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Exposition and sequencing to antiretrovirals in HIV-1 patients with triple-class antiretroviral failure, and harbouring protease resistance mutations

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Purpose of the study

To assess the characteristics of advanced HIV-1 infected patients with triple-class antiretroviral drug failure (NRTIs, NNRTIs and PIs), and harbouring protease mutations.

Methods

Retrospective, cross-sectional, multicenter study to identify adult patients with previous failure to NRTIs, NNRTIs and PIs, and a genotype with at least one major PI mutation plus = 4 protease mutations in all (IAS-USA guidelines).

Summary of results

326 patients identified by 82 treating physicians. Median age 43 years, 80% male, median length of HIV infection 12 years, acquired by IVDU in 40%, and by sexual intercourse in 58%. Patients had been treated with a median of 11 (IQR 9–13) drugs, five PIs, and eight (IQR 6–10) lines of treatment. The main reason for treatment change was virological failure. Median CD4 count 274 cells (median nadir CD4 176 cells), viral load 12,242 HIV-1 RNA copies/ml. CDC stage was C in 58% of them. Hepatitis C coinfection in 42%, and HBsAg-positive 5.6%. Treatment compliance was significantly lower in IVDU vs. non-IVDU (51% vs 72%, p = 0.0003). The most frequent major protease mutations were L90M (65%), V82A/F/S/T (60%), M46I/L (39%), I84V (23%), and G48V (11%). L63P, L10I, A71V, and M36I were the most frequently isolated accessory protease mutations. Nearly all patients harboured M184V, different patterns of TAMs, and NNRTI mutations that rendered inactive the first generation NNRTIs. Their first line of treatment was composed of an NRTI monotherapy in 44% of patients, and 55% had received an early regimen with only dual NRTI. The first PI was a non-boosted one in 77% of patients, and 92% have received a boosted PI later on. Most of them had recycled inactive drugs, mainly NRTIs, and partially active PIs.

Conclusion

Patients with advanced virological failure exposed to NRTI, NNRTI and PI share specific characteristics that drive a "classical" pathway to HIV-1 resistance. This pattern is composed of a burned reverse transcriptase with TAMs, M184V, NNRTI mutations, and a variety of protease mutations that render NRTI and first generation NNRTIs and PIs inactive. Most of them started their antiretroviral treatment with mono/dual NRTI therapy. Their first PI was non-boosted. The late onset of a boosted PI has not precluded the accumulation of protease resistance mutations in these patients.