Infosheet #29 *from the series* ***„For a Better QL of PLWHA"***

UNDER A SHADOW…

(The **XX International AIDS** Conference**,**
VII 2014, Melbourne)
(translated from Latvian)

The opening ceremony and the conference itself were overshadowed by the absence of delegates who died during a raid targeted at Malaysian aircraft. Among these was Martine de Schutter, known to many of us.
Delegates, even distantly knowing each other, sometimes greeted each other with "I am so glad you are here. I worried"...
The total of them at this conference was <14 000.
The conference theme was "Stepping up the Pace", and the UNAIDS is committed to ending AIDS by 2030 (90% of people with HIV diagnosed, 90% of them on treatment, and 90% of these with undetectable VL by 2020: **"90:90:90"**).

One of the main issues at the conference was, of course, a **cure for HIV**.
Quoting the popular writer Patricia Nell Warren: "Wildly excited stories about "AIDS cures" are popping up all over the news".
Conference provided the first report of a functional cure case that also seroconverted after advanced AIDS. The Argentine lady, now 51, was hospitalised in 1996 with AIDS wasting syndrome. She interrupted ART in 2007 due to lipodystrophy, and has no detectable HIV-1 RNA levels until now (600<CD4<900).
BUT "the virus can hang around for a very long time and pop up unexpectedly". This was shown by a recent discovery that the "cured" "Mississippi baby" (now 4 years old) still has HIV after having had an undetectable VL while off ART for more than 2 years.
So, "even very early is not early enough", and scientists need to learn how to eliminate long- lived reservoirs (i.e., the toughest problem is: latently infected cells versus productively infected cells).
A widely used strategy in HIV cure research to reactivate latent virus in resting cells is called "kick and kill". Its scenario is: once the virus is "woken up" and starts replicating, it becomes visible to the immune system and is susceptible to ARVs.
The first steps to disrupt HIV-1 latency (to make virus from silent to less silent) in patients on ART are: *Romidepsin* (a Danish research) and *Vorinostat* (poster LBPE07). Anyway, scientists have concluded that it does not look like these agents led to a significant reduction in the viral reservoir.
So, neither very early ART nor agents that re- activate latent virus are likely to be enough to enable a functional cure, or prolonged time off ART without disease progression.
During a press briefing it has been predicted that the cure field will move in the direction of therapeutic vaccines (my personal distrust in their success) or other immune- based therapies to be used in combination approaches.

So, this far only the "Berlin patient" case has led to an apparent sterilizing cure (after allogeneic bone marrow transplantation/ BMT).
The conference provided information on BMT in two Australian patients, which appeared to have cleared them of the virus. Anyway, BMT is not a cure for HIV, as it remains costly and a potentially dangerous procedure (poster LBPE21).

On the third day of the conference a huge throng filled the Convention centre's lobby. Suddenly, surrounded by lots of bodyguards, a man with a familiar face and surprisingly not tall at all passed the hall. Right upon arrival the former US President Bill Clinton started his presentation that was interrupted by a demonstration of activists challenging him to support a "**Robin Hood Tax**" (a small tax on financial transactions among banks, whose irresponsible actions have depleted the budgets of governments from around the world). Several countries already have similar taxes, e.g. UK and France. In his turn, the President described the achievements of UNITAID (a programme funded by a tax on airline ticket purchases).

The loudly acclaimed **WHO recommendation to initiate** ART in asymptomatic HIV patients **with CD4<500** was scrutinized by a simulating deterministic flow model. Implementation of these new guidelines should coincide with dramatic expansion in global ART supplies. Scientists came to a conclusion that failure to do this may paradoxically increase mortality in the short run and in the long run decrease the annual gain in life years from the ART supplies! (poster TUPE386).

The probability of a CD4<200 in an HIV patient with viral suppression and CD4>350 is very low. This data suggests **less frequent monitoring of CD4** counts in these patients (cohorts WEPE039; THPDB0205). As we know, there still are patients with CD4 around and below 350 among us...

Switching from first ART regimen while suppressed is associated with increased risk of subsequent virologic failure, as pronounced by researchers from Canadian CANOC cohort (oral TUAB0103).

