

# The 2013 Clinical Guidelines for the Diagnosis and Treatment of HIV/AIDS in HIV-Infected Koreans

The Korean Society for AIDS

While a variety of clinical guidelines for the diagnosis and treatment of HIV/AIDS are used extensively around the world, the implementation of such guidelines is not assured in Korea due to constraints with respect to the diagnostic tests and antiretroviral drugs currently available in the country. Consequently, the Committee for Clinical Guidelines for the Diagnosis and Treatment of HIV/AIDS of the Korean Society for AIDS was founded in 2010, and the first edition of the Korean guidelines was published a year later. However, due to the rapid discovery of new data in the field of HIV and the evolution of the clinical environment in Korea in the last few years, it has become necessary to revise the first set of guidelines. This guideline aims to provide comprehensive information regarding the diagnosis and management of HIV/AIDS in Korea. The recommendations contain important information for physicians working with HIV/AIDS in the clinical field. A brief summary of the revised guidelines and key changes to the original version of the guidelines are summarized below.

**Key Words:** HIV/AIDS, Diagnosis, Antiretroviral treatment, Guidelines

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\* The following recommendation is a practical guideline based on the current (2013.8) domestic Korean status, on the diagnosis and treatment of HIV infected patients. Rather than applying the following principle to the general, we recommended that patient treatment be based upon clinical decision making, according to the diversity of every individual patient.

\* The following recommendation can be used for educational and personal clinical practices, but it cannot be utilized for any commercial or clinical evaluation purposes. Those who wish to use the following guideline for any other purposes must admit a written form and must get written consent from the committee.

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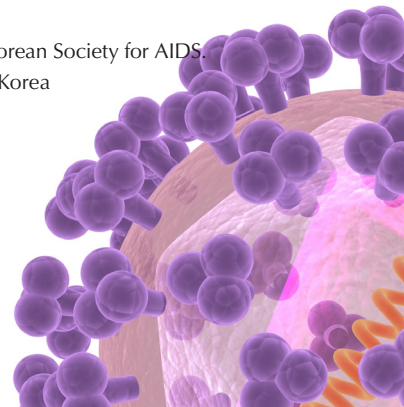
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## What's new in the guidelines?

The following key changes have been made to update the 2011 guidelines.

- 1) Bone mineral densitometry should be considered in men over the age of 50 years and post-menopausal women.
- 2) The previous guidelines did not recommend the initiation of antiretroviral therapy for patients with CD4+ T cell counts  $> 500/\text{mm}^3$ , but the new recommendations include offering antiretroviral therapy to all patients regardless of their CD4+ T cell counts. The new guidelines also favor the initiation of antiretroviral therapy for acute/recent HIV infection.
- 3) Tenofovir (TDF)/emtricitabine (FTC) is introduced as a preferred nucleoside analogue reverse transcriptase inhibitor (NRTI) backbone.
- 4) Zidovudine/lamivudine (3TC), which was the preferred NRTI backbone in the original guidelines, has been reclassified as an alternative NRTI backbone.
- 5) Raltegravir, an integrase strand transfer inhibitor (INSTI), has been reclassified as a preferred agent. It was considered an alternative agent in the original guidelines.
- 6) Nevirapine, which was advocated as an alternative non-nucleoside reverse transcriptase inhibitor (NNRTI), is no longer recommended.
- 7) Rilpivirine, an NNRTI, is introduced as an alternative NNRTI.
- 8) Sections on HBV/HCV screening and prevention have been added.
- 9) The recommendations for the pretreatment evaluation of HIV/HBV and HIV/HCV coinfection have been revised.
- 10) The HIV/HBV treatment guidelines have been revised according to the availability of tenofovir/emtricitabine.
- 11) The HIV/HCV treatment guidelines have been revised.
- 12) Recommendations for the monitoring of treatment responses to HBV/HCV infection have been added.

