Drug-Resistance Testing  (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel's Recommendations

For Antiretroviral Therapy-Naive Patients:

• HIV drug-resistance testing is recommended for persons with HIV infection at entry into care to guide selection of the initial antiretroviral therapy (ART) regimen (AII). If therapy is deferred, repeat testing may be considered at the time of ART initiation (CIII).

• Genotypic testing is recommended as the preferred resistance testing to guide therapy in antiretroviral (ARV)-naive patients (AIII).

• In special circumstances (e.g., in patients with acute or recent [early] HIV infection and in pregnant HIV-infected women, ART initiation should not be delayed while awaiting resistance testing results; the regimen can be modified once results are reported).

• Standard genotypic drug-resistance testing in ARV-naive persons involves testing for mutations in the reverse transcriptase (RT) and protease (PR) genes. If transmitted integrase strand transfer inhibitor (INSTI) resistance is a concern, providers should ensure that genotypic resistance testing also includes INSTI genotype testing (BIII).

For Antiretroviral Therapy-Experienced Patients:

• HIV drug-resistance testing should be performed to assist in the selection of active drugs when changing ART regimens in the following patients:
  • In patients with virologic failure and HIV RNA levels >1000 copies/mL (AI).
  • In patients with HIV RNA levels >500 copies/mL but <1000 copies/mL, drug-resistance testing may be unsuccessful but should still be considered (BII).
  • Drug-resistance testing should also be performed when managing suboptimal viral load reduction (AII).

• When a patient experiences virologic failure while receiving an INSTI-based regimen, genotypic testing for INSTI resistance should be performed to determine whether to include a drug from this class in subsequent regimens (AII).

• Drug-resistance testing in the setting of virologic failure should be performed while the person is taking prescribed ARV drugs or, if not possible, within 4 weeks after discontinuing therapy (AII). If more than 4 weeks have elapsed since the ARVs were discontinued, resistance testing may still provide useful information to guide therapy; however, it is important to recognize that previously selected resistance mutations can be missed (CIII).

• Genotypic testing is recommended as the preferred resistance testing to guide therapy in patients with suboptimal virologic response or virologic failure while on first- or second-line regimens (AII).

• The addition of phenotypic to genotypic testing is generally preferred for persons with known or suspected complex drug-resistance mutation patterns (BIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Co-Receptor Tropism Assays  (Last updated February 12, 2013; last reviewed February 12, 2013)

Panel's Recommendations

• A co-receptor tropism assay should be performed whenever the use of a CCR5 co-receptor antagonist is being considered (AI).

• Co-receptor tropism testing is also recommended for patients who exhibit virologic failure on a CCR5 antagonist (BII).

• A phenotypic tropism assay is preferred to determine HIV-1 co-receptor usage (AI).

• A genotypic tropism assay should be considered as an alternative test to predict HIV-1 co-receptor usage (BII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
HLA-B*5701 Screening  (Last updated December 1, 2007; last reviewed January 10, 2011)

<table>
<thead>
<tr>
<th>Panel's Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• The Panel recommends screening for HLA-B*5701 before starting patients on an abacavir (ABC)-containing regimen to reduce the risk of hypersensitivity reaction (HSR) (AI).</td>
</tr>
<tr>
<td>• HLA-B*5701-positive patients should not be prescribed ABC (AI).</td>
</tr>
<tr>
<td>• The positive status should be recorded as an ABC allergy in the patient's medical record (AII).</td>
</tr>
<tr>
<td>• When HLA-B*5701 screening is not readily available, it remains reasonable to initiate ABC with appropriate clinical counseling and monitoring for any signs of HSR (CIII).</td>
</tr>
</tbody>
</table>

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Initiation of Antiretroviral Therapy  (Last updated January 28, 2016; last reviewed January 28, 2016)