ART simplification
In a table below I have compiled the following strategies of switching from triple to dual therapies:

DUAL	**TRIPLE**	**STUDY/ COHORT**	**ABSTR.**	**COMPARISON**
lopinavir/r + *lamivudine (3TC)*	*lopinavir/r* + *3TC* or *FTC* + 1 nucleos(t)ide	OLE	LBPE17	Non- inferior, well tolerated, substantially less costly! Added benefit of preserving options
atazanavir/r +	*atazanavir/r* +	SALT	LBPE18	Non- inferior, effective, safe

lamivudine	2 nucleos(t)ides *(TDF + FTC* or *ABC + 3TC* or *ZDV + 3TC)*			compared to triple ART, which is expensive and can induce toxicity
PI/r (*darunavir* or *lopinavir* or other) + NNRTI or NRTI or *raltegravir* or *maraviroc*		HIV-COD	WEPE090	Useful option, with best results obtained when used to maintain a previously undetectable VL
ATV/r + *RAL*	*ATV/r* + *tenofovir DF* /+ *emtricitabine*	HARNESS	LBPE19	Well tolerated, but resulted in more (9,7% vs 2,7%) virologic rebound (VR) at week 24

BUT:

darunavir/r + *maraviroc*	*darunavir/r* + *emtricitabine* /+ *tenofovir*	MODERN	TUAB0101	Inferior efficacy (at week 48)!

Switching from twice- to once- daily

DRIVESHAFT study has shown that switching from twice- daily to once- daily *darunavir*/r (600/100mg x 2 vs 800/100mg x 1) in virologically suppressed patients maintains virologic control, and results in greater overall ARV adherence and reduction in LDL cholesterol (poster WEPE066). Note the reduced mg of *DTV*!

Single tablet regimens

While most cohorts have shown less side effects, virologic failures, better adherence and better or comparable viral oppression (posters MOPE054, WEPE069), Canadian scientists (CANOC) argue that single tablet regimens do not necessarily result in a more durable treatment. Most previous studies concluded that absence of toxicity was more important for a durable regimen than simplicity of administration (poster WEPDB0103).

Dose reductions

Reducing the dose may decrease adverse effects.
Although researchers from MiniZID study observed no difference in overall anaemia rate, reduced dose *AZT* (400mg) demonstrated improved safety and similar efficacy compared to standard dose (600mg) *AZT* (poster LBPE16)!

Some news on ARVs

Results of an Italian cross- sectional analysis suggest that presence of **neurocognitive impairment/** NCI **among *efavirenz* users is not** more common than in people not treated with *EFV*. Their tests measured: 1) concentration and speed of mental processing, 2) mental flexibility, 3) memory, 4) fine motor function and 5) visual- spatial ability. The factors independently associated with increased likelihood of NCI were: 1) older age, 2) HIV disease severity, 3) IDuse, and 4) hepC co- infection. Higher education and a current CD4>500 appeared to have a protective effect (nadir CD4 count, however, had no notable effect) (oral THAB0101).

The recently approved ***dolutegravir/ DTG*** (which also crosses blood/ brain barrier) marches its victory. It has demonstrated high rates of viral suppression even in treatment- experienced people who had virus with resistance to NRTIs (oral TUAB0104). According to network meta- analysis, *DTG* has a statistically higher probability of virologic suppression compared to all treatments and significantly greater increases in CD4 cells against *EFV* and *rilpivirine* (poster WEPE061).
A fixed- dose co- formulation containing *DTG* + *abacavir/ lamivudine* has already received scientific approval by the EMA and is expected to receive marketing approval (as *Triumeq*) within the next few months. If so, it will be the first one-pill, once- daily regimen not containing *tenofovir DF*, which some people wish to avoid due to its risk of kidney and bone toxicity.

From this info- sheet it may seem that the main emphasis during the conference was on ART, while it mainly dealt with **other AIDS- related issues**.
E.g., it is known that HIV+ individuals are more often **unemployed** than HIV- ones, while Dutch scientists from AGEhIV study concluded that HIV+ people aged 45-65 years who still participate in the labour process seem to function just as well at work as HIV- people of a similar age, although they were more often (6% vs 3%) partly unfit for work (poster MOPE131).

Speaking of other morbidities, results of an international study showed a new combination of drugs meant that **drug- resistant TB** could be cured in as little as 4 months, instead of 2 years!

Quite attractive, as usual, was **"the Global Village".** E.g., spectators were excited over the professionalism of a delegate from Tonga: his exquisite, although slow dance performance and the heartfelt song dedicated to the recently deceased ones.

Smokers' boudoir

It is among HIV patients that higher prevalence of smoking is being reported. Brazilian scientists in their cohort among HIV positives have proved that current smoking is significantly associated with incident **TB**. Former smoking does not seem to play a role (poster MOPE164).

Having put a cigarette aside -
Undoubtably yours -
A.Kalnins