## Initial assessment and follow-up tests

People living with HIV encounter various medical, psychological, and social problems. Every HIV-infected patient entering care should have a complete medical history, physical ex-

amination, and laboratory evaluation for subjective symptoms, underlying diseases, financial conditions, high-risk behaviors, and psychological elements. During the initial visit, a CD4+ T cell count/% proportion, plasma HIV-RNA (viral load), complete blood count including white blood cell differential count, chemistry profile, serologies for hepatitis A, B, and C, and screening tests for syphilis, toxoplasmosis, gonorrhea, and tuberculosis such as tuberculin skin tests, interferon (IFN)-release assays, or chest X-rays should be taken. In the case of advanced disease, a repeat test for tuberculosis is recommended when the CD4+ T cell count recovers over  $200/\text{mm}^3$  if the initial test for tuberculosis was negative. Genotypic resistance testing should be performed on entry into care to assess transmitted drug resistance, and bone mineral densitometry should be considered in men over the age of 50 years and post-menopausal women [1-3].

In people who are going to take highly active antiretroviral therapy (HAART), a CD4+ T cell count, HIV-RNA viral load (within the four-week period prior to HAART), pregnancy test (for women who are considering an efavirenz-based regimen), HLA-B\*5701 test (if considering abacavir use), and genotypic resistance test should be performed before HAART initiation [4, 5].

During HAART, the patient's CD4+ T cell count should be measured every 12–16 weeks, and this interval can be extended to 24–48 weeks if immunity is resumed after HAART and the patient is clinically stable. If the fasting lipid profile is normal, the recommended repetition interval is 48 weeks. However, a 24-week interval is suggested in the case of an abnormal result. In terms of fasting blood sugars, the recommended intervals are 12–24 weeks, with 12 and 24 weeks for abnormal and normal results, respectively. Serologic tests for viral hepatitis and opportunistic infection should be repeated every 48 weeks if the initial tests were negative.

## Conditions for the initiation of antiretroviral therapy

All adults with HIV infection should be offered HAART regardless of their CD4+ cell count. This recommendation is based on observational cohort data that all patients may benefit from HAART, as well as data from a randomized controlled trial that showed that HAART reduces the likelihood of HIV transmission while simultaneously providing clinical benefits to treated individuals [6-8]. In addition to the previously described data, recent evidence increasingly supports earlier initiation of HAART. Although no randomized con-

trolled trial has defined the optimal time of initiation, the available data are consistent with, and further strengthen, the recommendation for the early initiation of HAART.

Antiretroviral therapy is indicated for all pregnant women for both the mother's health and the prevention of HIV transmission to the infant [9]. Early initiation of antiretroviral therapy is recommended after starting active treatment for AIDS-defining illnesses. Persons with HIV-associated nephropathy should begin therapy as soon as the diagnosis is made because antiretroviral therapy improves survival and kidney function in these patients [10]. The risk of liver-related morbidity and mortality is increased in persons dually infected with HIV and HBV [11]. Infection with HIV also increases the risk of liver-related morbidity and mortality in persons dually infected with HCV. Antiretroviral therapy for patients coinfecting with HIV and the hepatitis virus reduces the progression of liver disease [12, 13]. A high viral load ( $> 100,000$  copies/mL) and rapid CD4+ T cell count decline ( $> 100/\text{mm}^3$  per year) are also conditions that favor the initiation of therapy regardless of CD4+ T cell count [14]. Antiretroviral therapy initiation is also recommended for patients with acute or recent HIV infection, with evidence of the benefits having been established [15, 16]. Despite increasing evidence for the benefits associated with earlier initiation of antiretroviral therapy, patients and clinicians should consider antiretroviral drug toxicities, the importance of adherence, and cost before the initiation of therapy.

