Journal of Clinical Virology 45 (2009) 72–75

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Case report

Virologic and immunologic responses to antiretroviral therapy among HIV-1 and HIV-2 dually infected patients: Case reports from Abidjan, Côte d'Ivoire

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ARTICLE INFO

Article history:
Received 12 November 2008
Received in revised form 26 February 2009
Accepted 6 March 2009

Keywords:
HIV-1/HIV-2
Dual infection
Antiretroviral therapy
Response to therapy

ABSTRACT

In four of five HIV-1 and HIV-2 dually infected patients treated with efavirenz-based therapy, viral load was undetectable for HIV-1 only, with limited increase in CD4+ counts. Both viral loads were undetectable and CD4+ counts increased in one patient treated with protease inhibitor regimen. Specific guidelines for treating HIV-dually infected patients are needed that should avoid the use of non-nucleoside reverse transcriptase inhibitors.

Published by Elsevier B.V.

1. Introduction

Infection with human immunodeficiency virus type one (HIV-1) or type two (HIV-2) causes depletion of CD4+ T cells and AIDS.[1] HIV-2 infection is endemic in West Africa, where an estimated 1–2 million cases exist.[2] HIV-2 has spread in the last decade to India and Europe.[3,4] Compared with persons infected with HIV-1, those infected with HIV-2 have a slower decrease in CD4+ T cell counts, lower mortality, lower rates of vertical and heterosexual transmission, and lower viral loads while asymptomatic.[1,4] Current treatment guidelines exclude treating HIV-2 infected patients with non-nucleoside reverse transcriptase inhibitors (NNRTIs) because HIV-2 isolates are intrinsically resistant to these molecules due to differences in amino acid sequences of one or more reverse transcriptase binding pockets.[5–7] In West Africa, where both HIV-1 and HIV-2 circulate, dual infection with the viruses is common.[8] However, very limited information exists on virologic and immunologic responses to antiretroviral therapy (ART) for dually infected patients, with treatment courses described for only four patients in three identified reports.[9–11] With an increasing number of HIV-infected patients in Africa receiving therapy through several initiatives, understanding how HIV-1 and HIV-2 dually infected patients respond to ART, is critical for developing treatment guidelines.

Treating dually infected persons with combinations of drugs that target only HIV-1 may effectively suppress HIV-1 viremia, but may not yield desirable effects against HIV-2 infection and may lead to HIV-2 disease progression. Here we describe changes in viral load, CD4+ T cell counts, and drug resistance profiles in a series of five dually infected patients in the first year of implementing ART in Côte d'Ivoire.

2. Methods

2.1. Background

In 1998, the Ministry of Health in Côte d'Ivoire in collaboration with the Joint United Nations' Program on AIDS (UNAIDS) established a drug access initiative to provide ART to HIV-infected patients. At the onset of this initiative, ART administered in the initiative included two- or three-drug antiretroviral regimens consisting of (a) nucleoside-analogue reverse transcriptase inhibitors (NRTIs: didanosine (DDI), stavudine (D4T), abacavir (ABC), lamivudine (3TC), zidovudine (ZDV)), and/or (b) a non-nucleoside-analogue reverse transcriptase inhibitor (NNRTI: efavirenz (EFV)) and/or a protease inhibitor (nelfinavir (NFV), indinavir (IDV)). For five patients analyzed, we retrospectively examined medical records from the first year of ARV treatment, and analyzed blood samples obtained during that year. These patients

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1386-6532/$ – see front matter. Published by Elsevier B.V.
doi:10.1016/j.jcv.2009.03.011

