNE 2023

ALL RECOMMENDATIONS P.1

Virologic and Immunologic Monitoring

- To assess a patient's response to ART and immunologic status and to identify when a change in ART regimen is needed, clinicians should perform HIV viral load and CD4 cell count testing as detailed in *Table 1: Recommended Viral Load and CD4 Count Monitoring in Non-Pregnant Patients With HIV*. (A1)
- Clinicians should address modifiable barriers to adherence and engagement in care to help ensure optimal virologic suppression. Modifiable barriers may include, but are not limited to, substance use, mental illness, other chronic medical conditions, ART-associated adverse medication effects, unstable housing, or low health literacy. (A2)
- Quarterly CD4 count monitoring is *no longer recommended* for non-pregnant patients receiving ART who have consistently undetectable HIV RNA levels and CD4 counts >200 cells/mm^3 (see Table 1 for recommended intervals). (A2)

Determining HIV Drug Resistance

- Clinicians should consult with an expert to interpret the results of resistance assays because such results can be complex. (A3)
  - The NYSDOH AI Clinical Education Initiative line is available for phone consultation: 866-637-2342.

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RESOURCES: DRUG RESISTANCE MUTATIONS

New resistance mutations and the emerging clinical significance of these mutations frequently change. See the following for more information on drug resistance mutations and resistance testing:

- Stanford University HIV Drug Resistance Database: https://hivdb.stanford.edu/
- IAS-USA 2022 Update of the Drug Resistance Mutations in HIV-1: https://www.iasusa.org/resources/hiv-drug-resistance-mutations/
- HIV Resistance Response Database Initiative: https://www.hivrdi.org/
- Los Alamos National Laboratory HIV Databases: https://www.hiv.lanl.gov/content/index
- HIV French Resistance Database: https://hivfrenchresistance.org/

← Use this code with your phone's QR code reader to go directly to a mobile-friendly version of the guideline.

¼-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Virologic and Immunologic Monitoring in HIV Care*. The full guideline is available at www.hivguidelines.org.

← Use this code with your phone's QR code reader to go to *HIV Resistance Assays*.

ALL RECOMMENDATIONS P.2

Determining HIV Drug Resistance *continued*

- Clinicians should perform genotypic resistance testing that includes the protease (A2), reverse transcriptase (A2), and integrase genes (B2) at baseline.
- For a patient experiencing treatment failure or incomplete viral suppression while taking oral ART, the clinician should perform resistance testing while the patient is still on therapy but no later than 4 weeks after stopping ART, to minimize the rapid return of wild-type virus when the selective pressure from ART is removed. (A2)
- For patients receiving CAB/RPV LA, the clinician should obtain resistance testing while the patient is still on or as soon as possible after they have discontinued effective ART, although the time limit for obtaining useful resistance information after discontinuation of CAB/RPV LA is unknown. (A3)
- Clinicians should perform coreceptor tropism testing before initiating a CCR5 antagonist. (A1)
- For patients whose treatment with a fusion inhibitor has failed, the clinician should test for fusion inhibitor resistance as a supplement to other genotypic resistance testing. (A2)

Note: Virologic failure is defined as a viral load >200 copies/mL.

KEY POINTS

Virologic and Immunologic Monitoring

- Quarterly HIV RNA monitoring remains appropriate for patients with a recent history of nonadherence, mental health disorders, substance use, homelessness, poor social support system, or other major medical conditions. Semiannual monitoring may be appropriate for patients with persistently undetectable HIV RNA and none of the above characteristics.
- Achieving and maintaining an undetectable viral load is always the goal of ART.

Determining HIV Drug Resistance

- Resistance testing is recommended when incompletely suppressive ART is interrupted. Because of the rapid return of wild-type virus without selective pressure from ART, testing is preferred before treatment is stopped. If the patient has already stopped ART, testing should be performed as soon as is practical and, if possible, no more than 4 weeks after cessation, before the return of wild-type virus. If resistance testing is performed more than 4 weeks after ART cessation, some mutations may no longer be detected by the assay and clinically relevant mutations may not be recognized. For patients who were receiving CAB/RPV LA, resistance testing should be done as soon as possible but may be useful any time after cessation of ART.