<table>
<thead>
<tr>
<th>Panel's Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Antiretroviral therapy (ART) is recommended for all HIV-infected individuals, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection (AI).</td>
</tr>
<tr>
<td>• ART is also recommended for HIV-infected individuals to prevent HIV transmission (AI).</td>
</tr>
<tr>
<td>• When initiating ART, it is important to educate patients regarding the benefits and considerations regarding ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.</td>
</tr>
</tbody>
</table>

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient  

(last updated July 14, 2016; last reviewed July 14, 2016)

Panel’s Recommendations

- An antiretroviral (ARV) regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors (NRTIs) in combination with a third active ARV drug from one of three drug classes: an integrase strand transfer inhibitor (INSTI), a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor (PI) with a pharmacokinetic (PK) enhancer (booster) (cobicistat or ritonavir).

- The Panel on Antiretroviral Guidelines for Adults and Adolescents (the Panel) classifies the following regimens as Recommended regimens for antiretroviral therapy (ART)-naive patients:

  **Integrase Strand Transfer Inhibitor-Based Regimens:**
  - Dolutegravir/abacavir/lamivudine—a for patients who are HLA-B*5701 negative (AI)
  - Dolutegravir plus either tenofovir disoproxil fumarate/emtricitabine—a (AI) or tenofovir alafenamide/emtricitabine (AII)
  - Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (AI)
  - Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (AI)
  - Raltegravir plus either tenofovir disoproxil fumarate/emtricitabine—a (AI) or tenofovir alafenamide/emtricitabine (AII)

  **Protease Inhibitor-Based Regimens:**
  - Darunavir/ritonavir plus either tenofovir disoproxil fumarate/emtricitabine—a (AI) or tenofovir alafenamide/emtricitabine (AII)

- On the basis of individual patient characteristics and needs, an Alternative regimen or, less frequently, an Other regimen, may be the optimal regimen for a particular patient. A list of Alternative and Other regimens can be found in Table 6.

- Given the many excellent options for initial therapy, selection of a regimen for a particular patient should be guided by factors such as virologic efficacy, toxicity, pill burden, dosing frequency, drug-drug interaction potential, resistance testing results, comorbid conditions, and cost. Table 7 provides guidance on choosing an ARV regimen based on selected clinical case scenarios. Table 8 highlights the advantages and disadvantages of different components in a regimen.

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials, observational cohort studies with long-term clinical outcomes, relative bioavailability/bioequivalence studies, or regimen comparisons from randomized switch studies; III = Expert opinion

*Lamivudine may substitute for emtricitabine or vice versa.*
Management of the Treatment-Experienced Patient

Virologic Failure  (Last updated April 8, 2015; last reviewed April 8, 2015)

<table>
<thead>
<tr>
<th>Panel’s Recommendations</th>
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<tbody>
<tr>
<td>• Assessing and managing a patient experiencing failure of antiretroviral therapy (ART) is complex. Expert advice is critical and should be sought.</td>
</tr>
<tr>
<td>• Evaluation of virologic failure should include an assessment of adherence, drug-drug or drug-food interactions, drug tolerability, HIV RNA and CD4 T lymphocyte (CD4) cell count trends over time, treatment history, and prior and current drug-resistance testing results.</td>
</tr>
<tr>
<td>• Drug-resistance testing should be performed while the patient is taking the failing antiretroviral (ARV) regimen (AI) or within 4 weeks of treatment discontinuation (AII). Even if more than 4 weeks have elapsed since ARVs were discontinued, resistance testing—although it may not detect previously selected resistance mutations—can still provide useful information to guide therapy (CIII).</td>
</tr>
<tr>
<td>• The goal of treatment for ART-experienced patients with drug resistance who are experiencing virologic failure is to establish virologic suppression (i.e., HIV RNA below the lower limits of detection of currently used assays) (AI).</td>
</tr>
<tr>
<td>• A new regimen should include at least two, and preferably three, fully active agents (AI). A fully active agent is one that is expected to have uncompromised activity on the basis of the patient’s treatment history and drug-resistance testing results and/or the drug’s novel mechanism of action.</td>
</tr>
<tr>
<td>• In general, adding a single ARV agent to a virologically failing regimen is not recommended because this may risk the development of resistance to all drugs in the regimen (BII).</td>
</tr>
<tr>
<td>• For some highly ART-experienced patients, maximal virologic suppression is not possible. In this case, ART should be continued (AI) with regimens designed to minimize toxicity, preserve CD4 cell counts, and delay clinical progression.</td>
</tr>
<tr>
<td>• When it is not possible to construct a viable suppressive regimen for a patient with multidrug resistant HIV, the clinician should consider enrolling the patient in a clinical trial of investigational agents or contacting pharmaceutical companies that may have investigational agents available.</td>
</tr>
<tr>
<td>• Discontinuing or briefly interrupting therapy may lead to a rapid increase in HIV RNA and a decrease in CD4 cell count and increases the risk of clinical progression. Therefore, this strategy is not recommended in the setting of virologic failure (AI).</td>
</tr>
</tbody>
</table>

