HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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VIROLOGIC AND IMMUNOLOGIC MONITORING AND RESISTANCE ASSAYS

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE SEPTEMBER 2018

ALL RECOMMENDATIONS P.1

Virologic and Immunologic Monitoring

- Regular monitoring of HIV RNA levels remains the most accurate and meaningful measure of effective ART (see *Table 1. Virologic and Immunologic Monitoring for Non-Pregnant Patients* for recommended intervals). (A1)
- Clinicians should monitor HIV RNA levels and CD4 counts according to the recommended intervals in Table 1. Follow-up visits should be scheduled more frequently as clinically necessary to address non-HIV-related conditions, secondary prevention, and issues that may affect adherence to ART or retention in care, such as substance use, mental health disorders, unstable housing, or need for supportive services. (A2)
- Clinicians should assess response to ART using viral load assays. (A1)
- CD4 cell counts should not be used for diagnosis of HIV infection. (A1)
- 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 are often complex. (A3)
  - The NYSDOH AIDS Institute's Clinical Education Initiative line is available for phone consultation: 800-637-2342.

KEY POINTS

- Quarterly HIV RNA monitoring remains appropriate for patients with a recent history of non-adherence, 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.
- Resistance testing is recommended when patients are interrupting incompletely suppressive ART. Because of the rapid return of wild-type virus without selective pressure from ART, testing is preferred before cessation of treatment. In cases where the patient has already stopped therapy, testing should be performed as soon as practical and no more than 4 weeks after cessation, before the return of wild-type virus. Mutations detected in this setting may provide useful information, but the absence of mutations does not rule out their presence in minor variants.

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/
- HIV Resistance Response Database Initiative: https://www.hivrdi.org/
- Los Alamos National Laboratory HIV Databases: https://www.hiv.lanl.gov/content/index

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 • 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

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

ALL RECOMMENDATIONS *(continued from P.1)* **P.2**

Determining HIV Drug Resistance *continued*

- When determining the optimal regimen for achieving viral suppression, clinicians should:
  - Perform genotypic resistance testing that includes the protease and reverse transcriptase genes:
    - At baseline, regardless of whether ART is being initiated. (A2)
    - In ART-naïve patients before initiation of ART [a]. (A2)
    - In patients experiencing treatment failure [b] or incomplete viral suppression; such testing should be performed while patients are still on therapy, but no longer than 4 weeks after stopping ART, given the rapid return of wild-type virus. (A2)
  - Perform co-receptor tropism testing prior to initiation of a CCR5 antagonist. (A1)
  - In cases where integrase or fusion inhibitor resistance is suspected, obtain these tests as a supplement to protease and reverse transcriptase testing. (A2)

Notes:

a. In the settings of pregnancy and acute infection, treatment should not be withheld while awaiting the results of resistance testing; adjustments may be made to the regimen once resistance results are available. See the NYSDOH AI guideline *Diagnosis and Management of Acute HIV*.

b. Virologic failure is defined as >200 copies/mL. See the NYSDOH AI guideline *Virologic and Immunologic Monitoring*.

Table 1: Virologic and Immunologic Monitoring for Non-Pregnant Patients [a]		
At Baseline	**HIV RNA Levels (copies/mL)**	**CD4 Lymphocyte Count (cells/mm³)**
All patients	Yes (A1)	Yes (A1)
Treatment Monitoring	**HIV RNA Levels (copies/mL)**	**CD4 Lymphocyte Count (cells/mm³)**
Following (1) initiation of ART or (2) a change in ART regimen after virologic failure [b] with new resistance to prior ART	• Within 4 weeks of initiation of ART or change in regimen (A3) • At least every 8 weeks until complete suppression [c] is documented (A3)	• Repeat at 12 weeks and then every 4 months until CD4 >200 cells/mm³ on two measurements obtained at least 4 months apart (A2); then monitor as below once suppressed
Following a change in ART to simplify treatment regimen or reduce toxicity for patients with suppressed virus	• Within 4 weeks after change in regimen to ensure continued suppression (A3); then monitor as below for suppressed	• Monitor as below for suppressed
Patients on ART who achieve complete suppression [c]	• At least every 4 months after complete suppression (A3) • May extend intervals to every 6 months in selected stable patients with CD4 counts >200 cells/mm³ after 1 year of complete suppression (B2)	• **If CD4 ≤300 cells/mm³:** At least every 6 months (B3) • **If CD4 >300 to ≤500 cells/mm³:** At least every 12 months (B2) • **If CD4 >500 cells/mm³:** Further monitoring is optional (B3)
Patients on previously suppressive ART with new HIV RNA [d] above the lower limit of detection using a highly sensitive assay [c]	• **All patients:** Assess for drug-drug interactions (A3) and for adherence (A3) • **Patients with viral load ≥500 copies/mL:** Have patient return within 2 weeks to repeat viral load test (A2) and obtain resistance testing (AI); obtain CD4 count if not done within previous 6 months (B3) • **Patients with viral load <500 copies/mL:** Repeat viral load test within 4 weeks to differentiate low level transient viremia ("blip") from virologic failure [b,e]. (A2). If viral load remains detectable on repeat test, obtain CD4 count if not done within previous 6 months (B3) and consider resistance testing [f] (B3)	
Patients not on ART: According to NYSDOH recommendations, ART is recommended for all patients with HIV. (See the NYSDOH AI guideline *When to Initiate ART*.)	• **If CD4 ≤500 cells/mm³:** At least every 4 months (A3) • **If CD4 >500 cells/mm³:** At least every 6 months (A3) • Continue to discuss ART initiation (A1)	• **If CD4 ≤500 cells/mm³:** At least every 4 months (A3) • **If CD4 >500 cells/mm³:** At least every 6 months (A3) • Continue to discuss ART initiation (A1)

Notes:

a. For monitoring HIV RNA levels and CD4 counts in pregnant women with HIV, see DHHS/AIDSinfo > *Recommendations for the Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States*.

b. Virologic failure is defined as the inability to achieve or maintain suppression of viral replication to an HIV RNA level <200 copies/mL.

c. Complete suppression is generally considered below the lower limit of detection of a highly sensitive assay (<20 to <50 copies/mL).

d. Patients with repeated intermittent low level viremia ≤200 copies/mL over a period of years without demonstrated failure may continue routine testing intervals.

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

f. 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.

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

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This ¼-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Resistance Testing*. The full guideline is available at www.hivguidelines.org.