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

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Treatment Goals (Last updated March 27, 2012; last reviewed March 27, 2012)

Eradication of HIV infection cannot be achieved with available antiretroviral (ARV) regimens even when new, potent drugs are added to a regimen that is already suppressing plasma viral load below the limits of detection of commercially available assays.[1] This is chiefly because the pool of latently infected CD4 T cells is established during the earliest stages of acute HIV infection[2] and persists with a long half-life, despite prolonged suppression of plasma viremia.[3-7] Therefore the primary goals for initiating antiretroviral therapy (ART) are to:

- reduce HIV-associated morbidity and prolong the duration and quality of survival,
- restore and preserve immunologic function,
- maximally and durably suppress plasma HIV viral load (see Plasma HIV RNA Testing), and
- prevent HIV transmission.

ART has reduced HIV-related morbidity and mortality[8-11] and has reduced perinatal[12] and behavior-associated transmission of HIV.[13-17] HIV suppression with ART may also decrease inflammation and immune activation thought to contribute to higher rates of cardiovascular and other end-organ damage reported in HIV-infected cohorts. (See Initiating Antiretroviral Therapy.) Maximal and durable suppression of plasma viremia delays or prevents the selection of drug-resistance mutations, preserves CD4 T-cell numbers, and confers substantial clinical benefits, all of which are important treatment goals.[18-19]

Achieving viral suppression requires the use of ARV regimens with at least two, and preferably three, active drugs from two or more drug classes. Baseline resistance testing and patient characteristics should guide design of the specific regimen. (See What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient.) When initial suppression is not achieved or is lost, rapidly changing to a new regimen with at least two active drugs is required. (See Virologic and Immunologic Failure.) The increasing number of drugs and drug classes makes viral suppression below detection limits an appropriate goal in all patients.

Viral load reduction to below limits of assay detection in an ART-naive patient usually occurs within the first 12–24 weeks of therapy. Predictors of virologic success include:

- high potency of ARV regimen,
- excellent adherence to treatment regimen,[20]
- low baseline viremia,[21]
- higher baseline CD4 count (>200 cells/mm^3),[22] and
- rapid reduction of viremia in response to treatment.[21,23]

Successful outcomes are usually observed, although adherence difficulties may lower the success rate in clinical practice to below the 90% rate commonly seen in clinical trials.[24]

Strategies to Achieve Treatment Goals

Achieving treatment goals requires a balance of sometimes competing considerations, outlined below. Providers and patients must work together to define individualized strategies to achieve treatment goals.

Selection of Initial Combination Regimen

Several preferred and alternative ARV regimens are recommended for use. (See What to Start.) Many of these regimens have comparable efficacy but vary to some degree in dosing frequency and symmetry, pill

burden, drug interactions, and potential side effects. Regimens should be tailored for the individual patient to enhance adherence and thus improve long-term treatment success. Individual regimen choice is based on such considerations as expected side effects, convenience, comorbidities, interactions with concomitant medications, and results of pretreatment genotypic drug-resistance testing.

Pretreatment Drug-Resistance Testing

Current studies suggest a 6%–16% prevalence of HIV drug resistance in ART-naive patients,[25-29] and some studies suggest that the presence of transmitted drug-resistant viruses may lead to suboptimal virologic responses.[30] Therefore, pretreatment genotypic resistance testing should be used to guide selection of the most optimal initial ARV regimen. (See Drug-Resistance Testing.)

Improving Adherence

Suboptimal adherence may result in reduced treatment response. Incomplete adherence can result from complex medication regimens; patient factors, such as active substance abuse and depression; and health system issues, including interruptions in patient access to medication and inadequate treatment education and support. Conditions that promote adherence should be maximized before and after initiation of ART. (See Adherence to Antiretroviral Therapy.)

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