**Rating of Recommendations:** A = Strong; B = Moderate; C = Optional

**Rating of Evidence:** I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
Poor CD4 Cell Recovery and Persistent Inflammation Despite Viral Suppression  (Last updated April 8, 2015; last reviewed April 8, 2015)

Panel’s Summary and Recommendations

• Morbidity and mortality from several AIDS and non-AIDS conditions are increased in HIV-infected individuals despite antiretroviral therapy (ART)-mediated viral suppression, and are predicted by persistently low CD4 T lymphocyte (CD4) cell counts and/or persistent immune activation.

• ART intensification by adding antiretroviral (ARV) drugs to a suppressive ART regimen does not consistently improve CD4 cell recovery or reduce immune activation and is not recommended (AI).

• In individuals with viral suppression, switching ARV drug classes does not consistently improve CD4 cell recovery or reduce immune activation and is not recommended (BIII).

• No interventions designed to increase CD4 cell counts and/or decrease immune activation are recommended at this time (in particular, interleukin-2 is not recommended [AI]) because none has been proven to decrease morbidity or mortality during ART-mediated viral suppression.

• Monitoring markers of immune activation and inflammation is not recommended because no immunologically targeted intervention has proven to improve the health of individuals with abnormally high biomarker levels, and many markers that predict morbidity and mortality fluctuate widely in individuals (AII).

• Because there are no proven interventions to improve CD4 cell recovery and/or inflammation, efforts should focus on addressing modifiable risk factors for chronic disease (e.g., encouraging smoking cessation, a healthy diet, and exercise; treating hypertension, hyperlipidemia) (AII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Regimen Switching in the Setting of Virologic Suppression  (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel’s Recommendations

• Advances in antiretroviral (ARV) treatment and a better understanding of HIV drug resistance make it possible to consider switching an effective regimen to an alternative regimen in some situations.

• The fundamental principle of regimen switching is to maintain viral suppression without jeopardizing future treatment options (AI).

• It is critical to review a patient’s full ARV history, including virologic responses, past ARV-associated toxicities, and cumulative resistance test results, if available, before selecting a new ART regimen (AI).

• Adverse events, the availability of ARVs with an improved safety profile, or the desire to simplify a regimen may prompt a regimen switch. Within-class and between-class switches can usually maintain viral suppression provided that there is no viral resistance to the ARV agents in the new regimen (AI).

• Consultation with an HIV specialist should be considered when considering a regimen switch for a patient with a history of resistance to one or more drug classes (BIII).

