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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 2014)☆

Expert Panel of GeSIDA and the National AIDS Plan

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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 strength and grade of the recommendation varies with clinical circumstances, number of CD4 cells, comorbid conditions and prevention of transmission of HIV. The objective of ART is to achieve an undetectable plasma viral load. Initial ART should always comprise a combination of 3 drugs, including 2 nucleoside reverse transcriptase inhibitors and a third drug from a different family (non-nucleoside reverse transcriptase inhibitor, protease inhibitor, or integrase inhibitor). This update presents the causes and criteria for switching ART in patients with undetectable plasma viral load and in cases of virological failure. An update is also provided for the specific criteria for ART in special situations (acute infection, HIV-2 infection, and pregnancy) and with comorbid conditions (tuberculosis or other opportunistic infections, kidney disease, liver disease, and cancer).

Executive summary 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 2014)

Palabras clave:
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RESUMEN

Se recomienda el TAR en todos los pacientes infectados por el VIH-1. La fuerza y gradación de la recomendación varía según la circunstancia clínica, número de CD4+, presencia de comorbilidades y prevención de la transmisión del VIH. El objetivo del TAR es lograr una CVP indetectable. El TAR de inicio debe ser siempre una combinación de tres fármacos que incluya una asociación de 2 análogos de nucleósido y otro fármaco de distinta familia (inhibidor de la transcriptasa inversa no nucleósido, inhibidor de la proteasa o inhibidor de la integrasa). Se exponen las causas y criterios para cambiar un TAR estando con CVP indetectable, así como en el fracaso virológico. Se actualizan igualmente los criterios específicos del TAR en situaciones especiales (infección aguda, infección por VIH-2, embarazo) o comorbilidades (tuberculosis u otra enfermedad oportunista, afectación renal, hepatopatías y neoplasias).

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 and mortality and reduced transmission of the human immunodeficiency virus

☆ See writing committee in Appendix A.

E-mail address: lopez_jos@gva.es

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[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 administration (efficacy, toxicity, resistance, tropism, pharmacologic interactions, use in special situations, and cost-effectiveness).

The complexity and speed with which changes occur necessitate frequent preparation and updating of guidelines on ART. For the last 15 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

- Every year, HIV-infected patients should undergo a physical examination. Pharmacological treatment should also be evaluated and a clinical history taken (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 appearance 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).

Plasma viral load

Plasma viral load (PVL) is a marker of the risk of progression and transmission of HIV.

Recommendation

- PVL should be determined before initiating ART (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 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

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

Recommendation

- Determination of the plasma concentration of antiretroviral drugs is not recommended for habitual 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 [morbid obesity], 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.

Recommendation

- Genotyping should be performed for detection of HIV resistance mutations in all patients, both at diagnosis of HIV infection and before initiating ART (if ART is deferred) (A-II).
- Genotyping should be performed for detection of HIV resistance mutations in all patients whose therapy has failed (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 multi-organ clinical syndrome observed during the first 6 weeks of treatment.

Recommendation

- HLA-B*5701 should be determined in all patients before initiating an ART regimen containing ABC (A-I).
- ABC should not be prescribed if the result of the HLA-B*5701 determination is positive (A-I).

Determination of tropism

A tropism assay is useful when prescribing maraviroc.

Recommendation

- Viral tropism should be determined before starting therapy with a CCR5 inhibitor (A-I)

Initial antiretroviral therapy

The main objectives of ART are to reduce HIV-associated morbidity and mortality, restore and preserve immune function,