Infosheet #27 *from the series* ***"For a Better QL of PLWHA!"***

IT IS NOT ALL ABOUT MONEY!

(the **VII IAS** Conference on **HIV Pathogenesis, Treatment** and **Prevention**, Kuala Lumpur, VI/VII 2013)

(Translation from Latvian)

This was the first time that the IAS conference was held in Asia, and in an Islamic country. It gathered >5000 participants and almost 200 volunteers.
Malaysia was chosen because its Government implemented policies that make this country a role model for the region. After the introduction of a National HR programme in 2005, ID users are accounting at 30% of new infections today (compared to 60% a decade ago)!
This country is experiencing a consistent downward trend in the annual rate of new HIV cases (from 28,5 in 2002 to 11,7 in 2012 per 100 000 population).
Actually, almost in all the Asian countries rates of new HIV infections are decreasing or stable.
So, Malaysia paved the way in harm reduction, Thailand – in safe sex, but Cambodia managed to combine the two.
Cambodia is on track to become one of the few countries in the world to successfully reverse its HIV epidemic and eliminate new infections by 2020. Annual new HIV infections in this very poor country plummeted from 20 000 in the early 1990s to ~1 300 in 2012.
So, **it is NOT all about money!** Tackling HIV is also largely dependent on the willingness, commitment and energy of national leaders to implement scientifically sound policies!
Here, some E European countries, in which millions are being invested without any "tangible" results, are coming into our minds…

The main event of this conference was releasing **the new WHO recommendations, 2013**. The new clinical treatment recommendation is to start ART in all individuals with CD4≤500. While the recommendation is "strong", it is not yet evidence- based (rather an expert opinion). Overall, these guidelines are political and aspirational, and driving global access to care.

Most optimistically, the conference highlighted several cases of **functional cure**.
Early initiation of cART during acute HIV infection can lead to control of viral replication after cessation of therapy in a rare subgroup of patients termed post treatment controllers (PTC).
A patient was treated with cART 3 months after HIV exposure (and 1 month after seroconversion) for 5.5 years, cART was stopped in 2004, and his VL still remains undetectable (CD4≈950) without ART since 9 years! However, the virus could be recovered in vivo in a humanized mouse model indicating the

persistence of replication competent virus. So, this unique German case suggests a functional cure rather than viral eradication after early onset cART.

Another case is so called "Boston patients". Both men with longstanding HIV infection who underwent bone marrow transplants have stopped (15 and 7 weeks ago) ART and have no detectable HIV in their blood. Remaining on ART, both men became undetectable by 8 months post- transplant. Since coming off ART this spring, they continue to have no detectable HIV DNA or RNA in their blood. While these results are exciting, they do not yet indicate that the men have been cured (virus could still be present in other tissues such as the brain or gastrointestinal track).

Unlike the Berlin Patient (see info- sheet #26), these patients received donor cells that are susceptible to HIV-1 infection.

And unlike the Mississippi child (who had undetectable VL after interrupting ART, initiated just after birth) (ibidem), Boston patients had established viral reservoirs prior to transplantation.

However, allogeneic hematopoietic stem cell transplantation is associated with 15 -20% mortality within the first few years. The procedure is very expensive, and patients may need long- term immunosuppressive medications. It is also unknown if such transplantation can eliminate the HIV reservoir in all infected patients (or if it will work in only a few select individuals).

And lastly, 14 patients in the VISCONTI cohort in France have maintained control of their HIV infection for a median of 7,5 years after ART interruption, showing that people who start treatment earlier (CD4>500) may have better chance of future control of HIV without medication.

Now, on **treatment simplification** strategies.

A Spanish study (WEPE514 at the poster exhibition) compared lopinavir/r and darunavir/r monotherapies, finding no significant differences in efficacy at 48 weeks between both treatment simplifications in patients with sustained virological suppression. The median change of CD4 was 3 and 71 cells/mm³ in DRV/r and LPV/r groups, respectively.

The same, Intelence and Darunavir Once a Day Study (INROADS, U.S.A) of etravirine (ETR) and darunavir/r (DRV/r) as dual therapy in treatment-experienced or treatment- naïve (with transmitted resistance) subjects showed that this dual therapy was generally effective and well- tolerated, with little resistance development (WEPE515).

On **dose reductions**.

Rebekah Puls from ENCORE1 study, Australia (WELBB01) showed that reduced dose EFV (400mg) has demonstrated non- inferior suppression of HIV replication compared to 600mg standard dose over 48 weeks. Besides, mean CD4+ T cell counts at week 48 were significantly higher for EFV400 versus EFV600 (difference = 25). Thus, 400mg EFV can be recommended as part of routine care! And this effective and reduced dose could yield meaningful cost savings.

Absence of drug toxicity is more important for a durable regimen than **simplicity of administration.**
Canadian clinical cohort (TUPDB0106) suggests that single tablet regimens (STR) do not necessarily result in a more durable treatment. Even with a higher pill burden and BID schedule, the initial use of RAL- based regimens was associated with a better outcome, concluded the speaker.

SAILING study (WELBB03) assessed dolutegravir (DTG), an investigational integrase inhibitor (INI) versus raltegravir (RAL) in INI- naïve patients with ≥2 class resistance and ongoing virologic replication. Patients received either DTG or RAL plus background regimen of no more than 2 agents. The presenter concluded that driven by higher virologic efficacy, **DTG was superior to RAL** in integrase naïve, treatment- experienced subjects through 48 weeks, with significantly less emergent resistance.

In "No Nuc No Boost" study (WEPE511) naïve HIV-1 infected patients with CCR5 virus received maraviroc (MRV), raltegravir (RAL) and Tenofovir/ Emtricitabine (TDF/FTC) for 24 weeks. Patients with VL<50 at week 20 stopped TDF/FTC at W24 and pursued MRV-RAL until W48. French scientists have concluded that **MRV-RAL maintenance therapy** following a 6 months induction phase with MRV-RAL-TDF-FTC has been well tolerated and **maintained virological efficacy** in these patients.
"No Nuc No Boost" results are in sharp contrast with those of the ROCnRAL study (presented at CROI 2013).

And finally, on hepatitis C.
Several combinations of ribavirin plus two Direct Acting Antivirals (DAAs) can cure HCV in 80% of treatment- naïve Genotype-1 patients, without use of interferon. Four next generation HCV DAAs, currently in Phase 3 development (daclatasvir, sofosbuvir, simeprevir, faldaprevir) has patent expiry in years 2026-2029. S African and UK scientists (TULBPE16) predicted their costs, assuming generic manufacture. They concluded that within the next 15 years, large- scale manufacture of ribavirin + 2 generic HCV DAAs is feasible, with target prices of $100-200 per 12 week treatment course. These low prices could make widespread access to HCV treatment in low and middle- income countries, and **potentially even HCV eradication, a realistic goal!**

Finishing on this optimistic note,
and being sorry for a somewhat "dry" compilation this time –
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AGIHAS
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