

# Early (Acute and Recent) HIV Infection

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| Panel's Recommendations                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| <ul style="list-style-type: none"> <li>Antiretroviral therapy (ART) is recommended for all people with HIV, including those with early<sup>a</sup> HIV infection <b>(AI)</b>. ART should be initiated as soon as possible after HIV diagnosis <b>(AII)</b>.</li> <li>The goals of ART are to suppress plasma HIV RNA to undetectable levels <b>(AI)</b>, prevent transmission of HIV <b>(AI)</b>, and preserve immune function <b>(AIII)</b>. Monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and antiretroviral (ARV) drug-related adverse effects should be done as recommended for people with chronic HIV infection <b>(AII)</b>.</li> <li>A blood sample for genotypic resistance testing should be sent to the laboratory before initiating ART <b>(AIII)</b>.             <ul style="list-style-type: none"> <li>Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes <b>(AIII)</b> for all people with early HIV.</li> <li>Genotype testing for integrase strand transfer inhibitor (INSTI) resistance should be performed for those who acquire HIV during or after the use of long-acting cabotegravir (CAB-LA) as pre-exposure prophylaxis (PrEP), if transmitted INSTI resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) <b>(AIII)</b>.</li> </ul> </li> <li>ART can be initiated before drug-resistance test results are available.             <ul style="list-style-type: none"> <li>For those without a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended<sup>b</sup> <b>(AIII)</b>:                 <ul style="list-style-type: none"> <li>Bictegravir (BIC)/tenofovir alafenamide (TAF)/emtricitabine (FTC)</li> <li>Dolutegravir (DTG) with (TAF or tenofovir disoproxil fumarate [TDF])<sup>c</sup> plus (FTC or lamivudine [3TC])</li> </ul> </li> <li>For those with a history of CAB-LA use as PrEP, genotype testing before starting ART should include screening for INSTI-resistance mutations <b>(AIII)</b>.                 <ul style="list-style-type: none"> <li>A regimen of cobicistat- (COBI)<sup>d</sup> or ritonavir-boosted darunavir (DRV) with (TAF or TDF)<sup>b</sup> plus (FTC or 3TC) is recommended while awaiting the results of the genotype testing <b>(AIII)</b>.</li> <li>Use of an empiric INSTI-containing regimen is not recommended unless genotype testing shows no evidence of INSTI resistance <b>(AIII)</b>. This is because INSTI resistance may be present in those who acquire HIV during and possibly after the use of CAB-LA as PrEP.</li> </ul> </li> </ul> </li> <li>In people with HIV RNA levels <math>\geq 200</math> copies/mL and who are taking PrEP, immediate initiation of an effective HIV treatment regimen is recommended while awaiting confirmation of HIV diagnosis <b>(AIII)</b>.</li> <li>Pregnancy testing should be performed in women of childbearing potential before initiating ART <b>(AIII)</b>.</li> <li>When the results of drug-resistance tests are available, the treatment regimen can be modified if needed <b>(AII)</b>.</li> <li>Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression <b>(AIII)</b>.</li> </ul> |
| <p><b>Rating of Recommendations:</b> A = Strong; B = Moderate; C = Weak</p> <p><b>Rating of Evidence:</b> I = Data from randomized controlled trials; II = Data from well-designed non-randomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |

<sup>a</sup> Early infection represents either acute or recent ( $\leq 6$  months) infection.

<sup>b</sup> Because of the low rates of transmitted INSTI resistance in the United States at present, even when there is suspicion that HIV was acquired from a partner with virologic failure while on an INSTI, an INSTI-based regimen can be started while awaiting the results of the INSTI genotype.

<sup>c</sup> TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

<sup>d</sup> COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

## Introduction

Acute HIV infection occurs soon after transmission and is typically characterized by the lack of anti-HIV antibodies and the presence of viremia, which can be detected by an HIV RNA test or p24 antigen test. Recent HIV infection is considered the period of  $\leq 6$  months after infection during which anti-HIV antibodies become detectable. Throughout this section, the term “early HIV infection” is used to refer to either acute or recent HIV infection. People with acute HIV infection may experience fever, lymphadenopathy, pharyngitis, skin rash, myalgia, arthralgia, and other symptoms; however, illness is generally nonspecific, and people can be asymptomatic or experience relatively mild symptoms.<sup>1-6</sup> Clinicians may fail to recognize acute HIV infection because its manifestations are similar to those of many other viral infections, such as COVID-19, influenza, and infectious mononucleosis. [Table 15](#) below provides clinicians with guidance to recognize, diagnose, and manage acute HIV infection.

