

Some baseline ZDV resistance mutations may not predict drug failure in patients treated with ZDV/3TC/IDV

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Background

Previous studies shown that baseline resistance is a predictive factor for a less favourable response to antiretroviral therapy either in patients primarily infected with resistant strains or in patients failing from a previous regimen. However, this is not always true. Adherence to therapy and the potency of the regimen can overcome some patterns of resistance.

Methods

Retrospective study, including 26 patients enrolled in the Department of Infectious Diseases of the University Hospital of Coimbra with sustained undetectable viral load (VL < 400 copies/mL) for at least five years after starting HAART. Frozen samples with a HIV-1 RNA viral load greater than 1000 copies/ml kept at -80°C were used for automated direct sequencing of the RT and Protease segments of the *pol* gene at baseline (before starting HAART).

Results

Twelve patients had a viral load of less than 400 copies/ml and were not sequenced.

Seven patients were drug naïve and no pattern of mutations could be detected.

Before starting HAART, seven patients had previously been treated with dual NRTI combination and the following patterns of mutations associated with resistance were found:

- K70R/M184V;
- M41L/D67N/K70R/L210W/T215Y;
- D67N/K70R;
- M41L/E44D/D67N/K70R/V118I/L210W/T215Y;
- D67N/K70R/T215F/K219Q;
- M41L/T215Y;
- K70R/T215Y.

A high degree of self-reported adherence (>95%) was a common feature. All responded to a combination regimen that included **ZDV/3TC/Indinavir**. Mean HIV-1 RNA viral load of the fourteen sequenced samples was 22.593 copies/mL, mean CD4 was 318 cells/mm³ (max. 920, min. 66). Mean variation of CD4 since 1997 was 466 cells (min. 280; max. 610).

Table 1. Characteristics of all sequenced patients

Characteristics	N=14
Men, n (%)	12 (85,7)
Caucasian, n (%)	14 (100)
Median age (min-max) years	41 (32-54)
Risk Factors	
Homosexual men, n (%)	5 (35,7)
Injection drug use, n (%)	2 (14,3)
Heterosexual men or women	4 (28,6)
Unknown	3 (21,4)
Mean 1997 CD4 cell count (min-max) cells/mm ³	318 (66-920)
Mean Gain of CD4 cell count (min-max) cells/mm ³	466 (280-610)
Mean (1997) plasma HIV1 RNA (min-max) copies/ml	22593 (893-1000000)

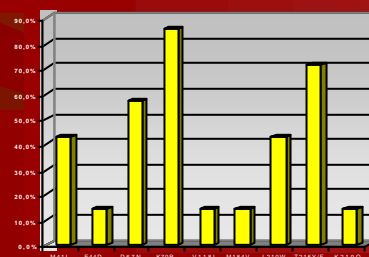


Figure 1. Frequency of NRTI resistance mutations in antiretroviral experienced patients (7).

Conclusions

Our data suggest that adherence to therapy and the potency of the HAART regimen are the strongest predictors of a long-term successful virologic and immunologic outcome. Both factors combined can overcome *in vivo* some patterns of resistance mutations associated with diminished susceptibility to AZT and 3TC. Prospective clinical trials are needed to validate data obtained in this retrospective study.

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