DRUG HOLIDAYS. YES OR NO?

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(translated from Latvian)

This conference is rated as the highest forum on scientific and clinical HIV and OI research.

The question when to start therapy is still essential.

The Washington university clinical study shows that a delayed start results in better virology outcomes and less opportunities for developing resistances. There is no evidence on an improved immune system or HIV eradication by starting early (abstr. #523).

Since the **first combination** fails in half of cases, it has to be chosen carefully (R. Murphy, MD). Mixing the 16 ARV drugs theoretically gives 3360 combinations. Here are some of them.

E.g., <u>ABC + AMP</u> quickly suppresses HIV- 1 replication and is usually well tolerated (#336).

 $\underline{NVR + ZDV + LMV}$ is equally effective in patients with low and even high VL (>100.000) (#517).

Once daily *Emtricitabine (FTC) + ddI + EFV* in therapy- naïve patients after 24 weeks lowered VL<400, increased CD4 cell count and was well tolerated (#518).

Once daily $\underline{EFV} + \underline{NVP}$ combination: it may be necessary to increase the EFV dose to 800 mg (#80).

<u>Single pill</u> combination of $\underline{ABC + LMV + ZDV}$ (twice daily) is biologically equal to its contents, has no dietary restrictions, is well- tolerated, easy to swallow and not disgusting (#98).

In order to evade **cross-resistance** – do not use combinations consisting of all the 3 ARV classes (#80)!

Using *NLF* as the first PI causes less cross- resistances compared to other PIs (dr. L. Prescott).

Discussion on **drug holidays** still goes on. 5/8 of patients on HAART had to restart therapy on the sixth week with their CD4 counts and CD4/CD8 ratios lowered. In contrast, patients on <u>Hydroxyurea + ddl</u> ("PANDA" clinical study) at the 8th week had a very small VL increase at stable CD4 and CD8 counts. This is the first study showing that STIs in chronically infected patients are feasible (#352).

60% of patients after 2 yrs on PIs are experiencing **lipodistrophy**. Switching to another ARV class does not guarantee its disappearance - lipodystrophy may not progress, though.

Some comparisons:

Comparing PIs: <u>AMP</u> is less prone to cause lipodystrophy than <u>IND</u>. $\underline{d4T}$ causes much more lipodystrophy cases than \underline{ZDV} (#756). 14% of patients after 3 years on $\underline{RTV} + \underline{SQV}$ are experiencing shrinkage in buttocks (D. W. Cameron).

While due to ARV combinations the virus is decreasing in bloodstream, it may continue replicating in sperm.

33% of men on PIs are experiencing **sexual dysfunction**. *Abbott* has a new salvage in its pipeline – an erectile medication *Uprima*. Its effect is reached in 75% of men who sucked the pill for 20 min. Compared to *Viagra* it has less of side effects.

Newly elaborated blood tests help to define the approximate timing of HIV infection. These tests have proved that **oral sex** has been the cause of HIV transmission in 8% of cases in San Francisco (abstr. #473).

A.Kalnins, AGIHAS