## Diagnosing Acute HIV Infection

Health care providers should consider a diagnosis of acute HIV infection in a person who has a suggestive clinical syndrome or in asymptomatic individuals who report recent engagement in activities that may put them at high risk of HIV acquisition (see [Table 15](#) below).<sup>7</sup> Individuals may not always disclose high-risk activities or perceive that such activities put them at risk for HIV acquisition. Thus, even in the absence of reported high-risk activities, health care providers should have a low threshold for considering a diagnosis of acute HIV infection. Health care visits to emergency departments provide an opportunity for health care providers to screen for acute or established HIV infection, as well as other sexually transmitted infections. Since 2019, the [United States Preventive Services Task Force](#) has recommended routine screening for HIV in adolescents and adults aged 15 to 65 years (Grade A recommendation). Testing of remnant blood specimens from an emergency department identified acute HIV infection in approximately 5 of 499 (1%) people presenting with flu-like symptoms.<sup>8</sup> Acute HIV infection was also diagnosed in 7 of 563 (1.2%) people presenting for evaluation of possible mononucleosis with negative heterophile antibody tests.<sup>9</sup> A study of HIV screening in nine emergency departments in six U.S. cities found that a new HIV diagnosis was made in 0.4% of 214,524 adolescents and adults, of whom 14.5% had acute HIV infection.<sup>10</sup> Current statistics on the prevalence of HIV in geographical areas in the United States can be found on the [AIDSVu](#) and Centers for Disease Control and Prevention (CDC) [AtlasPlus](#) websites.

The recommended initial laboratory HIV testing algorithm includes combination immunoassays that detect HIV-1 and HIV-2 antibodies, as well as HIV p24 antigen (Ag/Ab assays),<sup>11</sup> primarily due to their enhanced ability to detect acute HIV infection. Specimens that are reactive on an initial Ag/Ab assay should be tested with an immunoassay that differentiates HIV-1 from HIV-2 antibodies. Specimens that are reactive on the initial assay and have either a negative or indeterminate antibody differentiation test result should be tested for quantitative or qualitative HIV RNA; an undetectable HIV RNA test result indicates that the original Ag/Ab test result was a false positive. Detection of HIV RNA in this setting indicates that acute HIV infection is highly likely.<sup>11</sup> People presenting to care during the earliest days following HIV infection may have yet to develop a positive p24 Ag response, which typically occurs with viral load levels of  $>20,000$  to 30,000 copies/mL. In clinical settings with a

high probability of infection, quantitative or qualitative HIV RNA testing should be considered even if the HIV Ag/Ab test result is negative. HIV infection should be confirmed by repeat quantitative HIV RNA testing or subsequent testing to document HIV antibody seroconversion. People who receive antiretroviral therapy (ART) during acute or very early HIV infection may demonstrate weaker reactivity to screening antibody assays or incomplete HIV antibody evolution; may remain non-reactive to confirmatory antibody assays; and in the setting of sustained virologic suppression, may have complete or partial seroreversion.<sup>12-16</sup>

Providers should be aware that even a low-positive quantitative HIV RNA level (e.g., <200 copies/mL but detectable) in the setting of a negative or indeterminate antibody test result is consistent with acute HIV infection. When a low-positive quantitative HIV RNA test result is present at this level, the HIV RNA test should be repeated on a new blood specimen to confirm the diagnosis. Repeated false-positive HIV RNA test results are unlikely.<sup>2</sup> HIV RNA levels in acute infection are generally very high (e.g., >100,000 copies/mL)<sup>1,2,4</sup>; however, levels may be <200 copies/mL in the earliest weeks following infection as viral load continues to rise. In rare cases, however, such low HIV RNA levels also may represent a false-positive result. The previously proposed threshold of <3,000 copies/mL is based on historical data, which used laboratory methods that are now considered obsolete.<sup>17</sup> Improvements in plasma viral load methodology suggest that any positive result on a quantitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result may be consistent with acute HIV infection. Some health care facilities may still be using HIV testing algorithms that test only for anti-HIV antibodies. In such settings, when acute HIV infection is suspected in a person with a negative or indeterminate HIV antibody test result, a quantitative or qualitative HIV RNA test should be performed. A negative or indeterminate HIV antibody test result and a positive HIV RNA test result (<200 copies/mL)<sup>18</sup> indicate that acute HIV infection is highly likely.

