HIV CLINICAL RESOURCE ¼-FOLDED GUIDE

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DIAGNOSIS AND MANAGEMENT OF HIV-2 IN ADULTS

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE OCTOBER 2021

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 ➔

← 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.

DRUG NAME ABBREVIATION KEY:

3TC: lamivudine; **ABC:** abacavir; **ATV:** atazanavir; **BIC:** bictegravir; **COBI:** cobicistat; **DRV:** darunavir; **DTG:** dolutegravir; **EFV:** efavirenz; **EVG:** elvitegravir; **FTC:** emtricitabine; **RAL:** raltegravir; **RPV:** rilpivirine; **TAF:** tenofovir alafenamide; **TDF:** tenofovir disoproxil fumarate

OTHER ABBREVIATIONS:

Ab: antibody; **Ag:** antigen; **ART:** antiretroviral therapy; **CrCl:** creatinine clearance; **HBsAg:** hepatitis B surface antigen; **HBV:** hepatitis B virus; **HCV:** hepatitis C virus; **INSTI:** integrase strand transfer inhibitor; **NNRTI:** non-nucleoside reverse transcriptase inhibitor; **NRTI:** nucleoside/nucleotide reverse transcriptase inhibitor; **TB:** tuberculosis

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 3. (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*)
  - EFV and RPV, 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 (PrEP 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†)
  - DTG can be used instead of RAL in a PEP regimen if the exposed individual is not pregnant; if the individual is of childbearing potential, effective birth control should be in use.

Note: *As with HIV-1, TDF/FTC is active against HIV-2 and could be used as a PrEP regimen to prevent infection with HIV-2.*

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.

TABLE 1: PREFERRED ART REGIMENS FOR INITIAL TREATMENT OF NONPREGNANT ADULTS WITH HIV-2

Regimen	Comments	Rating
Available as a Single-Tablet Formulation		
ABC/3TC/DTG (Triumeq)	· Initiate ***only*** in patients confirmed to be negative for HLA-B*701, including when a "rapid-start" or "test-and-treat" initiation of ART occurs before baseline laboratory test results are available. · Initiate ***only*** in patients with CrCl ≥30 mL/min. · Consider underlying risk of coronary heart disease. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food.	A1
3TC/DTG (Dovato)	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Do not use in patients with HBV coinfection. · Do not initiate before HIV resistance tests results are available. · Do not initiate in patients with NRTI resistance, including the M184V/I mutation. · Do not initiate in patients with baseline HIV RNA levels >500,000 copies/mL until additional study data are available. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food.	A1
TAF 25 mg/FTC/BIC (Biktarvy)	· Initiate ***only*** in patients with CrCl ≥30 mL/min [d]. · Contains 25 mg of TAF, unboosted [c]. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after BIC; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. · Documented DTG resistance after initiation in treatment-naive patients is rare.	A1
Available as a Multi-Tablet Regimen With Once-Daily Dosing		
TAF 25 mg/FTC or TDF 300 mg/FTC *and* **DTG** (Descovy or Truvada *and* Tivicay)	· For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg of TAF, unboosted. · For TDF/FTC, initiate ***only*** in patients with CrCl ≥50 mL/min. · For TDF/FTC, consider bone mineral density. · Magnesium- or aluminum-containing antacids may be taken 2 hours before or 6 hours after DTG; calcium-containing antacids or iron supplements may be taken simultaneously if taken with food. · Documented DTG resistance after initiation in treatment-naive patients is rare.	A1
TAF 25 mg/FTC or TDF 300 mg/FTC *and* **RAL HD** (Descovy or Truvada *and* Isentress HD)	· For TAF/FTC, initiate ***only*** in patients with CrCl ≥30 mL/min. · Contains 25 mg of TAF, unboosted. · For TDF/FTC, initiate only in patients with CrCl ≥50 mL/min. · For TDF/FTC, consider bone mineral density. · Administer as TAF/FTC or TDF/FTC once daily and RAL HD 1200 mg once daily, dosed as two 600 mg HD tablets. · To date, no clinical trials have been conducted with TAF and RAL; data are based on bioequivalence pharmacokinetic studies. · Magnesium- or aluminum-containing antacids are contraindicated; coadministration of calcium-containing antacids is not recommended with RAL HD.	A2