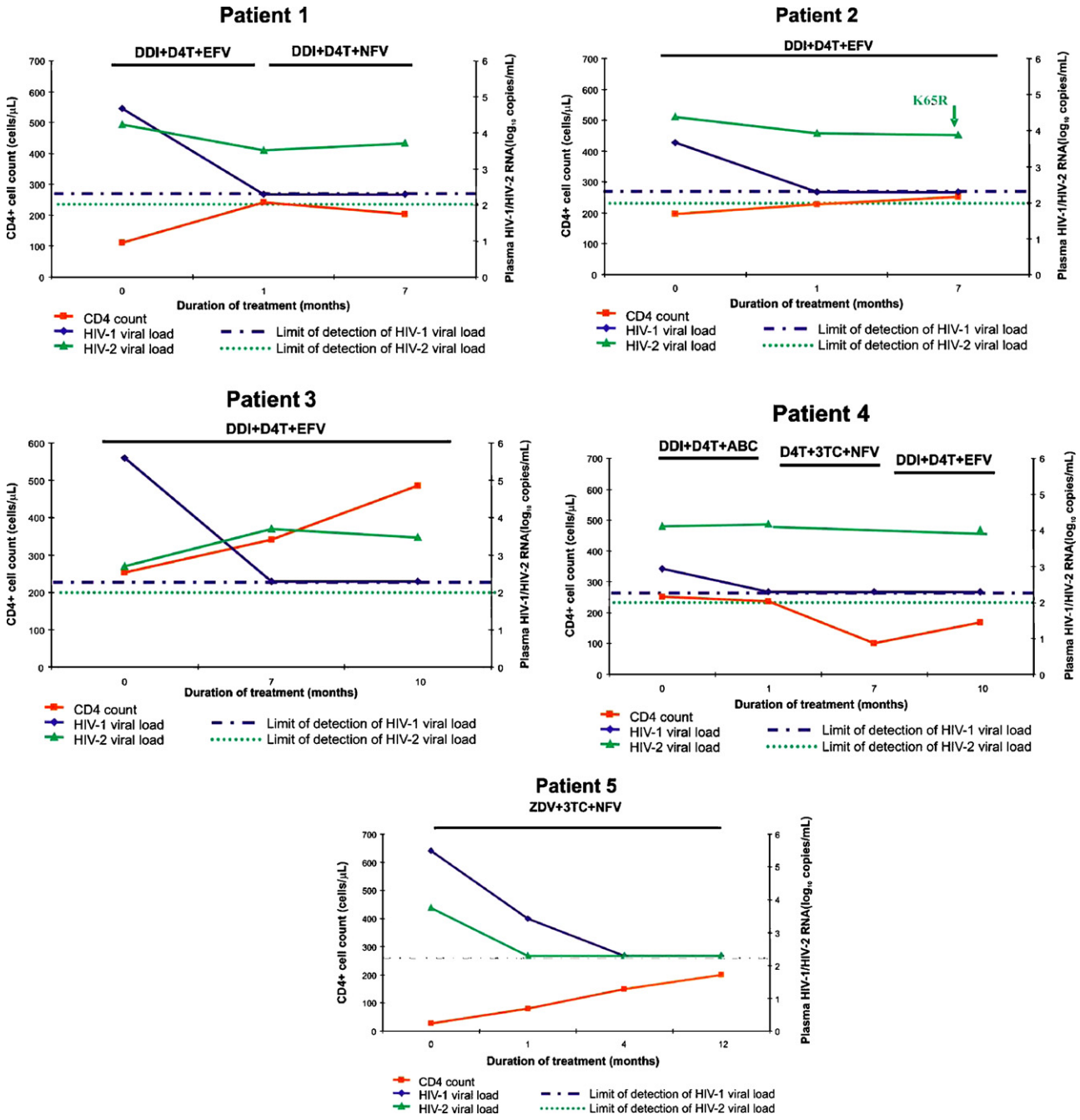

Fig. 1. CD4 counts, HIV-1 viral load and HIV-2 viral load values at different time points during the follow up period. Measurements done before initiating treatment are represented at time 0 on the *x*-axis.

were dually infected and had received different combinations of ART for several months. None of the patients had received ART prior to enrollment into the program.

2.2. Laboratory testing

We determined HIV antibody status using an ELISA-based testing parallel algorithm and HIV type-specific serodiagnosis was performed using a combination of monospecific ELISAs (Welcozyme HIV-1 and HIV-2 kit, Murex Diagnostics Limited, Temple Hill, Dartford, England). Dual infection was confirmed by DNA PCR testing on uncultured peripheral blood mononuclear cells (PBMCs) using HIV-1 and HIV-2 specific PCR primers from the protease gene as reported elsewhere.[12] HIV-1 RNA viral load in plasma was quantified by the Amplicor HIV-1 Monitor Assay, version 1.5 (Roche Diagnostic Systems, Branchburg, NJ, USA); this system has a limit of detection of 400 copies/ml. HIV-2 plasma viral load was quantified by a RT-PCR prototype assay (Roche Diagnostic Systems, Foster City, CA, USA),[13] which has a limit of detection of 100 copies/ml.

CD4+ T-cell count determinations were done using a FACScan flow cytometer (Becton Dickinson, San Jose, CA, USA). Antiretroviral drug resistance testing and analyses were done using the ViroSeq™ HIV-1 Genotyping System v2.0 (Celera Diagnostics, Alameda, CA). An in-house assay was used to determine HIV-2 drug resistance.[14] Adherence was scored based on a self-reported history of treatment interruption(s), missed drugs, or skipped pills.