## **Diagnosing Acute HIV Infection in People Taking Pre-Exposure Prophylaxis**

Four antiretroviral (ARV) options—oral emtricitabine (FTC) with either tenofovir alafenamide (TAF) or tenofovir disoproxil fumarate (TDF), intramuscular long-acting cabotegravir (CAB-LA), or subcutaneous lenacapavir—are now available for HIV pre-exposure prophylaxis (PrEP). People who acquire HIV while taking PrEP may sometimes have ambiguous HIV test results. A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating ART. Important considerations include the following:

- In people with HIV RNA level  $\geq 200$  copies/mL who are taking PrEP, immediate initiation of an effective HIV treatment regimen<sup>18</sup> is recommended while awaiting confirmation of HIV diagnosis **(AIII)**.
- In people taking PrEP who have a negative HIV antibody test result and a low-positive quantitative HIV RNA test result (<200 copies/mL), a confirmatory HIV antibody test and repeat quantitative plasma HIV RNA test should be performed, and results should be available before initiating ART.
- In rare cases, particularly when PrEP is transitioned to an ARV regimen and HIV RNA and antibody diagnostic testing are inconclusive, HIV DNA testing may be of value.<sup>19</sup> Options for confirming HIV infection and managing such cases are areas of evolving science summarized by the CDC.<sup>19</sup> Clinicians seeking urgent advice can contact the [Clinical Consultation Center's PrEP Service](#) at 1-855-HIV-PREP (or 1-855-448-7737).

## Acute HIV Infection in People Taking Long-Acting Cabotegravir for Pre-Exposure Prophylaxis

In the HPTN 083 trial, a pivotal trial of CAB-LA versus TDF/FTC for HIV PrEP with more than 2,000 participants enrolled in each arm, 25 incident cases of HIV were identified in the CAB-LA arm compared to 72 cases in the TDF/FTC arm.<sup>20,21</sup> Selection of a potent ARV regimen in people who develop acute HIV infection while taking CAB-LA for PrEP should consider that injectable cabotegravir (CAB) may remain detectable after treatment discontinuation, for up to 3 years in men and 4 years in women.<sup>22</sup> This long pharmacokinetic tail may contribute to the selection of drug-resistant variants in the setting of incident infection. In an extended analysis of HPTN 083, 34 cases of HIV infection were reported in the CAB-LA arm, with 6 of these cases occurring despite on-time CAB-LA injections.<sup>23,24</sup> Detection of HIV infection was delayed in 15 of 32 cases and was associated with waxing and waning HIV Ag/Ab, HIV antibody, and qualitative and quantitative HIV RNA test results (i.e., fluctuating between reactive/non-reactive, detectable/non-detectable).<sup>23</sup> Major resistance to an integrase strand transfer inhibitor (INSTI) occurred in 10 of the 32 cases evaluated. All 10 participants with INSTI resistance in the CAB-LA arm received their last CAB dose within 6 months of their initial HIV-positive site visit. While the risk of acquired INSTI resistance appears to wane after 6 months, this trend is based on few observations. These data reinforce the importance of screening for INSTI-resistance mutations when acute HIV infection is diagnosed in people taking CAB-LA or with a history of prior CAB-LA PrEP use **(AIII)**.

## Treating Early HIV Infection

The goals of ART during early HIV infection are to suppress plasma HIV RNA to undetectable levels **(AI)**, prevent the transmission of HIV **(AI)**, and preserve immune function **(AIII)**.<sup>25-27</sup> Importantly, as with chronic HIV infection, an individual's barriers to ART adherence and appointments should be assessed at the time of ART initiation (see [Adherence to the Continuum of Care](#)). ART should be initiated as soon as possible after a positive qualitative or quantitative HIV RNA test result **(AII)**. Same-day or rapid ART initiation in people with acute HIV has been shown to be safe, acceptable, and effective.<sup>28</sup> It is important to collect a new blood specimen for a confirmatory HIV antibody test and quantitative plasma HIV RNA test to verify the HIV diagnosis. Given the sensitivity of current HIV RNA assays,<sup>29</sup> a positive result by quantitative or qualitative plasma HIV RNA testing in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. HIV treatment does not need to be delayed while awaiting confirmation of HIV diagnosis. Some individuals may not accept their diagnosis or may decline ART initially for other reasons. Individuals who do not begin ART immediately should be maintained in care, and every effort should be made to initiate therapy as soon as they are ready.