TABLE 2: ALTERNATIVE ART REGIMENS FOR INITIAL TREATMENT OF NONPREGNANT ADULTS WITH HIV-2

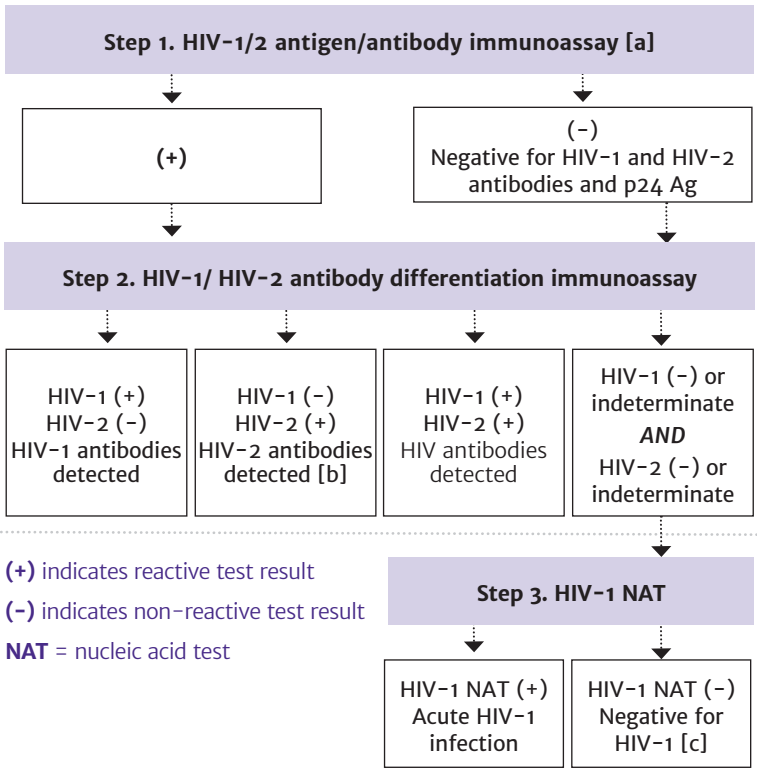
Regimen	Comments	Rating
Available as a Single-Tablet Formulation		
TAF 10 mg/FTC/ DRV/COBI (Symtuza)	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg TAF, boosted.	B2
TAF 10 mg/FTC/ EVG/COBI (Genvoya)	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg of TAF, boosted with COBI. · Separate dosing of cation-containing (Ca++, AL, Mg) antacids by 2 hours, either before or after dose of EVG.	B1
Available as a Multi-Tablet Regimen With Once-Daily Dosing		
TAF 25 mg/FTC or TDF 300 mg/FTC *and* **RAL** (Descovy or Truvada *and* Isentress)	· Initiate TAF/FTC ***only*** in patients with CrCl ≥30 mL/min. · Initiate TDF/FTC ***only*** in patients with CrCl ≥50 mL/min. · For TDF/FTC, consider bone mineral density. · Administer as TAF/FTC or TDF/FTC once daily and RAL 400 mg twice daily. · Magnesium- or aluminum-containing antacids are contraindicated; calcium-containing antacids are acceptable with RAL.	B3

TABLE 3: ART REGIMENS FOR INITIAL TREATMENT OF PREGNANT ADULTS WITH HIV-2*

· ABC/3TC (Epzicom) if HLA-B*5701 is negative and HBsAg is negative **OR** · TDF/FTC (Truvada)	**AND**	· RAL (Isentress) twice daily **OR** · DRV/r (Prezista *and* Norvir) twice daily

*Listed alphabetically; for specific details, see NYSDOH AI guideline *Selecting an Initial ART Regimen > Specific Factors to Consider and Discuss With Patients* and drug package inserts.

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.