"Terapia intermittente" con bictegravir/ emtricitabina/tenofovir alafenamide in una piccola coorte di pazienti con infezione da HIV, virologicamente soppressi.

Short cycle therapy with bictegravir/ emtricitabine/tenofovir alafenamide in a small cohort of virally suppressed people living with HIV.

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Riassunto

La terapia antiretrovirale intermittente si è dimostrata efficace e sicura, in alternativa al trattamento giornaliero, nel trattamento di persone che vivono con infezione da HIV e virologicamente soppressi. Descriviamo la nostra esperienza clinica riportando l'outcome virologico a 12 mesi in 12 pazienti virologicamente soppressi in terapia intermittente con bictegravir / emtricitabine /tenofovir alafenamide, somministrato 5 giorni a settimana (dal lunedì al venerdì).

Abstract

Short-cycle therapy has proven to be a safe and effective alternative to standard every-day antiretroviral treatment for HIV-1 infected suppressed patients.

Here we report 12-month virological outcome of 12 virally suppressed patients on short cycle therapy with bictegravir/emtricitabine/tenofovir alafenamide administered 5 days a week (Monday to Friday).

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Introduction

In recent years, several strategies have been studied to reduce the exposure of people living with HIV (PLWH) to antiretroviral drugs and to improve their adherence and quality of life, while maintaining safety and virological suppression. In particular, the "intermittent" or "short-cycle" therapy (SCT) has received considerable attention in France (1).

This strategy allows PLWH to take their antiretroviral drugs at standard doses and in combination for a limited number of consecutive days (generally 4 or 5 days) per week and interrupt the treatment during the weekend (Friday to Sunday or Saturday to Sunday).

Here, we report 12-month virological outcome in 12 virally suppressed patients on short cycle therapy with bictegravir / emtricitabine/tenofovir alafenamide, administered 5 days a week (from Monday to Friday).

Case series

In our Infectious Diseases Unit, in Trento (Northern Italy), we regularly follow 597 HIV-positive individuals. Among these, at the beginning of March 2022 twelve people on a stable bictegravir / emtricitabine /tenofovir alafenamide antiretroviral daily regimen, in virological suppression, started a "short-cycle" therapy (Monday to Friday), avoiding the single tablet on Saturdays and Sundays.

In **Table 1**, patients' characteristics at baseline are reported. Mean age was 55. 9 years (range 25-75). Three of them were women.

Mean antiretroviral therapy duration was 18 years (range 4-32 years) and duration of virological suppression was 12. 5 years (range 4-25 years). Mean time from diagnosis of HIV infection was 20 years (range 4-33 years). Most of them had a long history of antiretroviral therapy, with a mean number of 6 (range 1-13) previous antiretroviral regimens.

Table 1. Baseline patients' characteristics.

Age, years, mean (range)	55. 9 (25-75)
Sex. N (%)	
Males	9 (75%)
Female	3 (25%)
Risk factor for HIV acquisition	
MSM	7 (58%)
Heterosexual	1 (8%)
Intravenous drug use	4 (33%)
CDC Stage	
A	6 (50%)
B	3 (25%)
C	3 (25%)
Weight at switch to SCT, Kg, mean	72.1 Kg
Weight at 12-month follow-up, Kg, mean	71.7 Kg
HIV infection duration, years, mean (range)	20 (4-33)
Antiretroviral therapy duration, years, mean (range)	18 (4-32)
Virological suppression duration, years, mean (range)	12.5 (4-25)
Number of antiretroviral regimens before SCT, mean (range)	6 (1-13)
CD4 count at switch (n/µL), mean	683
CD4 count at 12-month follow-up (n/µL), mean	754

They had not experienced any virological failure, after starting their first antiretroviral regimen. All patients had plasma HIV RNA <20 copies/mL at the beginning of SCT. At the time of writing (July 2023) all patients were still aviremic and had a mean follow-up of 15.5 months (range 15-16 months). From the switch to SCT up to the last visit, lymphocytes CD4+ increased by 72 cells/ µL in average. Mean body weight was 72.1 Kg at the time of switch and 71.7 Kg after one year of SCT.

Discussion

In recent years, different strategies have been studied to reduce the exposure of PLWH to antiretroviral drugs and to improve their adherence and quality of life, while maintaining safety and virological suppression.

In particular, the "intermittent therapy" or SCT has received considerable attention.

This strategy allows PLWH to take their antiretroviral drugs at standard doses and in combination for a limited number of consecutive days (generally 4 or 5 days) per week, interrupting the treatment on the weekends (Friday to Sunday or Saturday to Sunday).

In our case series, all patients on SCT had a plasma viral load of less than 20 copies/mL for more than 12 months, no evidence of drug resistance mutations or failures with their regimens, before the beginning of the short- cycle therapy, and no co-infection with hepatitis virus.

Various studies have showed the virological safety of this strategy. First of these, the FOTO study, conducted in 2007 (2).

Then, the BREATHER study ("BREaks in Adolescent and child THerapy using Efavirenz and two nRtis"), a multicentric, randomized, controlled, open-label phase 2/3 trial, demonstrated the non-inferiority of a 5-days-per-week SCT compared to standard 7-days-per-week schemes in 199 adolescents taking efavirenz-based ART (3).

Recently, the ANRS 170 QUATUOR, a randomized, open-label, multicentric, non-inferiority trial demonstrated the non-inferiority of the 4days-on/ 3days-off strategy in a large cohort of HIV-infected suppressed patients on different ART regimens over 96- weeks follow-up period (4). As suggested in a 2017 document of a group of French experts on treatment optimization of suppressed persons living with HIV (5), we think that short cycle therapies could represent a feasible and valuable option for antiretroviral treatment optimization in selected individuals. This strategy could also be inserted in official guidelines. ■

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