Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

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What's New in the Guidelines? (Last updated February 12, 2013; last reviewed February 12, 2013)

The following key changes were made to update the March 28, 2012, version of the guidelines. Significant updates are highlighted throughout the revised guidelines.

Drug-Resistance Testing

In persons failing INSTI-based regimens, the panel now recommends that a genotypic assay for INSTI resistance should be performed to determine whether to include a drug from this class in subsequent regimens **(AII)**. Previously, the Panel recommended that INSTI resistance testing should be considered **(BIII)** in this setting.

Co-Receptor Tropism Assay

A genotypic tropism assay is now commercially available. The assay predicts HIV-1 co-receptor usage based on sequencing of the V3-coding region of HIV-1 *env*, the principal determinant of co-receptor usage. The Panel recommends that a genotypic tropism assay be used as an alternative to a phenotypic tropism assay before initiation of a CCR5 antagonist-containing regimen **(BII)**.

Initiating ART in Treatment-Naive Patients

The Panel has updated its recommendations on initiation of ART in treatment-naive patients. The Panel's recommendations are listed below.

- Antiretroviral therapy (ART) is recommended for all HIV-infected individuals to reduce the risk of disease progression.

  The strength and evidence for this recommendation vary by pretreatment CD4 cell count: CD4 count <350 cells/mm^3 **(AI)**; CD4 count 350 cells/mm^3 to 500 cells/mm^3 **(AII)**; CD4 count >500 cells/mm^3 **(BIII)**.
- ART also is recommended for HIV-infected individuals for the prevention of transmission of HIV.

  The strength and evidence for this recommendation vary by transmission risks: perinatal transmission **(AI)**; heterosexual transmission **(AI)**; other transmission risk groups **(AIII)**.
- Patients starting ART should be willing and able to commit to treatment and understand the benefits and risks of therapy and the importance of adherence **(AIII)**. Patients may choose to postpone therapy, and providers, on a case-by-case basis, may elect to defer therapy on the basis of clinical and/or psychosocial factors.

What to Start: Initial Combination Regimen for Antiretroviral-Naive Patients

The following changes and updates were made to this section:

- A rilpivirine (RPV)-based regimen is now recommended as an alternative NNRTI-based regimen **only** in patients with pre-treatment HIV RNA ≤100,000 copies/mL **(BI)**. This is based on results from clinical trials that show that the proportion of patients who experienced virologic failure at 96 weeks was greater in patients with pre-treatment HIV RNA >100,000 copies/mL than in patients with pre-therapy HIV RNA ≤100,000 copies/mL.
- Elvitegravir/cobicistat/tenofovir/emtricitabine (EVG/COBI/TDF/FTC) as a fixed-dose combination product is recommended as an alternative regimen for ART-naive patients with pre-treatment creatinine clearance >70 mL/min **(BI)**.

- The discussion on 3-NRTI regimens was removed from this section because 3-NRTI regimens are no longer recommended regimens for ART-naive patients.
- Tables 5a, 5b, 6, and 7 were updated to reflect the above changes.

Acute and Recent (Early) HIV Infection

- The term "early" HIV infection is now used when describing both the acute phase of HIV infection (i.e., immediately after HIV infection and before seroconversion) and recent (i.e., within first 6 months) HIV infection.
- The recommendation for initiation of ART in patients with early infection was changed from "should be considered optional **(CIII)**" to "should be offered **(BII)**."
- The section was updated to include a summary of recent randomized controlled trials that examined the role of time-limited ART in patients with early HIV infection.

HIV-Infected Women

- The recommendation on use of efavirenz (EFV) during pregnancy was updated to be in accord with the recommendation in the *Perinatal Antiretroviral Guidelines*. The key update includes the following statement: "Because the risk of neural tube defects is restricted to the first 5 to 6 weeks of pregnancy and pregnancy is rarely recognized before 4 to 6 weeks of pregnancy, EFV can be continued in pregnant women receiving an EFV-based regimen who present for antenatal care in the first trimester, provided the regimen produces virologic suppression **(CIII)**."
- The Panel also recommends that intravenous zidovudine use during labor may be omitted in women who have HIV RNA < 400 copies/mL near delivery **(BII)**. Oral combination ART should be continued during labor.

Drug-Drug Interaction

- This section includes new information under the heading "Pharmacokinetic (PK) Enhancing." The additional text describes the roles and mechanisms of ritonavir (RTV) and cobicistat (COBI) as pharmacokinetic enhancers to increase the exposure of antiretroviral drugs.
- Tables 14–16c have been updated with new pharmacokinetic interaction data, including known and predicted interactions involving EVG/COBI/TDF/FTC and other drugs.

Additional Updates

Minor revisions have also been made to the following sections:

- Introduction
- Adverse Effects of Antiretroviral Agents (and Table 13)
- ARV Drug Characteristics and ARV Drug Cost Tables (Appendix B)