Clinical trial data indicate that individuals who are treated during early HIV infection may experience immunologic and virologic benefits.<sup>26,30-41</sup> In addition, early HIV infection is considered a period of high infectivity,<sup>42</sup> and early ART substantially reduces the risk of HIV transmission.<sup>43-46</sup>

## Drug-Resistance Testing in the Setting of Early HIV Infection

Prior to the widespread use of INSTIs, data from the United States and Europe demonstrated that transmitted virus strains with resistance to at least one ARV drug were present in up to 16% of people with HIV.<sup>47,48</sup> In one study, 21% of isolates from people with acute HIV infection demonstrated resistance to at least one ARV drug, most commonly non-nucleoside reverse transcriptase inhibitors (NNRTIs).<sup>49-51</sup> The rate of transmitted INSTI resistance was reported to be ≤2.5% of the samples tested, and <0.5% with second-generation INSTIs.<sup>52-55</sup> Before initiating ART in a person with early HIV infection, a blood specimen should be sent for standard genotypic drug-resistance testing for mutations in the reverse transcriptase and protease genes **(AIII)**. Genotype

testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis occurs after receiving an INSTI-based regimen for post-exposure prophylaxis (PEP) **(AIII)**.<sup>22</sup>

Treatment should not be delayed pending resistance-test results. The test results should be used to modify the ARV regimen if necessary **(AII)**. In people with no history of CAB-LA use or use of an INSTI-based regimen for PEP, the Panel on Antiretroviral Guidelines for Adults and Adolescents does not currently recommend genotype testing for INSTI resistance given the low rate of transmitted INSTI resistance and the high barrier to resistance of bictegravir (BIC) and dolutegravir (DTG), unless transmitted INSTI resistance is a concern **(AIII)**.

## Considerations for Preventing HIV Transmission During Early HIV Infection

People with early HIV infection have a higher likelihood of sexual transmission of HIV to others. Prompt initiation of ART and sustained viral suppression to <200 copies/mL can prevent transmission of HIV to sexual partners. Individuals starting ART should use another form of prevention (e.g., condoms, PrEP for partners who are HIV negative, sexual abstinence) for at least the first 6 months of treatment and until they have a documented viral load of <200 copies/mL **(AII)**. Many experts would recommend confirming sustained viral suppression before assuming no risk of sexual transmission of HIV **(AIII)** (see [Antiretroviral Therapy to Prevent Sexual Transmission of HIV](#)).

## Antiretroviral Regimens for Early HIV Infection

ART should be initiated with one of the combination regimens recommended for people with chronic HIV infection **(AIII)** (see [What to Start](#)). Providers should inform individuals starting ART of the importance of adherence in achieving and maintaining viral suppression **(AIII)**. If available, the results of ARV drug-resistance testing or the resistance pattern of the source person's virus should be used to guide selection of the regimen. All women of childbearing potential should undergo a pregnancy test before initiating ART **(AIII)**.

For individuals who have not received CAB-LA as PrEP prior to diagnosis of acute HIV, one of the following INSTI-based regimens is recommended **(AIII)**:

- BIC/TAF/FTC
- DTG with (TDF or TAF) plus (3TC or FTC)

DTG and BIC are good treatment options because transmitted resistance to second-generation INSTIs in the United States is rare at present and both BIC and DTG have a high barrier to resistance.

For individuals who acquire HIV during and after the use of CAB-LA as PrEP:

- While awaiting integrase genotype results, the use of an INSTI-based regimen **is not recommended (AIII)**. The recommended regimen, until resistance testing confirms the absence of INSTI-resistance mutations, is a cobicistat (COBI)- or ritonavir (RTV)-boosted darunavir (DRV) with (TAF or TDF) plus (FTC or 3TC) **(AIII)**.

