Special Article
http://dx.doi.org/10.3947/ic.2015.47.3.205
Infect Chemother 2015;47(3):205-211
ISSN 2093-2340 (Print) · ISSN 2092-6448 (Online)

ic Infection & Chemotherapy

The 2015 Clinical Guidelines for the Diagnosis and Treatment of HIV/AIDS in HIV-Infected Koreans

The Korean Society for AIDS

The Committee for Clinical Guidelines for the Diagnosis and Treatment of HIV/AIDS of the Korean Society for AIDS was founded in 2010. The first edition of the Korean guidelines was published in 2011, and revised in 2013. The recommendations in the guideline contain important information for physicians working with HIV/AIDS in the clinical field. However, due to the rapid discovery of new data in the field of HIV and the evolution of the clinical environment in Korea, it has become necessary to revise the guideline again. This guideline aims to provide up-to-date comprehensive information regarding the diagnosis and management of HIV/AIDS in Korea. This guideline deals with issues regarding the initial assessment of newly diagnosed patients, timing of antiretroviral treatment (ART) initiation, preferred ART regimens in treatment-naïve as well as treatment-experienced patients and special populations such as HBV/HCV co-infected patients, or pregnant women. 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 (2014.11) 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.

Received: June 30, 2015
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1. What's new in the guidelines?

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

1) For the patient on a suppressive regimen whose CD4 count has consistently maintained, CD4+ T cell monitoring interval can be extended to every 6 months. Continued CD4+ T cell monitoring for virologically suppressed patients whose CD4+ T cell counts have been consistently >500 cells/mm^3 for at least 2 years may be considered optional.
2) Rilpivirine (RPV) is introduced as a preferred non-nucleoside reverse transcriptase inhibitor (NNRTI).
3) Elvitegravir (EVG)/cobicistat (COBI) is introduced as a preferred integrase strand transfer inhibitor (INSTI). It is available only as a single co-formulated tablet as tenofovir/emtricitabine/elvitegravir/cobicistat.
4) Didanosine (ddI)/lamivudine (3TC), which were advocated as an alternative nucleoside reverse transcriptase inhibitor (NRTI) backbone, are no longer recommended.
5) Sections on antiretroviral use in pregnant women have been added.

2. 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 examination, 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 performed. In the case of advanced disease, a repeat test for tuberculosis is recommended when the CD4+ T cell count recovers over 200/uL 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. Continued CD4+ T cell monitoring for virologically suppressed patients whose CD4+ T cell counts have been consistently >500 cells/mm^3 for at least 2 years may be considered optional. 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.

3. 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 controlled 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 to prevent 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-re-

lated morbidity and mortality in persons dually infected with HCV. Antiretroviral therapy for patients coinfected 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/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.

4. Initial combination regimens for the antiretroviral-naïve patient

The panel recommends one of the following antiretroviral regimens in treatment-naïve patients: 2 nucleoside reverse transcriptase inhibitor (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 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 [21-23]. Unboosted atazanavir may be used as an alternative drug when the preferred PI/r cannot be used [24]. However, unboosted atazanavir cannot be used with tenofovir. Efavirenz and Rilpivirine are the preferred drug when NNRTI is used [23, 25]. Raltegravir and elvitegravir/cobicistat can be used as a preferred INSTI [26]. Elvitegravir/cobicistat is available only as a single co-formulated tablet as tenofovir (TDF)/emtricitabine (FTC)/elvitegravir/cobicistat [27].

5. 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 past and current resistance test results 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].

6. 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 antiretroviral 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 coinfected patients regardless of CD4+ T cell count [40-42]. A combination of PegIFN plus ribavirin is the recommended backbone of therapy for HIV/HCV coinfected 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 coinfected patients [43-49].

7. Management of HIV-infected pregnant women

Women of childbearing potential should undergo pregnancy testing before initiation of efavirenz. Use of HAART during pregnancy has reduced the rate of perinatal transmission of HIV from approximately 30% to 0.1% to 0.5% [50]. Thus, HAART is recommended for all HIV-infected pregnant women. When selecting an antiretroviral regimen for a pregnant woman, clinicians should consider the known safety, and efficacy data for each agent.

Supplementary material

Guideline Korean version.

Supplementary material can be found with this article online http://www.icjournal.org/src/sm/ic-47-205-s001.pdf.

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