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in the spotlight

New ARVs Offer Virologic Suppression in Most Patients

Kimberly Y. Smith, MD, MPH

Newer antiretroviral (ARV) drugs in existing and novel classes are highly effective in treatment-experienced patients, but physicians must be careful to screen adequately for resistance patterns and sensitivity to agents, said Kimberly Y. Smith, MD, MPH, associate professor of medicine at Rush University Medical Center at a session on state-of-the-art HIV care at the 48th Annual ICAAC/IDSA 46th Annual Meeting in Washington, D.C., last month.

Recently approved ARVs offer virologic efficacy in multidrug-resistant patients, usually with minimal adverse events. Since few agents with demonstrated activity against multi-drug resistant virus are in the pipeline for the near future, Dr. Smith noted, "We need to get the most out of these new agents; thus, the most effective use of them requires strategic planning."

The entry inhibitor maraviroc provides a good example of the importance of carefully selecting a drug regimen based on patient profiles. While physicians are aware that maraviroc can be very effective in patients with R5-tropic virus, some might not be aware that the less sensitive first-generation tropism assay (Trofile) was recently replaced by a more sensitive one (Trofile ES). Trofile ES is expected to do a better job of identifying patients with low levels of X4 virus who are not good candidates for treatment with maraviroc.

Dr. Smith highlighted a regimen including three recently approved drugs—the protease inhibitor darunavir (with ritonavir) plus non-nucleoside reverse-transcriptase inhibitor etravirine plus integrase inhibitor raltegravir—that resulted in high rates of viral suppression and recovery of CD4+ cells in highly treatment-experienced patients. Further studies investigating this combination are ongoing.

New Drugs for the Treatment-Naïve?

The success of new ARVs in treatment-experienced patients has some wondering whether the drugs, particularly from the new classes, are appropriate for treatment-naïve patients. Some are and some are not, reported Dr. Smith.

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Maraviroc, in fact, was demonstrated to be less effective than efavirenz in the MERIT study, which was reported at the 2007 International AIDS Society (IAS) meeting. However, a poster presentation presented at the ICAAC/IDSA meeting suggested that maraviroc might have been more successful had the more sensitive tropism assay been available at the time.

Raltegravir has been shown to be as effective as efavirenz, reported Dr. Smith. A large phase III study comparing efavirenz to raltegravir (both in combination with fixed dose tenofovir plus emtricitabine) in treatment-naïve patients was presented by Lennox et al. at this year's meeting. This study demonstrated high rates of viral suppression in subjects on both treatment arms of the study, with fewer side effects observed in the raltegravir-treated subjects.

Etravirine will like be used less often in treatment-naïve subjects due to its twice daily dosing.

Of the new agents, only darunavir is currently recommended for use in treatment-naïve patients. Once-daily dosing of this agent has been proven to be highly effective in this population, and long-term efficacy and tolerability are being studied. Both the U.S. Department of Health and Human Services and IAS-USA guidelines include darunavir among its protease-inhibitor treatment options, and the Food and Drug Administration has recently approved this agent for treatment-naïve patients.

Dr. Smith advised physicians to address adherence issues for all patients before initiating or switching therapy. However, for physicians switching patients from a failing regimen, she said, "Don't wait too long, since additional mutations can accumulate that may affect the success of new agents."

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