A pharmacologically boosted protease inhibitor (PI)-based regimen (e.g., boosted DRV) is an option because resistance to PIs emerges slowly, and clinically significant transmitted resistance to PIs is uncommon. Therefore, boosted DRV plus (TAF or TDF) plus (FTC or 3TC) is generally recommended in this setting. Baseline laboratory testing recommended for individuals with chronic

HIV infection should be performed (see [Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy](#)). Individuals with hepatitis B virus/HIV coinfection should receive TDF/FTC or TAF/FTC as part of their ARV regimen.

Given the increasing use of TDF/FTC<sup>56-58</sup> and TAF/FTC as PrEP,<sup>59,60</sup> early HIV infection may be diagnosed in some people while they are taking TDF/FTC or TAF/FTC. In this setting, drug-resistance test results are particularly important; however, these regimens remain reasonable treatment options pending drug-resistance test results.

Abacavir/3TC **is not recommended** for treatment of acute HIV infection unless the person is known to be HLA-B\*5701-negative, and this information is rarely available in people with acute HIV infection. Additionally, due to relatively high rates of transmitted drug resistance for NNRTIs, agents in this drug class **are not recommended** as a component in the regimen of people initiating ART before the results of drug-resistance tests are available.

## Treatment Regimens for Early HIV Infection During Pregnancy

All women of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test **(AIII)**. Because early HIV infection, especially in the setting of high-level viremia, is associated with a high risk of perinatal transmission, all pregnant women with HIV should start combination ART as soon as possible to prevent perinatal transmission **(AI)**. COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters. For more information on the safety and efficacy of ARV use in pregnancy, refer to the [Perinatal Guidelines](#).

## Follow-Up After Antiretroviral Therapy Initiation

After ART initiation, monitoring of plasma HIV RNA levels, CD4 T lymphocyte cell counts, and adverse effects should be performed as described in [Laboratory Testing for Initial Assessment and Monitoring of People With HIV Receiving Antiretroviral Therapy](#) (i.e., HIV RNA testing 2–8 weeks after ART initiation, then every 4–8 weeks until viral suppression and every 3–4 months thereafter) **(AII)**.

**Table 15. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection**

| Suspicion of Acute HIV Infection                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
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| <ul style="list-style-type: none"> <li>Health care providers should consider the possibility of acute HIV infection in people with the signs, symptoms, or laboratory findings described below and in asymptomatic people with a possible acute (within 2–6 weeks) exposure to HIV.<sup>a</sup> <ul style="list-style-type: none"> <li>Signs, symptoms, or laboratory findings of acute HIV infection may include but are not limited to, one or more of the following: fever, lymphadenopathy, skin rash, myalgia, arthralgia, headache, diarrhea, pharyngitis, oral ulcers, leucopenia, thrombocytopenia, and transaminase elevation.</li> <li>High-risk exposures include sexual contact with someone who has HIV or is at risk of HIV infection, sharing needles, syringes, or equipment for drug preparation or injection, or any situation where a person's mucous membranes or broken skin come into contact with bodily fluids that may carry HIV.</li> </ul> </li> </ul> <p><b>Differential Diagnosis</b></p> <ul style="list-style-type: none"> <li>The differential diagnosis of acute HIV infection may include but is not limited to, viral illnesses such as COVID-19, EBV and non-EBV (e.g., CMV) infectious mononucleosis syndromes, influenza, viral hepatitis, streptococcal infection, or syphilis. Diagnosis of any STI should prompt HIV testing and consideration of acute HIV infection.</li> </ul> |
| Testing to Diagnose or Confirm Acute HIV Infection                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| <ul style="list-style-type: none"> <li>Acute HIV infection is defined as detectable HIV RNA or p24 antigen (the specific antigen used in currently available HIV-1/2 Ag/Ab combination assays) in the setting of a negative or indeterminate HIV antibody test result.</li> <li>A reactive HIV antibody test result or Ag/Ab combination test result must be followed by supplemental confirmatory testing.</li> <li>A negative or indeterminate HIV antibody test result in a person with a reactive Ag/Ab test result or in whom acute HIV infection is suspected requires plasma HIV RNA testing to diagnose acute HIV infection.</li> <li>A positive result on a quantitative or qualitative plasma HIV RNA test in the setting of a negative or indeterminate antibody test result indicates that acute HIV infection is highly likely. In this case, the diagnosis of HIV infection should be confirmed by subsequent documentation of HIV antibody seroconversion.</li> <li>A positive HIV Ag/Ab test result or a positive HIV RNA test result in the setting of a negative HIV antibody test result in a person taking PrEP should prompt immediate confirmation of HIV diagnosis. It is important to collect a new blood specimen to verify the HIV diagnosis before initiating HIV treatment.</li> </ul>                                                                                                         |
| Antiretroviral Therapy After Diagnosis of Early HIV Infection                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| <ul style="list-style-type: none"> <li>ART is recommended for all people with HIV, including those with early HIV infection <b>(AI)</b>. ART should be initiated as soon as possible after HIV diagnosis <b>(AII)</b>.</li> <li>Once initiated, the goals of ART are to achieve sustained plasma virologic suppression, prevent HIV transmission <b>(AII)</b>, and preserve immune function <b>(AIII)</b>.</li> <li>All women of childbearing potential who receive a diagnosis of early HIV infection should have a pregnancy test <b>(AIII)</b>.</li> <li>Pregnant women with early HIV infection should begin ART as soon as possible for their own health and to prevent perinatal transmission of HIV <b>(AI)</b>.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |

