HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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DIAGNOSIS AND MANAGEMENT OF HIV-2 IN ADULTS

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JULY 2019

ALL RECOMMENDATIONS *Please see full guideline for additional information* P.1

Diagnosis of HIV-2

- To diagnose HIV-2 infection, clinicians should follow the steps in the *CDC/APHL HIV Diagnostic Testing Algorithm* and the recommendations in the NYSDOH AI guideline *HIV Testing*. (A1)
- In individuals who are confirmed to have HIV-2 antibodies, clinicians should perform a clinical evaluation for HIV-2 infection that is similar in scope to the evaluation of patients with HIV-1. (A1) HIV-2 antibodies are confirmed by a reactive result to an HIV-1/2 or HIV-1/2 Ag/Ab immunoassay and a positive result for HIV-2 antibodies on an FDA-approved supplemental HIV-1/2 Ab differentiation assay.

Treatment of HIV-2

- Clinicians should recommend ART for all individuals diagnosed with HIV-2. (A2†)
- Clinicians should not prescribe any NNRTI for treatment of HIV-2 infection. (A*)
- Clinicians should recommend a single-tablet regimen that includes 2 NRTIs plus an INSTI as the initial treatment for adults with HIV-2 who are not pregnant and not planning to become pregnant, including those with acute HIV-2 infection (see Table 1). (A2)
- For individuals with HIV-1/HIV-2 coinfection, clinicians should:
  - Perform HIV-1 drug resistance testing to guide the choice of an initial regimen or to modify a regimen if virologic failure develops. (A2)
  - Recommend an ART regimen that will suppress both viruses effectively. (A*)

Monitoring ART in Individuals With HIV-2

- For individuals who are newly diagnosed with HIV-2, clinicians should perform the same laboratory and diagnostic testing currently recommended for individuals with HIV-1, with the exception of drug resistance testing, which is not available. (A3)

Continued on P.2 ➔

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

Monitoring ART in Individuals With HIV-2, continued

- Testing includes CD4 cell count, HIV-2 viral load, creatinine clearance, and status of coinfections such as HBV, HCV, and TB.
- Clinicians should use HIV-2 viral load testing and CD4 cell count to determine the effectiveness of an ART regimen in patients with HIV-2. (A2)
- If HIV-2 viral load testing is not available, clinicians should suspect treatment failure if individuals experience a sustained decrease in CD4 cell count or have clinical disease progression. (A2)
- If a clinical practice in New York State cannot obtain HIV-2 viral load testing from the Wadsworth Laboratory, clinicians should refer individuals with HIV-2 to a practice that has the ability to access HIV-2 viral load testing from the Wadsworth Laboratory. (A3)

Pregnancy and HIV-2

- Clinicians should recommend ART for all pregnant individuals with HIV-2. (A2†)
  - Clinicians should recommend one of the ART regimens in Table 2. (A3)
  - Clinicians should not delay initiation of ART in pregnant individuals even if there is no or limited access to HIV-2 viral load testing. (A2†)
- In selecting an ART regimen for a pregnant individual with HIV-2, clinicians should **not** include:
  - Boosted ATV, because of its lack of efficacy against HIV-2. (A*)
  - DTG prior to 8 weeks (see DTG safety statement in full guideline). (A2†)
  - EFV and RPV, which are the NNRTIs recommended for treatment of HIV-1 during pregnancy, because of a lack of efficacy against HIV-2. (A*)

Pre- and Post-Exposure Prophylaxis (PEP and PrEP*) for HIV-2

- Clinicians should recommend TDF/FTC *and* RAL as PEP after HIV-2 exposure (3TC may be substituted for FTC). (A2†)

* *As with HIV-1, TDF/FTC is active against HIV-2 and could be used as a pre-exposure prophylaxis (PrEP) regimen to prevent infection with HIV-2.*

Abbreviations: 3TC, lamivudine; Ag/Ab, antigen/antibody; APHL, American Public Health Laboratories; ART, antiretroviral therapy; ATV, atazanavir; CDC, Centers for Disease Control and Prevention; DTG, dolutegravir; EFV, efavirenz; FDA, U.S. Food and Drug Administration; FTC, emtricitabine; HBV, hepatitis B virus; HCV, hepatitis C virus; INSTI, integrase strand inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; RPV, rilpivirine; TB, tuberculosis; TDF, tenofovir disoproxil fumarate

Wadsworth Center Bloodborne Viruses Laboratory Services

The Wadsworth Center offers HIV-2 viral load testing, free of charge, for patients and healthcare providers in New York State. To submit a specimen for HIV-2 viral load testing, please contact the Bloodborne Viruses Laboratory at (518) 474-2163. Specific services include:

- Quantitative detection of HIV-2 RNA in plasma samples for baseline and subsequent monitoring of response to ART in patients with confirmed HIV-2 infection.
- HIV-2 RNA viral load testing during pregnancy. Contact the lab at (518) 474-2163 early in the patient's pregnancy to discuss the protocol and timing for testing.
- HIV testing for all newborns exposed to HIV (HIV-1 and HIV-2) in New York State, free of charge.
  - If a sample is reactive for HIV-2 antibodies, the Pediatric HIV Testing Service will perform a reverse transcription polymerase chain reaction (RT-PCR) test for qualitative detection of HIV-2 RNA.