• More intensive monitoring to assess tolerability, viral suppression, adherence, and laboratory changes is recommended during the first 3 months after a regimen switch (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
Considerations for Antiretroviral Use in Special Patient Populations

Acute and Recent (Earlya) HIV Infection  (Last updated January 28, 2016; last reviewed January 28, 2016)

<table>
<thead>
<tr>
<th>Panel’s Recommendations</th>
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<tbody>
<tr>
<td>• Antiretroviral therapy (ART) is recommended for all individuals with HIV-1 infection (AI) including those with earlya HIV-1 infection.</td>
</tr>
<tr>
<td>• Once initiated, the goal of ART is to suppress plasma HIV-1 RNA to undetectable levels (AIII). Testing for plasma HIV-1 RNA levels, CD4 T lymphocyte counts, and toxicity monitoring should be performed as recommended for patients with chronic HIV-1 infection (AII).</td>
</tr>
<tr>
<td>• Genotypic drug resistance testing should be performed before initiation of ART to guide the selection of the regimen (AII).</td>
</tr>
<tr>
<td>• ART can be initiated before drug resistance test results are available. Because resistance to pharmacokinetically enhanced protease inhibitors (PIs) emerges slowly and clinically significant transmitted resistance to PIs is uncommon, ritonavir-boosted darunavir (DRV/r) and tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) is a recommended regimen in this setting (AIII). For similar reasons, dolutegravir (DTG) plus TDF/FTC is also a reasonable option although data regarding transmission of integrase strand transfer inhibitor (INSTI)-resistant HIV and the efficacy of this regimen in early HIV infection is limited (AIII).</td>
</tr>
<tr>
<td>• When results of drug resistance testing are available, the treatment regimen can be modified if warranted (AII). In patients without transmitted drug resistant virus, therapy should be initiated with one of the combination regimens that is recommended for patients with chronic HIV-1 infection (see What to Start) (AIII).</td>
</tr>
<tr>
<td>• Patients starting ART should be willing and able to commit to treatment and should understand the importance of adherence (AIII). Patients may choose to postpone therapy, and providers, on a case-by-case basis, may recommend that patients defer therapy because of clinical and/or psychosocial factors.</td>
</tr>
</tbody>
</table>

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

a Early infection represents either acute or recent infection.
HIV-Infected Adolescents and Young Adults  (Last updated January 28, 2016; last reviewed January 28, 2016)

Key Summary and Panel’s Recommendations

- HIV-infected adolescents largely belong to two distinct groups—those who acquired HIV in infancy, and are heavily antiretroviral therapy (ART)-experienced, and those who acquired HIV more recently during their teens.

- ART is recommended for all HIV-infected individuals (AI) to reduce morbidity and mortality. Thus, ART is also recommended for ART-naive adolescents. However, before initiation of therapy, adolescents’ readiness and ability to adhere to therapy within their psychosocial context need to be carefully considered as part of therapeutic decision making (AIII).

- Once ART is initiated, appropriate support is essential to reduce potential barriers to adherence and maximize the success in achieving sustained viral suppression (AII).

- The adolescent sexual maturity rating can be helpful to guide regimen selection for initiation of or changes in ART as recommended by either these Adult and Adolescent ART Guidelines or the Pediatric ART Guidelines. These Adult/Adolescent Guidelines are more appropriate for postpubertal adolescents (i.e., sexual maturity rating IV or V) (AIII).

- Pediatric and adolescent care providers should prepare adolescents for the transition into adult care settings. Adult providers should be sensitive to the challenges associated with such transitions, consulting and collaborating with adolescent HIV care providers to insure adolescents’ successful transition and continued engagement in care (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
Summary of HIV-2 Infection