### Initial combination regimens for the antiretroviral-naïve patient

The panel recommends one of the following antiretroviral regimens in treatment-naïve patients: 2 NRTI + ritonavir-boosted protease inhibitor (PI/r) or protease inhibitor (PI); 2 NRTI + NNRTI; or 2 NRTI + INSTI. Tenofovir/emtricitabine and abacavir/lamivudine are the preferred NRTI backbones [17, 18]. Zidovudine/lamivudine or didanosine/lamivudine may be used when the aforementioned NRTI backbones are not suitable [19, 20]. Ritonavir-boosted darunavir, ritonavir-boosted atazanavir, and ritonavir-boosted lopinavir are the preferred drugs when PI/r (or PI) is used. Unboosted atazanavir may be used as an alternative drug when the preferred PI/r cannot be used [21-23]. However, unboosted atazanavir cannot be used [24] with tenofovir. Efavirenz is the preferred drug when NNRTI is used [23]. Rilpivirine may be used as an alternative NNRTI when efavirenz cannot be used [25, 26]. Raltegravir can be used as a preferred INSTI [27].

### Management of the treatment-experienced patient

Regular monitoring of plasma HIV-1 RNA is recommended to evaluate virologic response in treatment-experienced patients. When virologic failure (HIV-1 RNA level  $> 200$  copies/mL) is detected, a drug-resistance test should be done while the patient is taking the failing antiretroviral regimen. The goal of treatment for patients with virologic failure is to re-establish virologic suppression ( $< 50$  copies/mL). The patient's treatment history and resistance test results (past and current) should be used to identify at least two, preferably three, fully active agents for patients with virologic failure. If maximal viral suppression is not possible due to the limitations of active agents, antiretroviral therapy should be continued to avoid clinical deterioration [1, 28].

### Prevention, management, and treatment of chronic hepatitis B and C coinfection in HIV-infected patients

All HIV-infected patients should be tested for HBV and HCV infection, and assessed for immunity to hepatitis A. If patients are non-immune, vaccination is recommended. Hepatitis B surface antigen (HBsAg)-positive patients should be tested for HBV-DNA quantitatively before the initiation of HAART. Regardless of CD4+ T cell count or HBV treatment status, HAART-including agents with both anti-HIV and anti-HBV activity are recommended. As the NRTI backbone of HAART, a combination of TDF + FTC or TDF + 3TC is recommended [13, 29, 30]. If HBV treatment is needed and TDF cannot be used, the alternative option is entecavir in addition to a fully suppressive HAART [31]. Other options include peginterferon alfa (PegIFN) monotherapy or adefovir in combination with 3TC, FTC, or telbivudine in addition to a fully suppressive ARV regimen [13, 32, 33]. Entecavir, which is active against HIV, must be used in addition to a fully suppressive antiretroviral regimen [31, 34]. The discontinuation of agents with anti-HBV activity should be carefully monitored [35]. If HAART needs to be modified due to HIV virologic failure and the patient has optimal HBV suppression, the antiretroviral drugs active against HBV should be continued in combination with other suitable antiretroviral agents to achieve HIV suppression. Initial testing for HCV should be performed by measuring anti-HCV in the blood, and if positive, a confirmatory test measuring the plasma HCV-RNA level should be done quantitatively. In patients with HIV/HCV coinfection, pre-treatment

assessments prior to HCV treatment include the HCV genotype, IL-28B genotype, and stage of liver disease [36-39]. HAART should be considered for HIV/HCV coinfecting patients regardless of CD4+ T cell count [40-42]. A combination of PegIFN plus ribavirin is the recommended backbone of therapy for HIV/HCV coinfecting patients regardless of HCV genotype. If ribavirin cannot be used, PegIFN monotherapy is recommended. Potential drug-drug interaction and toxicity should be carefully monitored when treating HIV/HBV and HIV/HCV coinfecting patients [43-49].

## Supplementary material

Guideline Korean version.

Supplementary material can be found with this article online <http://www.icjournal.org/src/sm/ic-45-455-s001.pdf>.

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