Note: HIV-2 phenotypic and genotypic resistance testing is not offered at Wadsworth or commercially available in the United States.

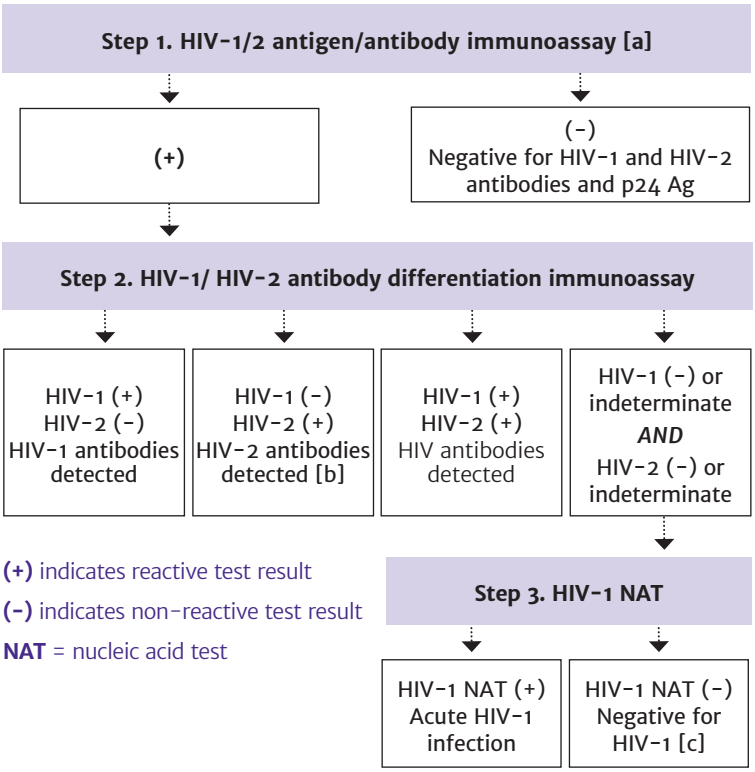
KEY POINTS

- In New York State, the standard of care for individuals with HIV-2 is to initiate and maintain ART in order to achieve an undetectable HIV-2 viral load.
  - If a protease inhibitor is being considered as part of an ART regimen for treatment of HIV-2, boosted darunavir is preferred.
  - Atazanavir **should not** be used because of its lack of potency in vitro against HIV-2.

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

This ¼-Folded Guide is a companion to the New York State Department of Health AIDS Institute guideline *Diagnosis and Management of HIV-2 in Adults*. The full guideline is available at www.hivguidelines.org.

Figure 2. Recommended HIV Testing Algorithm for Serum or Plasma Specimens [CDC. Updated January 2018]



1. Laboratories should conduct initial testing for HIV with an FDA-approved antigen/antibody immunoassay [a] that detects HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen to test for established HIV-1 and HIV-2 infection and for acute HIV-1 infection, respectively. No further testing is required for specimens that are non-reactive on the initial immunoassay. However, if there is a possibility of very early infection leading to a non-reactive initial antigen/antibody immunoassay, such as when recent HIV exposure is suspected or reported, then conduct an HIV-1 nucleic acid test (NAT), or request a new specimen and repeat the algorithm according to CDC guidance (1,4,5,6).
2. Specimens with a reactive antigen/antibody immunoassay result (or repeatedly reactive, if repeat testing is recommended by the manufacturer or required by regulatory authorities) should be tested with an FDA-approved supplemental antibody immunoassay that differentiates HIV-1 antibodies from HIV-2 antibodies. Reactive results on the initial antigen/antibody immunoassay and the HIV-1/HIV-2 antibody differentiation immunoassay should be interpreted as positive for HIV-1 antibodies, HIV-2 antibodies [b], or HIV antibodies, untypable (undifferentiated).
3. Specimens that are reactive on the initial antigen/antibody immunoassay and non-reactive or indeterminate on the HIV-1/HIV-2 antibody differentiation immunoassay should be tested with an FDA-approved HIV-1 NAT.
   - A reactive HIV-1 NAT result and non-reactive or indeterminate HIV-1/HIV-2 antibody differentiation immunoassay result indicates laboratory evidence of acute HIV-1 infection.
   - A negative HIV-1 NAT result and non-reactive or HIV-1 indeterminate antibody differentiation immunoassay result indicates an HIV-1 false-positive result on the initial immunoassay.
   - A negative HIV-1 NAT result and repeatedly HIV-2 indeterminate or HIV indeterminate antibody differentiation immunoassay result should be referred for testing with a different validated supplemental HIV-2 test (antibody test or NAT) or repeat the algorithm in 2 to 4 weeks, starting with an antigen/antibody immunoassay (3).
4. Laboratories should use this same testing algorithm, beginning with an antigen/antibody immunoassay on all serum or plasma specimens submitted for testing after a preliminary positive result from any rapid HIV test conducted in a CLIA-waived setting (7).