- Compared to HIV-1 infection, the clinical course of HIV-2 infection is generally characterized by a longer asymptomatic stage, lower plasma HIV-2 RNA levels, and lower mortality; however, progression to AIDS does occur.
- There have been no randomized trials addressing the question of when to start antiretroviral therapy or the choice of initial or second-line therapy for HIV-2 infection; thus, the optimal treatment strategy has not been defined.
- Although the optimal CD4 T lymphocyte (CD4) cell count threshold for initiating antiretroviral therapy in HIV-2 infection is unknown, therapy should be started before there is clinical progression.
- HIV-2 is intrinsically resistant to non-nucleoside reverse transcriptase inhibitors and to enfuvirtide; thus, these drugs should not be included in an antiretroviral regimen for an HIV-2 infected patient.
- Pending more definitive data on outcomes in an antiretroviral therapy-naive patient who has HIV-2 mono-infection or HIV-1/HIV-2 dual infection and requires treatment, an initial antiretroviral therapy regimen for these patients should include two nucleoside reverse transcriptase inhibitors plus an HIV-2 active boosted protease inhibitor or integrase strand transfer inhibitors.
- A few laboratories now offer quantitative plasma HIV-2 RNA testing for clinical care (see section text).
- Monitoring of HIV-2 RNA levels, CD4 cell counts, and clinical improvements can be used to assess treatment response, as is recommended for HIV-1 infection.
- Resistance-associated viral mutations to nucleoside reverse transcriptase inhibitors, protease inhibitors, and/or integrase strand transfer inhibitors may develop in HIV-2 infected patients while on therapy. However, no validated HIV-2 genotypic or phenotypic antiretroviral resistance assays are available for clinical use.
- In the event of virologic, immunologic, or clinical failure, second-line treatment should be instituted in consultation with an expert in HIV-2 management.
HIV and the Older Patient (Last updated January 28, 2016; last reviewed January 28, 2016)

Key Considerations When Caring for Older HIV-Infected Patients Receiving Antiretroviral Therapy (ART)

- Antiretroviral therapy (ART) is recommended for all patients regardless of CD4 T lymphocyte cell count (AI). ART is especially important for older patients because they have a greater risk of serious non-AIDS complications and potentially a blunted immunologic response to ART.

- Adverse drug events from ART and concomitant drugs may occur more frequently in older HIV-infected patients than in younger HIV-infected patients. Therefore, the bone, kidney, metabolic, cardiovascular, and liver health of older HIV-infected patients should be monitored closely.

- Polypharmacy is common in older HIV patients; therefore, there is a greater risk of drug-drug interactions between antiretroviral drugs and concomitant medications. Potential for drug-drug interactions should be assessed regularly, especially when starting or switching ART and concomitant medications.

- HIV experts, primary care providers, and other specialists should work together to optimize the medical care of older HIV-infected patients with complex comorbidities.

- Early diagnosis of HIV and counseling to prevent secondary transmission of HIV remains an important aspect of the care of the older HIV-infected patient.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion

Considerations for Antiretroviral Use in Patients with Coinfections

Hepatitis B (HBV)/HIV Virus Coinfection (Last updated July 14, 2016; last reviewed July 14, 2016)

Panel’s Recommendations

- Before initiation of antiretroviral therapy (ART), all patients who test positive for hepatitis B surface antigen (HBsAg) should be tested for hepatitis B virus (HBV) DNA using a quantitative assay to determine the level of HBV replication (AIII).

- Because emtricitabine (FTC), lamivudine (3TC), tenofovir disoproxil fumarate (TDF) and tenofovir alafenamide (TAF) have activity against both HIV and HBV, for patients coinfected with HIV and HBV, ART should be initiated with the fixed-dose combination of TDF/FTC or TAF/FTC, or the individual drug combinations of TDF plus 3TC as the nucleoside reverse transcriptase inhibitor (NRTI) backbone of a fully suppressive antiretroviral (ARV) regimen (AI).

- If TDF or TAF cannot safely be used, the alternative recommended HBV therapy is entecavir in addition to a fully suppressive ARV regimen (BI). Entecavir has activity against HIV; its use for HBV treatment without ART in patients with dual infection may result in the selection of the M184V mutation that confers HIV resistance to 3TC and FTC. Therefore, entecavir must be used in addition to a fully suppressive ARV regimen when used in HBV/HIV-coinfected patients (AII). Peginterferon alfa monotherapy may also be considered in certain patients (CII).

- Other HBV treatment regimens including adefovir alone or in combination with 3TC or FTC and telbivudine are not recommended for HBV/HIV coinfected patients (CII).

