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Consensus statement

Executive summary of the GESIDA/National AIDS Plan Consensus Document on Antiretroviral Therapy in Adults Infected by the Human Immunodeficiency Virus (Updated January 2016)

AIDS Study Group (GESIDA) of the Spanish Society of Infectious Diseases, Clinical Microbiology, the National AIDS Plan[1]

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ABSTRACT

In this update, antiretroviral therapy (ART) is recommended for all patients infected by type 1 human immunodeficiency virus (HIV-1). The objective of ART is to achieve an undetectable plasma viral load (PVL). Initial ART should comprise 3 drugs, namely, 2 nucleoside reverse transcriptase inhibitors (NRTI), and 1 drug from another family. Four of the recommended regimens, all of which have an integrase strand transfer inhibitor (INSTI) as the third drug, are considered a preferred regimen; a further 6 regimens, which are based on an INSTI, a non-nucleoside reverse transcriptase inhibitor (NNRTI), or a protease inhibitor boosted with cobicistat or ritonavir (PI/COBI, PI/r), are considered alternatives. The reasons and criteria for switching ART are presented both for patients with an undetectable PVL and for patients who experience virological failure, in which case the rescue regimen should include 3 (or at least 2) drugs that are fully active against HIV. The specific criteria for ART in special situations (acute infection, HIV-2 infection, pregnancy) and comorbid conditions (tuberculosis and other opportunistic infections, kidney disease, liver disease, and cancer) are updated.

Resumen ejecutivo del Documento de consenso de GESIDA/Plan Nacional sobre el Sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana (Actualización enero 2016)

Palabras clave:
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RESUMEN

Se recomienda tratamiento antirretroviral (TAR) a todos los pacientes con infección por VIH-1. El objetivo del TAR es lograr una carga viral plasmática (CVP) indetectable. El TAR inicial debe ser una combinación de 3 fármacos, que incluya 2 inhibidores de la transcriptasa inversa análogos de nucleósidos (ITIAN) y otro de distinta familia. Cuatro de las pautas recomendadas, todas las cuales tienen un inhibidor de la integrasa (INI) como tercer fármaco, se consideran preferentes, y otras 6, basadas en un INI, un inhibidor de la transcriptasa inversa no análogo de nucleósidos (ITINN) o un inhibidor de la proteasa potenciado con cobicistat o ritonavir (IP/COBI, IP/r), como alternativas. Se exponen las causas y los criterios para cambiar el TAR en los pacientes con CVP indetectable así como en los que presentan fracaso virológico, en cuyo caso el TAR de rescate debe incluir 3 (o al menos 2) fármacos plenamente activos frente al VIH. Se actualizan los criterios específicos del TAR en situaciones especiales (infección aguda, infección por VIH-2, embarazo) o comorbilidades (tuberculosis u otras enfermedades oportunistas, enfermedad renal, hepatopatías y neoplasias).

[1] See writing committee in Appendix A.

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Introduction

Since 1996, when the arrival of antiretroviral drugs made it possible to build potent combinations, antiretroviral therapy (ART) has led to huge health care benefits (reduced morbidity, mortality and transmission of the human immunodeficiency virus [HIV]). In parallel with these advances, ART has become complicated owing to the high number of drugs and families, as well as the many aspects affecting the appropriate choice of drugs (efficacy, toxicity, resistance, tropism, pharmacologic interactions, use in special situations, and cost-effectiveness).

The complexity and speed with which changes occur necessitate frequent updating of guidelines on ART. For the last 17 years, GESIDA and the National AIDS Plan have jointly edited a consensus document on ART in adults.[1] The present document updates previous recommendations in this population.

The objective of this consensus document is to provide health professionals who treat HIV-infected adults with up-to-date knowledge on ART and a series of recommendations based on scientific evidence that can act as guidelines in therapeutic decision making.

Clinical and laboratory evaluation as a guide for ART

Clinical evaluation

It is important to take an exhaustive clinical history, including physical and psychological data, treatment, habits, and risk practices. Specific aspects applying to women (e.g., desire to become pregnant and contraception) should be analyzed and a complete physical examination performed.

Recommendation

- A clinical history should be taken for all HIV-infected patients. The history should include an evaluation of the patient's drug therapy and comorbid conditions. The patient should also undergo a thorough physical examination, which should be repeated once a year (A-II).

Laboratory tests

In addition to specific determinations associated with HIV infection and its consequences, other tests should be ordered to take account of previous infections or cardiovascular risk factors.

Recommendation

- The initial laboratory workup should include a complete blood count, general biochemistry, and serology testing (*Toxoplasma*, cytomegalovirus, syphilis, HAV, HBV, and HCV). Viral load, CD4+ T-lymphocyte count, and primary resistance to HIV and HLA-B*5701 should also be determined (A-II).

CD4+ lymphocytes

The number of CD4+ T lymphocytes is the main marker of the risk of progression and onset of non-AIDS events.

Recommendation

- The absolute number and percentage of CD4+ T lymphocytes should be determined before initiating ART. Once therapy has started, these determinations should be made periodically to monitor the immune response (A-I).
- Determinations can be at longer intervals (up to 12 months) in stable patients with suppressed plasma viral load (PVL) and CD4+ T-lymphocyte counts >300–500 cells/μL (C-II).

Plasma viral load

PVL is a marker of the risk of progression and transmission of HIV.

Recommendations

- PVL should be determined before initiation of ART and regularly during treatment (A-II).
- PVL is the main parameter for evaluating the virological efficacy of ART and for defining virological failure (A-I).
- The objectives of virological suppression (VL <50 copies/mL) should be met both in ART-naïve patients and in those who have experienced previous therapeutic failure (A-II).
- PVL should be determined using a technique with a quantification limit of at least 50 copies/mL. The same technique should always be used (A-II).
- If decisions on therapy are to be taken based on PVL, they should be confirmed with a second determination (A-II).

Plasma concentration of antiretroviral drugs

The plasma concentration of antiretroviral drugs is correlated with efficacy and toxicity; therefore, determination of their levels could prove useful in certain situations.

Recommendations

- Determination of the plasma concentration of antiretroviral drugs is not recommended for regular monitoring of HIV-infected patients (A-II).
- Determination of the plasma concentration of antiretroviral drugs may be indicated in specific clinical situations (e.g., risk of pharmacological interactions, organ transplantation, extreme underweight or overweight, pregnancy, and renal or hepatic insufficiency) and to confirm suspected poor adherence to therapy (B-III).

Resistance of HIV-1 to antiretroviral drugs

Viral genome mutations are the consequence of rapid HIV-1 turnover and error-prone reverse transcriptase. The emergence of resistant mutations is associated with virologic failure. Resistance mutations can be either primary or secondary to virologic failure.

Recommendations

- Genotyping of reverse transcriptase and protease to detect HIV resistance mutations should be performed in all patients at diagnosis of infection and before initiating ART if this is deferred (A-II).
- Assessment of baseline integrase resistance mutations is only recommended when there is a high suspicion of transmission of resistance to integrase strand transfer inhibitors (INSTI) (C-III).
- Resistance should be studied by genotyping in all patients in whom virological failure has been confirmed. The study should include integrase resistance mutations if the patient's regimen includes an INSTI (A-I).

*Determination of the HLA-B*5701 allele*

The presence of the HLA-B*5701 allele is associated with hypersensitivity reaction to abacavir (ABC), a life-threatening multiorgan clinical syndrome observed during the first 6 weeks of treatment.

Recommendations

- HLA-B*5701 should be determined in all patients before initiating an ART regimen containing ABC (A-I).