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Hot News

Welcome to «Hot News», a section of AIDS Reviews written by the editors and invited experts which focuses on recently reported information believed to be of both impact and higher interest to the readership.

Lipid changes in the 2NN trial

Dyslipidemia is an important clinical problem in HIV-infected patients, particularly when they are receiving protease inhibitor (PI)-containing regimens. Switching to non-nucleoside analogues (NNA) has been attempted and different studies have demonstrated clear, but not identical, benefits with both efavirenz (EFV) and nevirapine (NVP). Replacing PI by NVP lowers both triglyceride (TG) levels and total cholesterol (TC)/HDLc ratios. These reductions may be associated with a lower cardiovascular risk. In contrast, EFV simplification studies have not shown similar results regarding TG, although the TC/HDLc ratio seems to be reduced. Direct comparisons between NVP and EFV in simplification trials (Negredo et al. CID 2002; 34: 456-62; Martínez et al. NEFA study, 9th CROI) have confirmed this advantage of NVP over EFV in patients suffering PI-related hyperlipemias.

No studies so far had directly compared NVP and EFV in drug-naive patients. In February 2003, the first results of the 2NN trial were reported (Van Leth et al. 10th CROI). This study is a 48-week randomized multicenter trial of first-line antiretroviral therapy with regimens containing either NVP, EFV or both drugs along with stavudine and lamivudine. A substudy of the lipid profile in patients who remained allocated to the original treatment arm up to week 48 (417, 289 and 127 subjects on NVP, EFV and NVP+EFV arms, respectively) was performed. Baseline characteristics were balanced between groups. Overall, TG, LDLc and HDLc levels increased in the three groups. However significant smaller increases in TG (p=0.010), larger increases in HDLc (p<0.001) and larger reductions in TC/HDLc ratios (p<0.001) were achieved in patients under NVP compared with those under EFV (table 1).

Despite the increased proportion of patients with total hypercholesterolemia in all treatment arms at 48 weeks, the percentage of patients with TC/HDLc ratios above 6.5 remained stable in the EFV arm in respect to baseline, but declined significantly in the NVP arm, mainly due to changes in HDLc (table 2).

Tabla 1.

	NVP arm		EFV arm		NVP+EFV arm	
Variables	Baseline	Change	Baseline	Change	Baseline	Change
TC (mmol/l)	4.00	0.98	4.00	1.12	4.06	1.39
LDL (mmol/l)	2.35	0.57	2.37	0.50	2.45	0.76
HDL (mmol/l)	1.00	0.37*	1.00	0.24	0.97	0.41
TC/HDL	4.29	–0.36*	4.37	0.04	4.53	–0.17
TG (mmol/l)	1.52	0.12*	1.43	0.37	1.42	0.44

*p<0.05 compared to efavirenz

Tabla 2.

	% pts with TC > 240 mg/dl Week		% pts with TC/HDLc ratio >6.5 Week	
	0	48	0	48
NVP	1.9	14.2	5.3	4.5
EFV	1.4	12.9	5.9	6.3
NVP+EFV	0.8	22.8	5.5	7.9

Two main conclusions may be drawn from this study. Firstly, a complete lipid profile is essential in order to explore the different lipid behavior of antiretroviral drugs. Secondly, NVP may exert unique advantages on lipids and this benefit should be taken into account when antiretroviral therapy is planned to be prescribed for patients at increased risk for coronary heart disease.

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Unsafe medical procedures are not the main route of HIV infection in sub-Saharan Africa

A recent report suggested that high HIV infection rates in sub-Saharan Africa could be related to unsafe medical procedures (Gisselquist & Potterat, J STD & AIDS 2003;14:162-73). These authors stated that HIV infection rates were much higher than expected from sexually transmitted diseases. However, Polly et al. (Nature 2003;422:679) compared the spread of HIV versus that of HCV, which is mainly transmitted parenterally, in the same geographic region. They found that HIV spread much faster, despite being 6 times less infectious via parenteral routes than HCV (Goldmann, J Allergy Clin Immunol 2002;110(suppl):21-6). In South-Africa, HIV and HCV prevalences were at similar rates in the early nineties, but HIV rose from 0.7 to 24.5% during the last decade (1990-2000), while HCV prevalence has remained relatively stable. The use of unsterile medical equipment and contaminated blood supplies are not the predominant mechanisms of spread of HIV in sub-Saharan Africa. Therefore, preventive measures should continue to focus on sexual transmission, in order to reduce HIV prevalence in that part of the world.

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Oral transmission of HIV

When exposed to high levels of HIV, the cells lining the mouth can develop a low-level infection, a finding that increases our understanding of the risks of oral transmission of the disease. Researchers from California reported their findings past March (Liu et al. J Virol 2003; 77: 3470-6). The majority of HIV type 1 infections occur via mucosal contact, and there are several reports indicating that the oral mucosa may be one route of exposure," say the researchers. "It is difficult to confirm that oral mucosa is a major transmission portal because of the correlation between oral-genital contact and other transmission risk behaviors." In the study, the authors tested the ability of HIV to infect oral mucosal cells known as normal human oral keratinocytes (NHOK). They found that when exposed to high concentrations of the virus, the cells established a low-level, productive infection that could subsequently transfer to other cells in the body.

"Human saliva contains several types of anti-HIV activity that may help protect an individual against a small virus inoculum. However, if individuals are exposed to inocula containing a heavy viral load, it is conceivable that the oral epithelium could be infected and thus serve as a beachhead for HIV-1 infection," say the authors. Therefore, preventive measures against sexual transmission of HIV should include oral sex.

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SIVcpz divergence may suggest the virus was acquired through interspecies transmission

The group from Beatrice Hahn (Santiago et al. J Virol 2003;77:2233-42) recently succeeded in amplifying the entire genome of a new SIV (TAN1) from wild *Pan troglodytes schweinfurthii*, using only non-invasive fecal samples. It is the second strain characterized from this East-African chimpanzee subspecies. The two viruses in this subspecies seem to be clustering together, but are still genetically very divergent (20 to 40% amino acid divergence). The high genetic distance they show in respect to other members of the HIV-1/SIVcpz lineage (30 to 50% amino acid divergence) raises questions about the origin of chimpanzee viruses.

The divergence of SIV within chimpanzees (*P t troglodytes and P t schweinfurthii*) approaches the one between the other SIV lineages from different monkey species. In addition, the virus does not seem to spread easily among chimpanzees. Santiago et al. reported of unpublished findings showing that within a small chimpanzee community at the Gombe National Park, SIV does not spread from an identified index case. A different simian origin of the chimpanzee virus would also fit with surprising low prevalences of SIV in both wild and captive chimpanzees, in contrast to the high prevalences of SIV seen in various other monkey species (Peeters et al. Emerg Infect Dis 2002;8:451-7). It is time to look for more evidence of interspecies transmission from smaller monkeys to chimpanzees.

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