- Discontinuation of agents with anti-HBV activity may cause serious hepatocellular damage resulting from reactivation of HBV; patients should be advised against stopping these medications and carefully monitored during interruptions in HBV treatment (AII).

- If ART needs to be modified due to HIV virologic failure and the patient has adequate HBV suppression, the ARV drugs active against HBV should be continued for HBV treatment in combination with other suitable ARV agents to achieve HIV suppression (AIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional
Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
HIV/Hepatitis C Virus Coinfection

(last updated July 14, 2016; last reviewed July 14, 2016)

Panel Recommendations

- All HIV-infected patients should be screened for hepatitis C virus (HCV) infection. Patients at high risk of HCV infection should be screened annually and whenever HCV infection is suspected.
- Antiretroviral therapy (ART) may slow the progression of liver disease by preserving or restoring immune function and reducing HIV-related immune activation and inflammation. For most HCV/HIV-coinfected patients, including those with cirrhosis, the benefits of ART outweigh concerns regarding drug-induced liver injury. Therefore, ART should be initiated in all HCV/HIV-coinfected patients, regardless of CD4 T lymphocyte (CD4) cell count (AI).
- Initial ART regimens recommended for most HCV/HIV-coinfected patients are the same as those recommended for individuals without HCV infection. However, when treatment for both HIV and HCV is indicated, the regimen should be selected with special considerations of potential drug-drug interactions and overlapping toxicities with the HCV treatment regimen (see discussion in the text below and in Table 12).
- Combined treatment of HIV and HCV can be complicated by drug-drug interactions, increased pill burden, and toxicities. Although ART should be initiated for all HCV/HIV-coinfected patients regardless of CD4 cell count, in ART-naive patients with CD4 counts >500 cells/mm³ some clinicians may choose to defer ART until HCV treatment is completed (CIII).
- In patients with lower CD4 counts (eg, <200 cells/mm³), ART should be initiated promptly (AI) and HCV therapy may be delayed until the patient is stable on HIV treatment (CIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion
Panel’s Recommendations

- Selection of a tuberculosis (TB)-preventive treatment for HIV-infected individuals coinfected with latent tuberculosis infection (LTBI) should be based on the individual’s antiretroviral therapy (ART) regimen as noted below:
  - Any ART regimen can be used when isoniazid alone is used for LTBI treatment (AII).
  - Only efavirenz (EFV)- or raltegravir (RAL)-based regimens (in combination with either abacavir/lamivudine [ABC/3TC] or tenofovir disoproxil fumarate/emtricitabine [TDF/FTC]) can be used with once-weekly isoniazid plus rifapentine (AIII).
  - If rifampin or rifabutin is used to treat LTBI, clinicians should review Tables 18 through 19e to assess the potential for interactions among different antiretroviral (ARV) drugs and the rifamycins (BIII).

- All HIV-infected patients with active TB who are not on ART should be started on ART as described below:
  - In patients with CD4 counts <50 cells/mm³: Initiate ART as soon as possible, but within 2 weeks of starting TB treatment (AI).
  - In patients with CD4 counts ≥50 cells/mm³: Initiate ART within 8 weeks of starting TB treatment (AIII).

- In all HIV-infected pregnant women: Initiate ART as early as feasible, for treatment of maternal HIV infection and to prevent mother-to-child transmission (MTCT) of HIV (AIII).

- In patients with tuberculous meningitis: Caution should be exercised when initiating ART early, as high rates of adverse events and deaths have been reported in a randomized trial (A).

- Rifamycins are critical components of TB treatment regimens and should be included for HIV-infected patients with active TB, unless precluded because of TB resistance or toxicity. However, rifamycins have a considerable potential for drug-drug interactions. Clinicians should review Tables 18 through 19e to assess the potential for interactions among different ARV drugs and the rifamycins (BIII).

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = Data from randomized controlled trials; II = Data from well-designed nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion