

# Practice Guidelines

## HIV Prevention and Treatment with ART: International Antiviral Society Updates Recommendations

### Key Points for Practice

- ART should be prescribed and treatment barriers addressed soon after HIV infection is diagnosed.
- Before starting treatment, obtain HIV-1 RNA levels and a CD4 cell count; test for viral hepatitis, and perform blood chemistry testing and HIV genotyping for reverse transcriptase inhibitors and protease inhibitors.
- Assess treatment history, tolerance of various treatment options, other current medications, and results of previous resistance testing before changing therapy.

From the *AFP* Editors

**Antiretroviral therapy (ART)** is the key to preventing and managing human immunodeficiency virus (HIV) infection. Based on the availability of new medications and treatment options, the USA Panel of the International Antiviral Society has updated its 2016 recommendations. The full guidance addresses when to start ART in patients with active opportunistic infection or malignancy; appropriate regimens, including in unique situations (e.g., pregnancy); switching regimens; laboratory monitoring; patient engagement and adherence; cost considerations; HIV infection prevention; and future directions.

### Treatment Initiation

The following recommendations are based on evidence from at least one randomized controlled trial from a peer-reviewed journal. Unless a person has expressed interest in not initiating treatment, physicians should prescribe ART

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immediately after HIV infection is diagnosed, including addressing treatment barriers to allow for ART initiation at the first office visit as appropriate. Most persons with opportunistic infections should receive ART within two weeks of diagnosis. Before starting treatment in any patient, HIV-1 RNA measurement; CD4 cell count; HIV genotyping for nucleoside reverse transcriptase inhibitors (NRTIs), non-NRTIs, and protease inhibitors; laboratory testing to identify active viral hepatitis; and blood chemistry testing should be performed; treatment may be initiated while awaiting results. If planning to prescribe abacavir (Ziagen), testing for *HLA-B\*5701* allele also should be performed and results obtained. If a patient has a CD4 count lower than 200 cells per  $\mu\text{L}$  ( $0.20 \times 10^9$  per L), he or she should receive prophylaxis for *Pneumocystis pneumonia*. Pregnant women with HIV infection should start ART for their own benefit, as well as to reduce the risk of transmission to the fetus.

All of the following primary regimen options have similar evidence supporting their use:

- bicitgravir/tenofovir alafenamide/emtricitabine (Biktarvy);
- dolutegravir/abacavir/lamivudine (Triumeq); and
- dolutegravir (Tivicay) plus tenofovir alafenamide/emtricitabine (Descovy).

If these options are not available or indicated, then secondary options include:

- darunavir/cobicistat (Prezcobix) plus tenofovir alafenamide/emtricitabine or tenofovir disoproxil fumarate/emtricitabine (Truvada);
- darunavir (Prezista) boosted with ritonavir (Norvir) plus tenofovir alafenamide/emtricitabine or tenofovir disoproxil fumarate/emtricitabine;
- efavirenz/tenofovir disoproxil fumarate/emtricitabine (Atripla);
- elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine (Genvoya) or elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine (Stribild); and
- raltegravir (Isentress) plus tenofovir disoproxil fumarate/emtricitabine (tenofovir alafenamide/emtricitabine also is an option).

If a patient has an HIV RNA level less than 100,000 copies per mL and a CD4 cell count greater than 200 cells per  $\mu\text{L}$ , rilpivirine/tenofovir alafenamide/emtricitabine (Odefsey) or rilpivirine/tenofovir disoproxil fumarate/emtricitabine

(Complera) is the recommended secondary option. For any of these regimens containing tenofovir alafenamide/emtricitabine in which cost is a concern or the medication is unavailable, tenofovir disoproxil fumarate/emtricitabine or tenofovir disoproxil fumarate/lamivudine (Cimduo) is an effective option for patients without kidney or bone disease. For initial treatment, regimens with two medications combined as opposed to standard three-drug regimens are only rarely required; for example, for patients who cannot take abacavir, tenofovir alafenamide, or tenofovir disoproxil fumarate.

Based on evidence from nonrandomized clinical studies, cohort studies, or case-control studies, ART should be started right away for patients with a malignancy, taking into consideration interactions with other medications. Primary *Mycobacterium avium* complex prophylaxis is not necessary in addition to effective ART. Based on the group's consensus, non-NRTIs and abacavir are not recommended for quick ART initiation, cryptococcal disease prophylaxis is not necessary in areas with a low incidence that have appropriate treatment resources, and tenofovir disoproxil fumarate is not appropriate for persons at risk of or who have kidney or bone disease.

### Treatment Changes

Common reasons for treatment changes include simplifying the regimen, addressing comorbid conditions, managing adverse effects or interactions, and for insurance purposes. Based on evidence from at least one randomized controlled study from a peer-reviewed journal, before making any changes to treatment, the patient's treatment history, tolerance of various treatment options, other current medications, and results of previous resistance testing should be assessed. When opting to change treatment, patients with NRTI mutations should not change from a boosted protease inhibitor to a medication with a low barrier to resistance (e.g., non-NRTI, raltegravir). For patients who have achieved virologic suppression but have a high risk of renal toxicity or bone disease, switching from tenofovir disoproxil fumarate to tenofovir alafenamide is recommended; however, other medications should first be reviewed to determine if dosing adjustments are needed. When opting to switch patients from three medications to two in the setting of virologic suppression, dolutegravir/rilpivirine (Juluca) is an option for those without previous failure or medication resistance, with long-term follow-up to confirm sustainability. When making treatment changes because of virologic failure with a non-NRTI, dolutegravir combined with two NRTIs is recommended. In virologic failure, the addition of one active agent to the existing regimen is not recommended.

Based on evidence from nonrandomized clinical studies, cohort studies, or case-control studies, when switching from three medications to two in the setting of virologic suppression, a boosted protease inhibitor with lamivudine or dolutegravir with lamivudine is an option for patients without previous failure or medication resistance, with long-term follow-up to confirm sustainability. Treatment of patients with HIV and hepatitis B virus infection should include three medications, two of which should be active against hepatitis B virus, typically tenofovir alafenamide or tenofovir disoproxil fumarate combined with lamivudine or emtricitabine; two-medication regimens are not recommended. Treatment with boosted protease inhibitors or dolutegravir alone is not an option when switching treatment methods in the setting of virologic suppression. In virologic failure, resistance testing should be performed on the currently failing regimen or within four weeks of discontinuation. Confirmation of virologic failure is recommended; if resistance to treatment is confirmed, the patient should be switched to another treatment based on results of the resistance testing.

Based on the group's consensus, the patient's HIV viral load should be reviewed one month after any treatment change to confirm virologic suppression. When viral suppression is achieved, patients taking older antiretroviral medications known to have toxicities should continue to be monitored for subtle adverse effects; a treatment change is warranted only if toxicities are identified. When switching regimens for virologic failure with a combination of medications that includes an integrase strand transfer inhibitor, a boosted protease inhibitor combined with two NRTIs, at least one of which should be active, is the first choice for treatment. Dolutegravir twice per day combined with one active medication may be an option in patients in whom raltegravir or elvitegravir has failed. When resistance to multiple classes of medications is identified, medications from new classes should be used whenever possible.

**Guideline source:** International Antiviral Society–USA Panel

**Evidence rating system used?** Yes

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**Guideline developed by participants without relevant financial ties to industry?** No

**Recommendations based on patient-oriented outcomes?** No

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