Highlights of the 2010 Recommendations of the IAS–USA Panel Antiretroviral Treatment of Adult HIV Infection

In January 2010, the current panel of the International AIDS Society–USA convened to review its 2008 antiretroviral therapy guidelines for the treatment of HIV-infected adults. In light of new and emerging data, the panel updated its recommendations concerning when to start antiretroviral therapy, the choice of initial regimens, patient monitoring, and changes for virologic failure. A full article detailing the recommendations appears in the *Journal of the American Medical Association* (Thompson MA, Aberg JA, Cahn P, et al. Antiretroviral Treatment of Adult HIV Infection: 2010 Recommendations of the International AIDS Society–USA Panel, *JAMA*. 2010;304[3]:321-333) and is available free of charge by visiting **http://jama.ama-assn.org/cgi/content/full/304/3/321**. Below are selected highlights.

When to Start

Clinicians should confirm patient readiness for treatment before initiating antiretroviral therapy.

Treatment is recommended for
- Asymptomatic individuals with CD4+ cell counts of 500/μL or less
- Regardless of CD4+ cell count, patients who
  - Are symptomatic
  - Are pregnant
  - Have a plasma HIV-1 RNA level greater than 100,000 copies/mL
  - Have experienced a rapid decline in CD4+ cell count >100/μL/year
  - Are coinfected with hepatitis B or C virus
  - Are older than 60 years of age
  - Have HIV-associated renal disease
  - Have cardiovascular disease or are at high risk
  - Have an opportunistic infection, including tuberculosis
  - Have symptomatic primary HIV infection
  - Are involved in circumstances involving a high risk of HIV transmission, such as serodiscordant couples

Treatment should be considered for
- Asymptomatic individuals with CD4+ cell counts greater than 500/μL unless the patient is an elite controller (plasma HIV-1 RNA level < 50 copies/mL) or has a stable CD4+ cell count and low-level viremia in the absence of antiretroviral therapy. There is no CD4+ cell count at which treatment initiation is contraindicated.

What to Start

The initial regimen should be individualized according to resistance testing results, predicted virologic efficacy, toxicity and tolerability, pill burden, dosing frequency, drug-drug interactions, comorbidities, and patient and practitioner preference.

The initial recommended regimen consists of
- Fixed-dose combinations when possible for patient convenience.
- A combination of 2 nucleoside or nucleotide analogue reverse transcriptase inhibitors (nRTIs) (tenofovir/emtricitabine, or abacavir/lamivudine as an alternative).
- A potent third agent from another class, such as the nonnucleoside reverse transcriptase inhibitor (NNRTI) efavirenz, a ritonavir-boosted (/r) protease inhibitor (PI) such as atazanavir/r or darunavir/r, or the integrase strand transfer inhibitor raltegravir, unless being reserved for later use when resistance mutations are present. Alternatives are lopinavir/r or fosamprenavir/r, nevirapine, or maraviroc.

Patient Monitoring

The goal of therapy, even in heavily pretreated patients, should be to suppress plasma HIV-1 RNA below the limits of quantification by commercially available assays. Baseline genotypic testing for drug resistance should be performed for all treatment-naive patients and in cases of confirmed virologic failure. Tropism testing is essential before a CC chemokine receptor 5 (CCR5) inhibitor is used.

Monitoring of plasma HIV-1 RNA levels is indicated
- Frequently when therapy begins or is changed because of virologic failure (every 2 weeks to 8 weeks after initiation, every 4 weeks to 8 weeks until suppressed, and then every 3 months to 4 months for at least the first year)
- On a continuing basis until the viral load becomes undetectable and for some time thereafter at 6-month intervals once the viral load is suppressed for a year and the CD4+ cell count stabilizes at 350 cells/μL or higher in treatment-adherent patients

Changes for Virologic Failure

Reasons for virologic failure should be assessed, including poor adherence, drug interactions, intercurrent infections, and recent vaccinations.

Recommendations regarding changes in treatment include the following:

- Virologic failure of an initial regimen should be identified and treated as early as possible with at least 2, preferably 3, fully active drugs (usually including a ritonavir-boosted PI) to avoid the accumulation of resistance mutations.
- Design of a new regimen should consider the patient's previous drug exposure, previous and current resistance profiles, drug interactions, and history of intolerance and toxicity.
- For PI/r failures, PI resistance does not always emerge, and strategic sequencing of PIs should be based upon results of resistance testing. If some degree of PI resistance exists, darunavir/r is preferred over lopinavir/r or tipranavir/r because of superior tolerability and toxicity and substantial drug interactions with tipranavir. If not previously used, an NNRTI may be included, provided that potential drug interactions are considered.
- For NNRTI failures, the new combination usually should include a PI/r or a drug from a new class if a PI/r is not possible. Etravirine may be a useful component of a new regimen but must be supported by a potent combination including a PI/r. Depending on the resistance profile and available options, inclusion of drugs from new drug classes (raltegravir or maraviroc) should be considered. Monotherapy with a PI/r should be avoided unless other drugs cannot be considered for reasons of toxicity or tolerability.
- For multidrug resistance, 3 active drugs, including new classes of agents (integrase strand transfer inhibitors or entry inhibitors) and PIs with activity against resistant strains, such as darunavir/r or tipranavir/r, should be used. Etravirine can be paired with darunavir/r (but not tipranavir/r) and may be of value, depending on the number of NNRTI mutations present. Enfuvirtide may be an option if no other new class can be used.
- Treatment interruptions should be avoided except in the context of clinical trials.
- Other reasons for changing therapy include management of toxicity, enhancement of tolerability, and simplification of therapy.

Future Directions

Whether in resource-limited or resource-rich settings, too many patients with HIV infection still present for treatment with advanced disease and thus do not benefit from the tremendous advances made in antiretroviral therapy. Universal voluntary HIV testing, comprehensive prevention services, and early linkage to care and treatment are urgently needed. Full implementation of these recommendations will require addressing social and structural barriers to receipt of health care as well as the pervasive stigma and discrimination associated with an HIV diagnosis.

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