Official journal of the Spanish Society of Chemotherapy

Marta Rosas[1,2]
Santiago Moreno[1,2,3]

Global strategy in the treatment of HIV infection in 2022

[1]Servicio de Enfermedades Infecciosas. Hospital Universitario Ramón y Cajal. Madrid. Spain
[2]Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS). Madrid.
[3]Universidad de Alcalá (UAH). Madrid. Spain

Revista Española de Quimioterapia
doi:10.37201/req/s03.08.2022

ABCTRACT

The treatment of HIV infection has become a cornerstone for the global control of the pandemic due to its benefits on individual health and for preventing the transmission of HIV. It should be started in all people with HIV infection and as quickly as possible. Ideally, it should be started on the same day of diagnosis or, failing that, within the first 7 days. Antiretroviral regimens with excellent efficacy, no significant toxicity, and convenient administration are currently available for initiation of antiretroviral treatment. They can incorporate two or three drugs and are always based on a second-generation integrase inhibitor.

Keywords: HIV, antiretroviral therapy, dolutegravir, bictegravir.

INTRODUCTION

The treatment of HIV infection has become a cornerstone for the global control of the pandemic. Antiretroviral treatment (ART) not only has benefits on the individual health of people, by reducing complications and improving survival, but also prevents the transmission of HIV, significantly reducing the appearance of new infections. For all these reasons, it is crucial to incorporate into clinical practice the results of clinical trials and observational studies that guarantee therapeutic success with the minimum risk for patients.

There are national and international guidelines with recommendations for the treatment of HIV based on the best scientific evidence [1-5]. Surely the most important part of these guidelines is the one that refers to the initial treatment of HIV infection. When and with what to start ART is key, since in many cases it can determine the overall evolution of a patient. For this reason, we will briefly summarize the main recommendations in this regard collected from the most followed guides.

Correspondence:
Dr. Santiago Moreno Guillén
Servicio de Enfermedades Infecciosas, Hospital Universitario Ramón y Cajal, Carretera de Colmenar, Km. 9,100
28034 Madrid, Spain
E-mail: smguillen@salud.madrid.org

WHEN TO START ANTIRETROVIRAL TREATMENT

The optimal time to start ART has evolved over time. After the results of randomized clinical trials on the optimal time to start treatment to preserve the health of patients [6] and prevent transmission of infection [7] and large observational studies [8], the recommendation is unanimous: ART should be started in all person with HIV regardless of other factors, such as the presence of clinical symptoms, CD4+ T cell count, and viral load levels. In this way, patients and the community are benefited, the quality and quantity of life of patients is increased and the appearance of new cases is avoided, helping to control the pandemic.

The unanimity in this recommendation has led to pursuing a more demanding objective. The standard of treatment included not starting ART until an initial visit had been made with the patient, the pros and cons of treatment had been discussed, and the necessary tests had been ordered to choose the best therapeutic regimen. From the patient's first office visit, initiation of ART could be delayed by 3 to 6 weeks. Some clinical trials and observational studies showed that this delay could be associated with worse outcomes in patients [9]. For this reason, WHO and other organizations and institutions changed their recommendations and propose starting ART as soon as possible, ideally in the first week after diagnosis (rapid start). Furthermore, if the patient is prepared, the recommendation would be to start ART the same day as diagnosis (immediate start).

Conclusion. Antiretroviral treatment should be started in all people with HIV infection and as quickly as possible. Ideally, it should be started on the same day of diagnosis or, if not possible, within the first 7 days.

WITH WHAT TO START ANTIRETROVIRAL TREATMENT

Also in this regard, considerable unanimity has been reached in the different guidelines. The variety of regimens and drugs that were once part of the recommended regimens for initiating ART have been greatly simplified. It should be clarified that all the guidelines include regimens of choice, understanding that they are applicable to the vast majority of patients, but the regimens considered alternative may perfectly be the regimens of choice for a patient and even a group of patients.

The current recommendations can be summarized in two points:

1. How many drugs should be included in an initial regimen: The magic figure of 3 drugs has been altered by the results of randomized clinical trials [10]. A two-drug regimen alone has been shown in these clinical trials to be noninferior to a three-drug regimen in terms of virologic efficacy, rate of discontinuation due to toxicity, rate of any grade undesirable effects, and rate of resistance. after failure. Since the publication of these trials, all the guidelines include the two-drug regimen made up of lamivudine (3TC) and dolutegravir as the drug of choice for starting ART. The guidelines differ in the limitations for this double regimen as initial therapy, including high viral loads (>500,000 copies HIV RNA/ml), low CD4 count (<200 cells/mm3), active infection by the hepatitis B virus (surface antigen positive), pregnancy, absence of transmitted resistance tests before starting ART, and rapid initiation of ART.

