Comparison of resistance profiles between patients starting nevirapine and efavirenz in EuroSIDA

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The subsequent development of the EuroSIDA genotypic resistance database has allowed a re-investigation of this question. Using stored plasma samples, genotypic resistance at the start of the NNRTI regimen (baseline) was determined to assess whether variations in resistance between those starting either of the two NNRTIs could explain the virological outcome.

OBJECTIVES
In HIV-infected patients starting NVP- or EFV-containing regimens:

To compare the rate of virological failure after adjusting for ARV resistance found to be present at baseline.

To compare resistance profiles at baseline and failure time.

METHODS
For patients with unsuppressed baseline viral load (>500 copies/mL), virological failure was defined as two consecutive viral loads >500 copies/mL, at least 6 months after starting NNRTI regimen (any time after start of regimen for those with viral load >500 copies/mL at baseline). Time to virological failure (the first of these two values) was analysed using Cox proportional-hazards models with follow-up to permute virological viral load measurement.

The Rega algorithm v6.3 was used to interpret ARV resistance. Resistance to nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs) and NNRTIs was defined as at least one drug in the class showing full or intermediate resistance.

RESULTS
Table 1: The baseline characteristics of the 452 patients who started an NNRTI-containing regimen (232 NVP and 220 EFV) were displayed. ARV-naive patients were 44% (NVP) and 46% (EFV), p=0.20.

There were similar levels of baseline NNRTI resistance in the two groups (4% NVP and 5% EFV, p=0.92). NNRTI resistance was also similar (4% NVP and 6% EFV, p=0.92) however PI resistance was slightly higher in the EFV group (7% NVP and 9% EFV, p=0.02).

Figure 1: The percentage of patients with virological failure over time is shown. In total, 221 (49%) NVP patients, 95% confidence interval (CI) (46%-52%) and 104 (47%) EFV patients, CI (44%-50%) had experienced virological failure by one year, p=0.01.

Figure 2: The relative hazards (RH) of experiencing virological failure were adjusted for variables considered to be potential confounders in the previous EuroSIDA analysis (number of previous NNRTIs/PIs, previous AIDS, year started CART, baseline CD4 count, CD4 nadir, viral load, max ever viral load) with the addition of number of active non-NNRTI drugs in the regimen defined by the Rega score (median 5.5 for NVP, 5.5 for EFV, p=0.55), and whether or not the NNRTI in the regimen was active.

The adjusted RH on EFV compared to NVP was 0.85, 95% CI (0.60-1.20), p=0.33, displayed in Figure 2. Adjustment for type of NRTI backbone and duration of previous therapy did not change results.

Table 2: Among patients who experienced virological failure, 95% NVP and 95% EFV patients had resistance test results available at time of failure. NNRTI resistance was found to be fairly similar and was high in both groups (86% NVP and 75% EFV, p=0.09), as was NRTI and PI resistance.

Restricting to patients who started an NNRTI regimen at time of failure as well as having a resistance test at 92% of the 248 NVP patients and 96% of the 156 EFV were negative for these drugs and also may be more likely to receive NNRTI due to their lower genotypic resistance profile.

CONCLUSIONS
Baseline resistance profiles in patients starting NVP- and EFV-containing regimens cannot explain the difference in virological outcome found in this analysis.

Randomised trials have only investigated virological efficacy in ARV-naive patients.

REFERENCES


Figure 1: Kaplan-Meier plot of % of patients with virological failure over time

Figure 2: Adjusted relative hazards of virological failure

Figure 3: New NNRTI resistance mutations