Table 1: Recommended Viral Load and CD4 Count Monitoring in Non-Pregnant Patients With HIV [a]

Event	HIV RNA Viral Load	CD4 Cell Count	Comments
Entry into care	Baseline viral load (A1)	Baseline CD4 cell count (A1)	· If a patient is not taking ART, recommend initiation [b] (A1) · Monitor as below
Patients Taking ART			
ART initiation or change to address virologic failure	· Within 4 weeks after ART start or change (A3) · At least every 8 weeks until complete virologic suppression is documented (A3)	· 12 weeks after ART initiation · Every 4 months until CD4 count >200 cells/mm^3 is obtained on 2 measurements at least 4 months apart (A2), then monitor as below once virologic suppression is achieved	· Virologic failure occurs when a viral load <200 copies/mL is either not achieved or not maintained · Virologic suppression is defined as a viral load <20 to <50 copies/mL obtained with a highly sensitive assay
ART change for simplification or due to adverse effects	Within 4 weeks after ART change, then as below (A3)	Monitor as below for documented virologic suppression	––
Documented viral suppression	· At least every 4 months (A3) · May extend interval to 6 months in patients stable on ART with CD4 count >200 cells/mm^3 and complete viral suppression for 1 year (B2)	· At least every 6 months if CD4 count is ≤350 cells/mm^3 (B2) · Optional if CD4 count is >350 cells/mm^3 (B2)	––
New HIV RNA ≥500 copies/mL after previous viral suppression	· Repeat viral load test 2 weeks after first result (A2)	Obtain CD4 cell count if previous result is >6 months old (B3)	· Assess for adherence and drug-drug interactions (A3) · Obtain resistance testing (A1)
New HIV RNA level over the limit of detection of sensitive assays, 20 to 50 copies/mL, but <500 copies/mL after previous viral suppression	· epeat viral load test within 4 weeks to differentiate low-level transient viremia ("blip") from virologic failure [c] (A2)	If repeat viral load is detectable, obtain CD4 cell count if previous result is >6 months old (B3)	· Assess for adherence and drug-drug interactions (A3) · If repeat viral load is detectable, consider resistance testing [d] (B3) · Patients with low-level viremia ≤200 copies/mL over a period of 12 months without demonstrated failure may continue routine testing intervals of at least every 4 months [e]
Patients Taking Antiretroviral Therapy (ART)			
CD4 cell count ≤500 cells/mm^3 (A2)	At least every 4 months	At least every 4 months	At every visit, recommend ART initiation [b]
CD4 cell count >500 cells/mm^3 (A2)	At least every 6 months	At least every 6 months	At every visit, recommend ART initiation [b]

Abbreviation: ART, antiretroviral therapy

Notes:

a. For recommendations on virologic monitoring in pregnancy, see DHHS: *Recommendations for the Use of Antiretroviral Drugs During Pregnancy and Interventions to Reduce Perinatal HIV Transmission in the United States*.

b. See the NYSDOH AI guideline *Rapid ART Initiation*.

c. An ART regimen should not be changed based on a single viral load elevation. The risk of virologic rebound (breakthrough) increases when values are ≥500 copies/mL.

d. Standard genotypic tests may not provide resistance results when viral load is low. For repeated low-level viremia, an assay that detects resistance mutations in archived proviral DNA is available; however, clinical data are insufficient to recommend for or against its use in the patient care setting.

e. In patients with low-level viremia, clinicians should consult with an experienced HIV care provider; low-level viremia can be due to multiple causes, and its clinical effect is not clear.

Table 3: FDA-Approved Quantitative HIV-1 RNA Assays for Viral Load Monitoring

Test Name	Method	Lower and Upper Limits of Quantification (LOQ)
Abbott RealTime HIV-1 (Abbott Laboratories)	Real-time PCR	· 40 copies/mL [a] · 10,000,000 copies/mL
Cobas AmpliPrep/Cobas TaqMan HIV-1 Test, version 2.0 (Roche Diagnostics)	Real-time PCR	· 20 copies/mL · 10,000,000 copies/mL
Cobas HIV-1 quantitative NAT for use on Cobas 6800/8800 systems (Roche Diagnostics)	Real-time PCR	· 20 copies/mL · 10,000,000 copies/mL
Cobas TaqMan HIV-1 Test, v2.0 for use with the high pure system (Roche Diagnostics)	Real-time PCR	· 34 copies/mL · 10,000,000 copies/mL

Abbreviation: FDA, U.S. Food and Drug Administration; LOQ, limit of quantification; NAT, nucleic acid test, PCR, polymerase chain reaction.

Note:

a. This lower LOQ applies when 1.0 mL of plasma is used. When 0.5 and 0.2 mL of plasma are used, the lower LOQ is 75 copies/mL and 150 copies/mL, respectively.