Infosheet #32 *from the series* ***"For a Better QL of PLWHA!"***

LONGEVITY RECORD: 43 YEARS!

(the **XIII** International Congress
"**HIV Drug Therapy**",
Glasgow, 2016. X)
(translated from Latvian)

This congress is quite friendly to community educators from most different countries, with our biggest friend – prof. Ian Weller, Organizing Committee member, who has been knighted for services to HIV/AIDS research.

The well- known **target 90%:90%:90%** (*90% of PLWHA diagnosed, 90% of them on treatment, and 90% of those with undetectable VL by 2020)* was discussed again.
Seems that Sweden may be the first to achieve it.
An opening lecture challenged the current model of drug pricing by showing mark-ups that are commonly >1000 times higher than production costs and that make many medicines now largely unaffordable in high income countries. The analysis was presented by dr Andrew Hill who was speaking of **another target: 90$:90$:90$**, meaning that costs of making drugs to treat HIV, TB and hepatitis are now so low that each disease could be treated for less than 90$/year.
Many frequently prescribed ARV drugs go off patent:

DRUG	AVAILABLE AS GENERICS	BECOMING AVAILABLE AS GENERICS /GOING OFF PATENT
efavirenz	V	
lamivudine	V	
abacavir/lamivudine		2016
lopinavir/r		2016
emtricitabine		2017
tenofovir		2017
tenofovir/lamivudine		2017
atazanavir/r		2018
darunavir/r		2019

Generic competition and pricing transparency have the potential to drive down ART costs by 90% *(if purchasers are well informed about the real costs of manufacture).*
A. Hill's research group has calculated the minimum price a generic manufacturer could make a drug for: e.g., *tenofovir/lamivudine* – for 67$/year.

Current global targets for elimination of HIV will not be reached without price reductions, dr Hill concluded *(keynote lecture KL2)*.

Nadir CD4 counts, advanced age and hepC co-infections are known predictors of poorer immune recovery following HAART. As high CD8 count was associated with inflammatory non-AIDS related clinical events, scientists from Hong Kong researched its impact on immune recovery. They discovered that patients with low pre- HAART CD8 *(<800)* had a higher chance of achieving a higher CD4 count. Instead, **a high pre- HAART CD8 count *(CD8>800)*** gave a high odds of **poorer immune outcome**. While CD4 is a useful prognostic marker, the strength of prediction increased with the addition of baseline CD8 count *(using a cut-off of 800)*, researchers concluded *(poster 374)*.

Now, on **switching strategies**.
EFV remains a widely used 3rd agent with increasing numbers of patients switching due to CNS toxicities. A pilot study by British scientists showed that **switching *EFV* to *DTG*** was associated with significant improvement in CNS toxicity *(P209)*.

A multi-national study was comparing long term *(96- week)* efficacy and safety in virologically suppressed participants after **switching from *tenofovir (TDF)* to *TAF*** *(tenofovir alafenamide)*. Researchers have concluded that renal and bone safety parameters of patients improved *(oral125)*.

4 examples of **treatment simplification**:
1) ATLAS-M trial, Italy:
Its 96-week data demonstrated non-inferiority and even superior efficacy of treatment simplification to **dual therapy *(DT)* of *atazanavir*/r + *lamivudine*** as compared to continuation of the triple therapy *(atazanavir/r + 2 NRTIs)*.
A numerically higher rate of VF was observed in the triple therapy (TT) arm.
Switch to DT was associated with improved renal function over TT continuation, but also with increased cholesterol and bilirubine levels.
The speaker remarked that DT would reduce the cost of treatment *(O121)*.

2) A Spanish prospective study:
In this study researchers demonstrated the efficacy and safety of **dual therapy** with ***lamivudine + PI/r (darunavir/r or lopinavir/r)***, with 97% remaining free of VF after 48 weeks and improvement in renal involvement. The median **increase in CD4 count** was +35 and +80 cells at 6 and 12 months. By contrast, a significant increase in total cholesterol and LDL cholesterol is expected initially with partial recovery at 48 weeks *(P103)*.

3) TALENT study, China
is the first phase III trial of an **injectable** long-acting *(LAI)* HIV drug – a new fusion inhibitor, *albuvirtide*, under development in China. The interim *(48 weeks)* analysis suggests that **once-weekly *albuvirtide*** in combination with *lopinavir/r* is

clinically practical, well tolerated and non-inferior to standard triple regimen of *lopinavir/r + 2 NRTIs (0336)*.

Several **monotherapy** studies have been conducted as well:
4) DOLUMONO trial, Netherlands.
In this study *DTG* could be taken with or without food, but if VL became detectable *(>20)*, participants were told to take *DTG* with a meal *(as this boosted drug levels)*. Of 103, 102 patients had a VL<200 at week 24: 98% *(49/50)* on MONO and 100% *(53/53)* on continued cART. ***DTG* monotherapy** was therefore **non-inferior** to continued cART and well tolerated. At 24 weeks, more patients on DOLUMONO had statistically insignificant low level viremia *(50<VL<200 in 3/49 vs 0/53).*
Although these results are promising, longer follow-up is needed as more patients on DOLUMONO had low-level viremia *(O333)*.

While a significant proportion of people retain viral suppression in the monotherapy arms of these studies, the unpredictability of viral rebound, sometimes after many years of viral suppression and in the context of good adherence, suggests that the promising early data with *DTG* should be rethought to include *lamivudine* as dual therapy.

On **lipodystrophy *(LD)*** again.
Scientists from Barcelona hypothesized that lipodystrophy would increase the risk of co-morbidities and death. Instead, from their 20 year longitudinal cohort study they discovered that **patients with lipoatrophy *(LA)* had** significantly **higher CD4 cell counts** *(572 vs 492)*, higher proportion of viral suppression in plasma *(87% vs 69%)* and higher haemoglobin *(146 vs 145)* at the end of follow-up compared with patients without any LA. Patients with any LD *(LA or lipohypertrophy*) had significantly higher total cholesterol and triglycerides at the end of follow-up relative to patients without LD respectively. Between 1999 and 2015 the mortality rate in people who had any LD was 0,9%/year but in people without it, it was 2,1%/year. The risk of developing an AIDS-related condition was lower in people with LD *(1,55% vs 2,8% without LD)*. Patients with LD had a lower risk of certain co-morbidities as well.
Scientists have proved that LD is a marker for better adherence to ART *(O213)*.

During a community evening lecture the presenter, proving that doctors often have a good sense of humour, introduced shortened ART drug names instead of *"Do, Re, Mi..."* in the well-known song from the *"Sounds of Music"*:
"When you treat, you begin with....
The first three drugs just happen to be...".

As optimistic was the conclusion on a registered **longevity** with HIV diagnose: **43 years!**

Indestructibly yours -
A. Kalnins, AGIHAS