Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV

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Antiretroviral therapy (ART) has reduced HIV-related morbidity and mortality at all stages of HIV infection\textsuperscript{1-4} and has reduced HIV transmission.\textsuperscript{5-8} Maximal and durable suppression of plasma viremia delays or prevents the selection of drug-resistance mutations, preserves or improves CD4 T lymphocyte (CD4) cell numbers, and confers substantial clinical benefits, all of which are important treatment goals.\textsuperscript{9,10} 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 cohorts with HIV (see Initiating Antiretroviral Therapy). Despite these benefits, eradication of HIV infection cannot be achieved with available antiretrovirals (ARVs). Treatment interruption has been associated with rebound viremia, worsening of immune function, and increased morbidity and mortality.\textsuperscript{11} Thus, once initiated, ART should be continued, with the following key treatment goals:

\begin{itemize}
  \item Maximally and durably suppress plasma HIV RNA;
  \item Restore and preserve immunologic function;
  \item Reduce HIV-associated morbidity and prolong the duration and quality of survival; and
  \item Prevent HIV transmission.
\end{itemize}

Achieving viral suppression currently requires the use of combination ARV regimens that generally include three active drugs from two or more drug classes. Baseline patient characteristics and results from drug resistance testing should guide design of the specific regimen (see What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient). When initial HIV suppression is not achieved or not maintained, changing to a new regimen with at least two active drugs is often required (see Virologic Failure). The increasing number of ARV drugs and drug classes makes viral suppression below detection limits an achievable goal in most patients.

After initiation of effective ART, viral load reduction to below limits of assay detection usually occurs within the first 12 to 24 weeks of therapy. Predictors of virologic success include the following:

\begin{itemize}
  \item Low baseline viremia;
  \item High potency of the ARV regimen;
  \item Tolerability of the regimen;
  \item Convenience of the regimen; and
  \item Excellent adherence to the regimen.
\end{itemize}

### Strategies to Achieve Treatment Goals

#### Selection of Initial Combination Regimen

Several ARV regimens are recommended for use in ART-naive patients (see What to Start). Most of the recommended regimens have comparable efficacy but vary in pill burden, potential for drug interactions and/or side effects, and propensity to select for resistance mutations if ART adherence is suboptimal. Regimens should be tailored for the individual patient to enhance adherence and support long-term treatment success. Considerations when selecting an ARV regimen for an individual patient include potential side effects, patient comorbidities, possible interactions with concomitant medications, results of pretreatment genotypic drug-resistance testing, and regimen convenience (see Table 7).

#### Improving Adherence

Suboptimal adherence may result in reduced treatment response. Incomplete adherence can result from complex medication regimens; patient-related factors, such as active substance abuse, depression, or...
the experience of adverse effects; 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 the Continuum of Care).

References


