Rate of viral rebound in 539 patients with < 50 copies/mL on efavirenz-containing regimens, according to concomitant use of 3TC or ddI.

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Background: Results from recently reported trials (eg ACTG384, ES30009) have highlighted the fact that the effect of some antiretroviral drugs is dependent on which other drugs are used in conjunction.

Patients: We followed 539 patients in EuroSIDA who had attained <50 cps/mL on HAART, without previously virologically failing HAART and were currently on a regimen containing efavirenz plus zdv/3TC, zdv/ddI, d4T/3TC or d4T/ddI (other combinations were used infrequently). Time zero was the date of attaining <50 on the efavirenz-containing regimen or – in those who simplified by switching to efavirenz – the date of starting efavirenz. We included patients who were naïve or nucleoside experienced at start of HAART. Follow-up was to viral rebound (two consecutive values >400 cps/ml), stopping ART or switching to a non-efavirenz regimen, or last available viral load. A group of 1656 people on protease inhibitor (PI)-regimens (nelfinavir, indinavir, saquinavir (sgc) or ritonavir boosted PI) were used for comparison.

Results: During 677.7 person years of follow-up on the efavirenz regimen, 28 patients experienced virological rebound (rate 4.1 /100 pyrs). For with 3TC (and hence not ddI) included in the regimen the rebound rate was 3.1 (18/589.6 pyrs) compared with 11.4 (10/88.1 pyrs) for those using ddI (and not 3TC) (rate ratio 3.3; p=0.004, after adjustment for age, gender, risk group, pre-HAART nuc use, whether efavirenz was in the original HAART and time from start of HAART in a Poisson regression model). In contrast, for those on PI-regimens the rebound rates were 7.5 (231/3061.5) and 10.3 (30/291.8) (adjusted rate ratio 1.2). In a model containing both types of regimens, the interaction between efavirenz use (vs. PI) and 3TC use (vs. ddI) was statistically significant (p=0.03). In a re-parameterised model, the adjusted rate ratios for PI with 3TC, PI with ddI and efavirenz with ddI were 2.4 (p=0.0004), 2.8 (p=0.0007) and 3.0 (p=0.005), respectively, compared with efavirenz with 3TC. No such interaction was detected with zidovudine / d4T. Results based on 6 months updated follow-up will be presented.

Conclusions: These results suggest that the durability of efavirenz-containing regimens may depend on concurrent use of 3TC, although it is difficult to identify with certainty if these results reflect a positive modifying effect of use of 3TC or a negative effect of ddI.