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Lowering HIV fitness and replication rate by administration of lamivudine alone, in extensively resistant HIV-infected patients, as a "bridging" strategy towards optimized salvage regimens

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Background

HIV-infected patients harbouring a lamivudine-resistant virus, seem to take benefit from a continued lamivudine monotherapy, versus combined antiretroviral treatment (cART) interruption, since a reduced HIV replication is selected by the maintenance of lamivudine-related M184 mutation. The mid-term outcome of isolated lamivudine therapy in multi-drug-resistant patients with very restricted therapeutic options, waiting for novel drug classes, is reported.

Methods

Six patients aged 23-49 years (4 males and 2 females, one of them with perinatal infection), with HIV disease treated since 13.8 ± 6.2 years with 10.3 ± 4.7 therapeutic lines, experienced repeated virological-immunological failures due to an extensive HIV genotype resistance, which finally led to a complete 3-class resistance, and no residual therapeutic options, when excluding the use of a fusion/integrase/co-receptor inhibitors, without the possibility to optimize the therapeutic background. A concurrent toxicity was also present:combined lipodistrophy syndrome, dyslipidemia, and insulin resistance (3,2, and one patients, respectively).

Results

At the time of lamivudine monotherapy initiation, the median viremia was 36,000 HIV-RNA copies/mL, while the median CD4+ count was 344 cells/μL. Despite a previous diagnosis of AIDS in 4/6 patients, at the time of therapeutic switch the clinical situation was stable. During the monthly follow-up with lamivudine monotherapy, ranging from 8 to 24 months (mean 9.9 ± 5.2) months, no HIV-associated signs-symptoms occurred, previous cART-associated laboratory toxicity significantly ameliorated, and no significant differences were found as to virological-immunological markers of HIV disease. A fluctuating viremia was noticed in all cases, with a median value at the end of follow-up of 44,000 HIV-RNA copies/mL, while no significant loss of CD4+ count occurred (median final levels:322 cells/μL). Two-four nucleos(t)ide mutations, and 2-5 protease mutations were deselected during the follow-up, but the M184 mutation remained. All these patients were allowed to re-introduce a cART with novel drug classes, according to the availability of an optimized therapeutic background in the subsequent months.

Discussion

When extensive HIV resistance does not leave therapeutic options, lamivudine monotherapy performed with a strict monitoring in clinically stable patients with no compromised virological-immunological figures, is a potentially safe choice. Waiting for the novel cART associations, the exploitment of lamivudine resistance on HIV replication-fitness represents an ultimate therapeutic approach to these difficult-to-manage subjects.

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