[a] The FDA-approved singe-use rapid HIV-1/HIV-2 antigen/antibody immunoassay can be used as the initial assay in the laboratory HIV testing algorithm for serum or plasma. If any instrumented antigen/antibody test is available, it is preferred due to its superior sensitivity for detecting HIV during acute infection (1,2).

[b] This includes specimens reported as HIV-2 positive with HIV-1 cross-reactivity (3).

[c] Refer to last bullet, item 3 above.

1) Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations https://stacks.cdc.gov/view/cdc/23447
2) Use of the Determine HIV 1/2 Ag/Ab Combo Test with Serum or Plasma in the Laboratory Algorithm for HIV Diagnosis https://stacks.cdc.gov/view/cdc/48472
3) Technical Update on HIV-1/2 Differentiation Assays https://stacks.cdc.gov/view/cdc/40790
4) Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm https:/stacks.cdc.gov/view/cdc/45930
5) Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV-United States, 2016 https://stacks.cdc.gov/view/cdc/38856
6) Web content: How Soon Can Clinicians Rule Out Infection? https://www.cdc.gov/hiv/testing/clinical/index.html
7) Web content: Clinical Laboratory Improvement Amendments https://wwwn.cdc.gov/clia/

TABLE 1: ART Regimens for Initial Treatment of Nonpregnant Adults With HIV-2*

PREFERRED REGIMENS

Single-Tablet Regimens	Comments
ABC/3TC/DTG [Triumeq]	· Initiate ***only*** in patients confirmed to be negative for HLA-B*5701. · Initiate ***only*** in patients with creatinine clearance (CrCl) ≥50 mL/min. · Consider underlying risk of coronary heart disease. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Clinicians should refer to the DHHS *Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States* when choosing an initial regimen for individuals of childbearing potential. · In patients with HIV/HBV coinfection, this regimen should be used in conjunction with other anti-HBV drugs.
TAF 25 mg/FTC/BIC [Biktarvy]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg of TAF, unboosted.

ALTERNATIVE REGIMENS

Single-Tablet Regimens	Comments
TAF 10 mg/FTC/COBI/DRV [Symtuza]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg TAF, boosted.
TAF 10 mg/FTC/COBI/EVG [Genvoya]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg of TAF, boosted with COBI.
Once-Daily Multi-Tablet Regimens	**Comments**
ABC/3TC *and* **RAL HD** [Epzicom *and* Isentress HD]	· Initiate ***only*** in patients confirmed to be negative for HLA-B*5701 and negative for HBsAg. · Consider underlying risk of coronary heart disease. · ABC/3TC once daily, RAL HD 1200 mg once daily dosed as two 600 mg HD tablets.
TAF/FTC *and* **DRV/RTV** [Descovy *and* Prezista *and* Norvir]	· Carefully consider drug-drug interactions with RTV. · Initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg TAF, boosted. Use with caution in individuals with stage 3 chronic kidney disease.
TAF/FTC *and* **DRV/COBI** [Descovy *and* Prezcobix]	· Carefully consider drug-drug interactions with COBI. · Initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg TAF, boosted. Use with caution in individuals with stage 3 chronic kidney disease.
TAF 25 mg/FTC *and* **DTG** [Descovy *and* Tivicay]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Contains 25 mg of TAF, unboosted. · Clinicians should refer to the DHHS *Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States* when choosing an initial regimen for individuals of childbearing potential.
TAF 25 mg/FTC *and* **RAL HD** [Descovy *and* Isentress HD]	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · To date, no clinical trials have been conducted with TAF; data are based on bioequivalence pharmacokinetic studies. · Contains 25 mg of TAF, unboosted. · TAF/FTC once daily and RAL HD 1200 mg once daily dosed as two 600 mg HD tablets.

TABLE 2: ART Regimens for Initial Treatment of Nonpregnant Adults With HIV-2 [1]

· ABC/3TC (Epzicom) [2] *OR* · TDF/FTC (Truvada)	*PLUS*	· RAL (Isentress) [3] *OR* · DRV/r (Prezista *and* Norvir) [3]

Drug name abbreviations key: 3TC, lamivudine; ABC, abacavir; DRV/r, darunavir/ritonavir; FTC, emtricitabine; RAL, raltegravir; TDF, tenofovir disoproxil fumarate

Notes:
1. Listed alphabetically.
2. Prescribe ABC/3TC only if the patient is HLA-B*5701 negative and HBsAg is negative.
3. Dosed twice daily.