**Table 15. Identifying, Diagnosing, and Treating Acute and Recent HIV Infection**

- A blood sample for genotypic drug-resistance testing should be obtained before initiating ART to guide the selection of the regimen **(AIII)**, but ART should be initiated as soon as possible, often before resistance-test results are available. If resistance is subsequently identified, treatment should be modified as needed.
- Standard genotypic drug-resistance testing should be performed for mutations in the reverse transcriptase and protease genes **(AIII)** for all people with early HIV. Genotype testing for INSTI resistance should be performed for those who acquire HIV during or after the use of CAB-LA as PrEP, if transmitted INSTI resistance is suspected, or if HIV diagnosis is made after receiving an INSTI-based regimen for PEP **(AIII)**.
- ART can be initiated before the results of drug-resistance testing are known. For individuals who do not have a history of using CAB-LA as PrEP, one of the following ARV regimens is recommended **(AIII)**:
  - o BIC/TAF/FTC **(AIII)**; or
  - o DTG with (TAF or TDF)<sup>b</sup> plus (FTC or 3TC) **(AIII)**
- For individuals with a history of using CAB-LA as PrEP, genotypic resistance testing performed before starting ART should include screening for INSTI-resistance mutations **(AIII)**. Recommended regimens include the following:
  - o (DRV/c<sup>c</sup> or DRV/r) with (TAF or TDF)<sup>b</sup> plus (FTC or 3TC)—pending the results of the genotype **(AIII)**. Empiric INSTI-containing regimens **are not recommended (AIII)**, because INSTI resistance may be present in those who acquire HIV during the use of CAB-LA and possibly up to 4 years after.

<sup>a</sup> In some settings, activities that increase the risk of HIV infection may not be recognized or perceived as risky by the health care provider, the person at risk, or both. Thus, even in the absence of reported high-risk activities, symptoms and signs consistent with acute retroviral syndrome should motivate health care providers to consider a diagnosis of acute HIV infection.

<sup>b</sup> TAF and TDF are two forms of tenofovir that are approved in the United States. TAF has fewer bone and kidney toxicities than TDF, whereas TDF is associated with lower lipid levels. Safety, cost, and accessibility are among the factors to consider when choosing between these drugs.

<sup>c</sup> COBI should be avoided in pregnancy because lower concentrations of COBI and DRV have been reported during the second and third trimesters.

**Key:** 3TC = lamivudine; Ag/Ab = antigen/antibody; ART = antiretroviral therapy; ARV = antiretroviral; BIC = bictegravir; CAB-LA = long-acting cabotegravir; CMV = cytomegalovirus; COBI = cobicistat; DRV = darunavir; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EBV = Epstein-Barr virus; FTC = emtricitabine; INSTI = integrase strand transfer inhibitor; PEP = post-exposure prophylaxis; PrEP = pre-exposure prophylaxis; STI = sexually transmitted infection; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate

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