HIV CLINICAL RESOURCE ▪ ¼-FOLDED GUIDE

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DIAGNOSIS AND MANAGEMENT OF HIV-2 IN ADULTS

NYSDOH AIDS INSTITUTE HIV CLINICAL GUIDELINE JUNE 2023

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

Diagnosis of HIV-2

- To diagnose HIV-2 infection, clinicians should follow the standard HIV laboratory testing algorithm. (A1) (see Figure)
- 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 Ag/Ab combination immunoassay and a positive result for HIV-2 Abs on an FDA-approved supplemental HIV-1/HIV-2 Ab differentiation immunoassay.

Treatment of HIV-2

- Clinicians should recommend ART for all individuals diagnosed with HIV-2. (A2†)
- Before initiating ART in patients with HIV-2, clinicians should perform all of the standard laboratory testing recommended for patients with HIV-1 except for HIV drug resistance testing, which is not available. (A3)
  - Testing includes CD4 cell count, HIV-2 viral load, creatinine clearance, and status of coinfections such as HBV, HCV, and TB.
- 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 Tables 1 and 2). (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*)

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

Monitoring ART

- Clinicians should monitor the virologic and immunologic status of patients with HIV-2 by performing viral load and CD4 count testing at the same intervals recommended for patients with HIV-1.
  - Because HIV-2 viral load testing is available in NYS only through the Wadsworth Center, clinicians who do not have access to Wadsworth Center laboratory testing services should refer patients to practices that do. (A3)
  - Clinicians should continue to monitor CD4 count every 6 months in all patients with HIV-2, even those with persistent viral suppression. (B2)
- If HIV-2 viral load testing is not available, clinicians should suspect treatment failure if patients experience a sustained decrease in CD4 count, defined as a 30% decrease in CD4 count or a 3-point decrease in CD4%, confirmed by repeat testing (B2), or have clinical disease progression. (A2)
- If patients with HIV-2 have either virologic or immunologic treatment failure, clinicians should consult with an experienced HIV-2 clinical management specialist. (A3)

Management of HIV-2 in Pregnancy

- 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 ART initiation 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*)

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†)
  - DTG can be used instead of RAL in a PEP regimen.

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

Wadsworth Center Bloodborne Virus Laboratory

The Wadsworth Center Bloodborne Viruses Laboratory 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, Pediatric HIV Testing (518-486-9605) will perform a reverse transcription polymerase chain reaction test for qualitative detection of HIV-2 RNA.

Note: HIV-2 phenotypic and genotypic resistance testing is not offered at the Wadsworth Center 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 to achieve an undetectable HIV-2 viral load.
- If a protease inhibitor is being considered as part of an ART regimen for HIV-2 treatment, boosted darunavir is preferred.
- Atazanavir **should not be used** because of its lack of potency in vitro against HIV-2.

DRUG NAME ABBREVIATION KEY:

3TC: lamivudine; **ABC:** abacavir; **ATV:** atazanavir; **BIC:** bictegravir; **CAB:** cabotegravir; **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; **Al:** aluminum; **ART:** antiretroviral therapy; **Ca:** calcium; **CrCl:** creatinine clearance; **HBsAg:** hepatitis B surface antigen; **HBV:** hepatitis B virus; **HCV:** hepatitis C virus; **INSTI:** integrase strand transfer inhibitor; **Mg:** magnesium; **NNRTI:** non-nucleoside reverse transcriptase inhibitor; **NRTI:** nucleoside/nucleotide reverse transcriptase inhibitor; **TB:** tuberculosis

← 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.

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. · Mg- or Al-containing antacids may be taken 2 hours before or 6 hours after DTG; Ca-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. · Contains 25 mg of TAF, unboosted. · Mg- or Al-containing antacids may be taken 2 hours before or 6 hours after BIC; Ca-containing antacids oriron supplements may be taken simultaneously if taken with food.	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. · Documented DTG resistance after initiation in treatment-naive patients is rare. · Mg- or Al-containing antacids may be taken 2 hours before or 6 hours after DTG; Ca-containing antacids or iron supplements may be taken simultaneously if taken with food.	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 1,200 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. · Mg- or Al-containing antacids are contraindicated; coadministration of Ca-containing antacids is not recommended with RAL HD.	A2

Table 2: Alternative ART Regimens for Initial Treatment of Nonpregnant Adults With HIV-2

