New HIV treatment guidelines indicate importance of early, individualized antiretroviral treatment

July 18 2010

Advances in antiretroviral treatment (ART) have shown that the progressive immune system destruction caused by HIV infection, including AIDS, can be prevented, indicating the importance of beginning ART early, when a person with HIV infection is without symptoms, according to the 2010 recommendations of the International AIDS Society-USA Panel, published in the July 21 issue of *JAMA,* a theme issue on HIV/AIDS. This shift to earlier therapy is made possible by the increased understanding of the negative consequences of ongoing HIV replication and the development of newer drugs providing the potential for potent viral suppression in initial and subsequent therapy.

Melanie A. Thompson, M.D., of the AIDS Research Consortium of Atlanta and chair of the International AIDS Society-USA Antiretroviral Therapy Guidelines Panel, presented the recommendations of the panel at a JAMA media briefing at the International AIDS Conference in Vienna.

"Successful ART is associated with dramatic decreases in AIDS-defining conditions and their associated mortality. Expansion of treatment options and evolving knowledge require revision of guidelines for the initiation and long-term management of ART in adults with HIV infection," the authors write. Since the 2008 International AIDS Society-USA ART guidelines, new data have emerged regarding timing of therapy, optimal regimen choices, monitoring, and newer drugs are better understood in

terms of efficacy, toxicity, and potential uses in HIV management. New relevant HIV data and research since 2008 was reviewed by the panel for the 2010 recommendations

When to Start

"The prominence of non-AIDS events as a major cause of morbidity and mortality in those with ongoing HIV replication suggests that early ART initiation may further improve the quality and length of life for persons living with HIV," the authors write. They add that patient readiness for treatment is a key consideration when deciding when to initiate ART. There is no CD4+ cell count threshold at which initiating therapy is contraindicated. Initiation of therapy is recommended for asymptomatic individuals with CD4+ cell counts at 500/µL or below. Treatment should be considered for asymptomatic individuals with CD4+ cell counts greater than 500/µL and is recommended regardless of CD4+ cell count for patients with symptomatic established HIV disease. Therapy is also recommended for patients with other conditions such as pregnancy, age older than 60 years, hepatitis B or C virus coinfections, HIV-associated kidney disease, active or high risk for cardiovascular disease, opportunistic diseases, symptomatic primary HIV infection, and situations in which there is high risk for HIV transmission such as serodiscordant (one HIV-infected and one HIV-uninfected) partners. Once initiated, ART should be continued, except in the context of a clinical trial. Risk reduction counseling should be a routine part of care at each patient-clinician interaction.

What to Start

According to the authors, components of the initial and subsequent regimens must be individualized, particularly in the context of concurrent (occurring at the same time) conditions. Fixed-dose

combinations are recommended when possible for convenience. Tenofovir plus emtricitabine is the recommended nRTI (nucleoside or nucleotide analogue reverse transcriptase inhibitor) combination in initial therapy. Zidovudine plus lamivudine should be reserved for instances in which neither tenofovir nor abacavir combinations can be used. The recommended third component should be efavirenz or a ritonavir-boosted protease inhibitor (particularly atazanavir or darunavir) or the integrase inhibitor raltegravir. Three or 4 nRTIs alone are not recommended for initial therapy. There are also considerations for initial therapy in patients with specific conditions.

Monitoring

Plasma HIV-1 RNA levels should be monitored frequently when treatment is initiated or changed for virologic failure until viral load decreases below detection limits and regularly thereafter, the authors write. Once the viral load is suppressed for a year and CD4 + cell counts are stable at 350/uL or greater, viral load and CD4+ cell counts can be monitored at intervals up to 6 months in patients with dependable adherence. Baseline genotypic testing for resistance should be performed in all patients who have not received treatment before and in cases of confirmed virologic failure. The goal of therapy, even in heavily pre-treated patients, should be HIV-1 RNA suppression below commercially available assay quantification limits.

When to Change and What To Change To

According to the authors, maintenance of regimen potency is the objective when switching ART regimens. Virologic failure of an initial regimen (confirmed measurable viremia [presence of the virus in the blood stream]) should be identified and treated as early as possible with at least 2 (and ideally 3) fully active drugs to avoid the accumulation of

resistance mutations. Depending on the resistance profile and options available, inclusion of agents from new drug classes should be considered. Monotherapy with a ritonavir-boosted protease inhibitor should be avoided unless other drugs cannot be considered for reasons of toxicity or tolerability. Design of a new regimen should consider previous drug exposure, previous and current resistance profile, drug interactions, and history of intolerance or toxicity. Treatment interruptions should be avoided, except in the context of controlled clinical trials.

"... far too many HIV-infected persons present for medical care with advanced disease, both in wealthy and resource-limited settings. Universal voluntary HIV testing, comprehensive prevention services, and early linkage to care and treatment are necessary to ensure that advances in ART are made available during earlier disease stages. Advances in ART have shown that AIDS, as traditionally defined, can be prevented. One of the greatest challenges is that full implementation of these guidelines will require addressing social and structural barriers to diagnosis and care, as well as the pervasive stigma and discrimination associated with an HIV diagnosis," the authors conclude.

More information: JAMA. 2010;304[3]:321-333.

Provided by JAMA and Archives Journals