Effectiveness of first-line antiretroviral therapy based on NNRTIs vs ritonavir-boosted PIs in HIV-1 infected patients with high plasma viral load

Imaz, A1; Llibre, J2; Navarro, J3; Curto, J1; Clotet, B2; Crespo, M3; Murillo, O1; Ferrer, E1; Saumoy, M1; Tiraboschi, J1 and Podzamczer, D1

1Hospital Universitari de Bellvitge, Department of Infectious Diseases, Barcelona, Spain. 2Hospital Universitari Germans Trias i Pujol, Barcelona, Spain. 3Hospital Universitari Vall d’Hebron, Barcelona, Spain.

Purpose of the study
Few clinical trials have compared non-nucleoside reverse transcriptase inhibitors (NNRTI) and ritonavir-boosted protease inhibitors (PI/r) as initial combined antiretroviral therapy (cART) for HIV-1-infected patients with high plasma viral load (pVL), and non-conclusive results have been reported. We compared the effectiveness between NNRTI and PI/r as first-line cART for HIV-1-infected patients with high pVL.

Methods
Observational retrospective study of 664 consecutive treatment-naive HIV-1-infected patients with pVL (HIV-1 RNA) > 100,000 copies/mL who initiated NNRTI or PI/r-based cART between 2000–2010 in three University hospitals. Only currently preferred or alternative regimens in clinical guidelines were included. Primary endpoint: percentage of therapeutic failures at week 48. Virologic failure was defined as: a) lack of virologic response ( < 1 log RNA HIV-1 decrease in first 3 months); b) RNA HIV-1 > 50 c/mL at week 48; c) confirmed rebound > 50 c/mL after a previous value < 50 c/mL. Intent-to-treat (ITT noncompleter = failure) and on-treatment (OT) analyses were performed.

Results
62% of patients initiated NNRTI-regimens (83% efavirenz) and 38% PI/r-regimens (62% lopinavir/). Baseline characteristics: male 83%; median age 39 yrs; median CD4 count: 212/μL (NNRTI 232 vs PI/r 177, p = 0.028); pVL 5.83 log10 c/mL (NNRTI 5.43 vs PI/r 5.55, p = 0.007); AIDS 24% (NNRTI 21% vs PI/r 29%, p = 0.015). NNRTI backbones were tenofovir plus 3TC or FTC in 72%. The percentage of therapeutic failure was higher in the PI/r group (ITT NC = F 26% vs 18%, p = 0.012) with no differences in virologic failures (PI/r 5%, NNRTI 6%, p = 0.688). The rate of treatment changes due to toxicity and/or voluntary discontinuations was higher in the PI/r group (15% vs 8%, p = 0.008). A multivariate analysis adjusted for age, gender, CD4 count, VL and AIDS showed NNRTI vs PI/r as the only variable associated with treatment response (OR 0.61, 95% CI 0.41–0.88). Median pVL and rate of resistance at virologic failure were higher in patients receiving NNRTI (3.97 vs 2.49 log copies/mL, p < 0.001 and 62% vs 12%, p = 0.004, respectively).

Conclusions
Initial NNRTI-regimens showed higher effectiveness compared with PI/r-regimens in HIV-1-infected patients with high pVL, although virologic failure rates were low and comparable. Resistance emergence was more frequent and pVL higher in patients failing NNRTI. However, more patients initiating PI/r-based regimens changed or discontinued therapy.