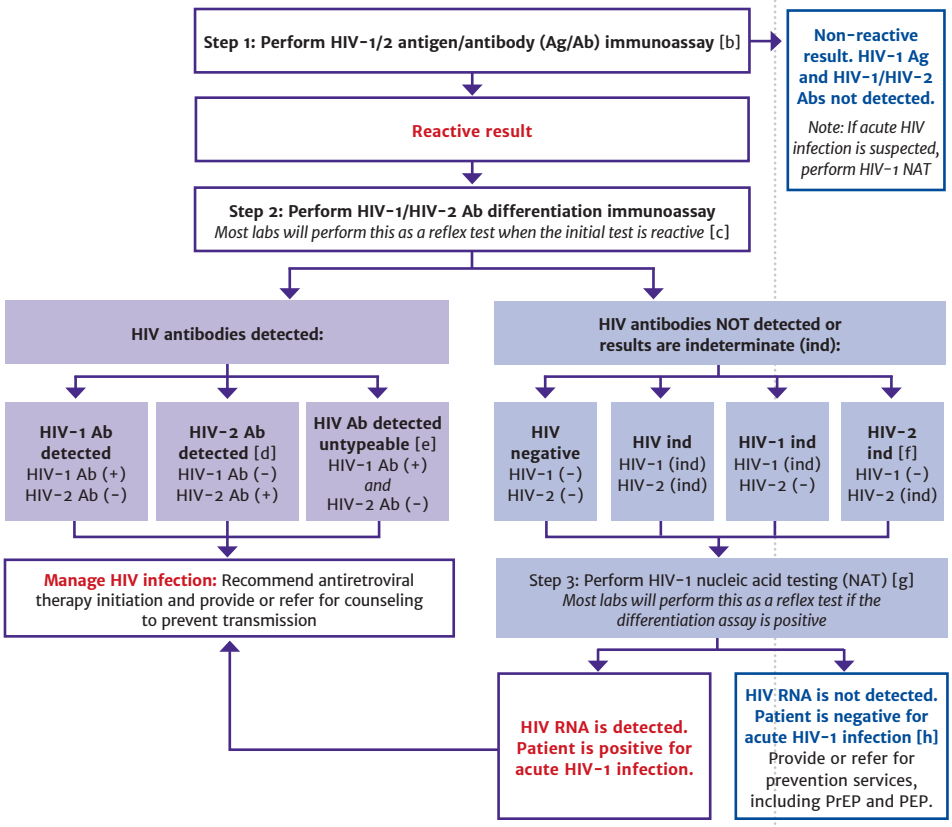
Regimen	Comments	Rating
Available as a Single-Tablet Formulation		
TAF 10 mg/FTC/DRV/COBI (Symtuza)	· Initiate ***only*** in patients with CrCl ≥30 mL/min. · Carefully consider drug-drug interactions with COBI. · Contains 10 mg TAF, boosted with COBI.	B2
TAF 10 mg/FTC/EVG/COBI (Genvoya)	· Initiate ***only*** 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 Al-, Ca-, and Mg-containing antacids by 2 hours, either before or after EVG.	B1
Available as a Multi-Tablet Regimen With Twice-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. · Al- or Mg-containing antacids are contraindicated; Ca-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** · TAF/FTC (Descovy) **OR** · TDF/FTC (Truvada) **OR** · TDF/3TC (multiple brands)	**AND**	· DTG (Tivicay) **OR** · 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: HIV Laboratory Testing Algorithm [a]



Abbreviations: Ab, antibody; Ag, antigen; APHL, Association of Public Health Laboratories; CDC, Centers for Disease Control and Prevention; ind, indeterminate; FDA, U.S. Food and Drug Administration; NAT, nucleic acid test; NYSDOH, New York State Department of Health; PEP, post-exposure prophylaxis; PrEP, pre-exposure prophylaxis.

Notes:

a. Adapted from CDC *2018 Quick reference guide: Recommended laboratory HIV testing algorithm for serum or plasma specimens* and *APHL Suggested reporting language for the HIV laboratory diagnostic testing algorithm*.
b. APHL and CDC continue to recommend that laboratories use an FDA-approved instrumented HIV-1/HIV-2 Ag/Ab immunoassay as the initial assay in the laboratory HIV testing algorithm for serum or plasma due to their superior sensitivity for detecting acute HIV infection. However, the FDA-approved single-use rapid HIV-1/HIV-2 Ag/Ab immunoassay may be used as the initial assay in the laboratory HIV testing algorithm for serum or plasma if an instrumented assay is not available.
c. Become familiar with the laboratory's internal testing algorithm and results-reporting policies. Many labs will reflex additional screening steps (such as HIV Ab differentiation immunoassay and HIV RNA) on the original sample without supplemental orders. Other labs may require additional samples or supplemental orders to complete all steps in the algorithm.
d. This includes specimens reported as HIV-2 positive with HIV-1 cross-reactivity.
e. Further testing may be performed to determine type.
f. Per the Geenius package insert, specimens with this final assay interpretation should be retested with a new cartridge. If the final assay interpretation is again HIV-2 indeterminate, it should be reported as such and followed with an HIV-1 NAT.
g. Most laboratories reflex directly to an HIV-1 RNA test without requiring an additional test order or new specimen, either by performing the test in-house or referring the specimen to another laboratory. If the laboratory is unable to or does not automatically reflex directly to the RNA test, clinicians should order an HIV-1 RNA test as soon as possible. To reflex directly to an HIV-1 RNA test, a test kit approved by either the FDA or NYSDOH to aid in diagnosing HIV-1 infection is required. If HIV-1 RNA is detected, acute HIV-1 is present, and clinicians should proceed with clinical evaluation. If no HIV-1 RNA is detected, the initial immunoassay result is presumed false positive.
h. 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) if available. Alternatively, redraw and repeat algorithm in 2 to 4 weeks to assess HIV-2 infection.