2. With which drugs should ART be started: in both triple and dual regimens, the central element is a second-generation integrase inhibitor (dolutegravir or bictegravir in triple regimens, dolutegravir in dual regimen). Along with the integrase inhibitor, two nucleoside reverse transcriptase inhibitor analogs are associated in triple regimens, or a single analog in double regimens. The constant nucleoside analog is 3TC or FTC in all regimens. Furthermore, in three-drug regimens, some guidelines only include tenofovir alafenamide (TAF) while others also include tenofovir disoproxil fumarate (TDF) or abacavir. Table 1 shows the main initial therapeutic regimens included in the guidelines, which are usually recommended to be administered as a single pill. With these regimens, virological efficacy is achieved in practically all patients, with very low toxicity and the absence of resistance mutations in case of failure.

It should be noted that some scientific societies include two additional drugs: the integrase inhibitor raltegravir and the non-nucleoside analogue doravirine, having demonstrated its efficacy and low toxicity in clinical trials [3].

Conclusion. Antiretroviral regimens with excellent efficacy, no significant toxicity, and convenient administration are currently available for initiation of antiretroviral treatment. They can incorporate two or three drugs and are always based on a second-generation integrase inhibitor.

Table 1 Main therapeutic regimens recommended for initial ART.

Type of regimen	Drugs
Triple (3 drugs)	Bictegravir/FTC/TAF
	Dolutegravir/3TC/abacavir
	Dolutegravir + FTC/TAF
Dual (2 drugs)*	3TC/dolutegravir

FTC, emtricitabina; TAF, tenofovir alafenamide; 3TC, lamivudine
*With caveats (variable according to the different guidelines)

CONFLICT OF INTEREST

Authors declare no conflict of interest

REFERENCES

1. WHO. Guidelines for Managing Advanced HIV Disease and Rapid Initiation of Antiretroviral Therapy. https://www.ncbi.nlm.nih.gov/books/NBK475977/pdf/Bookshelf_NBK47.
2. Department of Health and Human Services. Panel on Antiretroviral Guidelines for Adults and Adolescents. https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/0.
3. European AIDS Clinical Society (EACS). European AIDS Clinical Society (EACS) guidelines V.11.0. https://www.eacsociety.org/media/final2021eacsguidelinesv11.0_oct2021.pdf
4. GeSIDA. Documento de consenso de GeSIDA/plan nacional sobre el sida respecto al tratamiento antirretroviral en adultos infectados por el virus de la inmunodeficiencia humana. https://gesida-seimc.org/wp-content/uploads/2022/05/GuiaGeSIDAPlanNacionalSobreElSidaRespectoAlTratamientoAntirretroviralEnAdultosInfectadosPorElVirusDeLaInmunodeficienciaHumanaActualizacionEnero2022.pdf.
5. Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2020 recommendations of the international antiviral society-USA panel. JAMA 2020; 324: 1651–69.
6. INSIGHT START Study Group. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. N Engl J Med. 2015;373:795-807.
7. Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral Therapy for the Prevention of HIV-1 Transmission. N Engl J Med. 2016;375:830-9.
8. Rodger AJ, Cambiano V, Bruun T et al. Risk of HIV transmission through condomless sex in serodifferent gay couples with the HIV-positive partner taking suppressive antiretroviral therapy (PARTNER): final results of a multicentre, prospective, observational study. Lancet 2019; 393: 2428–38.
9. Mateo-Urdiales A, Johnson S, Smith R et al. Rapid initiation of antiretroviral therapy for people living with HIV. Cochrane Database Syst Rev 2019; issue 6: CD012962. panel. JAMA 2020; 324: 1651–69.

10. Cahn P, Sierra Madero J, Arribas JR et al. Dolutegravir plus lamivudine versus dolutegravir plus tenofovir disoproxil fumarate and emtricitabine in antiretroviral-naive adults with HIV-1 infection (GEMINI-1 and GEMINI-2): week 48 results from two multicentre, double-blind, randomised, non-inferiority, phase 3 trials. Lancet 2019; 393: 143–55.