Infosheet #28 *from the series* ***"For a Better QL of PLWHA!"***

NOT ONLY SUCCESS…

(the **XXI CROI:**
Conference on **Retroviruses** and **Opportunistic Infections**,
Boston, III. 2014)

(translated from Latvian)

This was my first conference I did not find any breakthrough in it. Nevertheless, it provided enough of valuable information!

On success and failure:
HIV VL had rebounded to detectable levels in both "Boston patients" who had previously undergone stem cell transplantation and later discontinued HIV treatment.
These cases differ from the "Berlin patient" *(see infosh. #23)* who apparently remains HIV-free 7 years after stem cell transplants from a donor with a double mutation *(CCR5-delta-32)* that makes cells resistant to HIV entry *(the "Boston patients'" donors had stem cells susceptible to HIV infection).*
The first patient experienced HIV re-emergence 3 months into his treatment interruption, while the second – 8 months. Both men experienced rapid HIV replication, reaching VL in the millions. After restarting ART both patients are doing well.
Researchers summarized that long- lived tissue reservoirs that are inaccessible to testing may have contributed to viral rebound. This implies that even a few remaining HIV-uninfected cells may be enough to allow full viral rebound once protective ART is stopped.
These cases suggest that a functional cure for HIV will be difficult to achieve if even a small amount of residual virus remains in the body *(oral 144LB).*

Starting from the beginnings:
Scientists are closer to resolve the origins of all HIV1 groups, so: two ape species *(gorillas from SW Cameroon)* are involved in the **origin of HIV1 in humans** *(o.51).*

As we already know, replication- competent **HIV-1 can persist for extremely long periods** of time despite effective treatment with HAART. Dr M. Lichterfeld's *(Boston hospital)* data suggest that T- memory stem cells *(an exquisitively rare population of T cells with stem cell- like properties)* harbour high levels of HIV1 DNA in patients treated with suppressive HAART. HIV1 DNA levels in these cells remain stable for many of ART, and their relative contribution to the total viral reservoir increases over time.
The increasing understanding in this field may be translated into improved clinical strategies for inducing HIV1 eradication *(0.54).*

A fact also is that patient's genotype influences outcome of HIV infection and treatment. So, scientists from Switzerland tested doctors' perception and predictive power of a **custom genotyping.**
According to their survey, 57% of physicians said they found the information (potentially) useful. In 12% of instances, the treating physician would have been inclined to prescribe a different treatment; 16% would consider additional laboratory tests and 34% would discuss cardiovascular risk factors.

Thus, the interim analysis demonstrates a modest predictive power of the genetic testing and its eventual lead to a change in clinical decisions *(poster 505).*

A low CD4/CD8 ratio *(<1)* in elderly HIV- adults is associated with increased morbidity and mortality. A subset of HIV+ adults receiving ART fails to normalize this ratio, even after a normal peripheral CD4 count is obtained.
While CD4 counts predict mortality in those with low CD4, in those with adequate CD4 recovery, high CD8 might drive adverse outcomes. In both scenarios, the CD4/CD8 retains the predictive importance of both CD4 and CD8 cells.
According to the evaluation of a group of scientists, a persistently low CD4/CD8 ratio during otherwise effective ART is associated with increased innate and adaptive immune activation, an immunosenescent phenotype, and higher risk of morbidity/ mortality.
This ratio may prove useful in monitoring response to ART and could identify a unique subset of individuals needed of novel therapeutic interventions *(p.242).*

The impact, particularly on clinical outcomes, of **low- level viremia** *(LLV)* 50-500 remains unknown. Current US guidelines define viral failure *(VF)* as a confirmed VL>200.
Investigators have discovered that among patients virologically suppressed 3-9 months after starting ART, LLV 200-500 was strongly associated with VF, but not with AIDS events or death. LLV 50-200 had little impact on VF or clinical outcome.
Neither type of ART regimen *(NNRTI- vs PI/r- based)* nor cumulative duration of LLV were associated with clinical or virological outcomes *(p.1014).*

A study by Swedish physicians indicates a low prevalence of **HIV- associated neurocognitive disease** *(HAND) (see infosh. #26)* in a well treated cohort with low prevalence of confounding factors. The majority *(75%)* performed normally in all 4 tests *[1) psychomotor function/ attention; 2) speed of information processing/ attention; 3) learning; 4) working memory].* Memory and concentration difficulties were associated with symptoms of depression and low CD4 count *(p.474).*

Efficacious **dose reduction** may provide added clinical benefit by reducing dose- related toxicities as well as lower costs.
ENCORE1 study is still going on. It has already proved *(see info- sheet #27)* that EFV400 is virologically non –inferior to EFV600mg. While BMS representatives are speaking about efficacy and resistance problems, results from the ENCORE1 sub- study challenge the currently defined PK targets for therapeutic success *(p.510).*

Selenium deficiencies *(see infosh. #6;10)*, indicated by low plasma Se concentrations, have been documented among HIV positives, especially with low Se level in soil *(like in Latvia) (on the other hand, it is known that human body can synthesize the missing microelements).* But evidence of effect of Se supplementation on VL and CD4 outcomes from trials has given mixed results.
The given trial provided Se 200mcg per day or placebo to ART- naïve HIV+ patients *(average baseline CD4=555).*
As a result, the rate of CD4 depletion was reduced by 44% among patients receiving Se. Average decline in CD4 over 24 months were 54 cells among the Se arm and 95 cells among the placebo arm.
Investigators found no treatment effect for the composite outcome or viral suppression. They also found no significant differences between groups for adverse events.

The investigators state that in ART- naïve HIV+ adults, 24 month Se supplementation was safe and significantly decreased the rate of measured immune decline.
Se supplementation may be an inexpensive and effective intervention when started in early stages of HIV disease *(p.552LB).*

Smokers' corner:
Investigators are stating: among treated HIV+ individuals more life years may be lost through smoking than through HIV.
Excess mortality associated with smoking increases markedly with age *(p.1011).*

Inevitably yours –
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