Infosheet #35 *from the series* ***"For a Better QL of PLWHA!"***

HAIR LOSS?

(the **XXVI CROI:**
Conference on **Retroviruses** and **Opportunistic Infections**,
III, 2019, Seattle)

(translated from Latvian)

While local bums and weirdies prepare themselves for a new day using the Washington State Convention Centre ground floor's toilet, 4000 conference participants are gathering in the huge building's upper floors. The preeminent HIV research meeting in the world - CROI - has started.

As this is a non-commercial conference *(only the pharma's leading scientists are present),* it has no exhibition. Instead, the hall abounds with posters. It makes almost 4 kilometres to pass all *(over a 1000)* of them.

Among participants, there are also 23 community educator scholarships' awardees from N America, W Europe and the rest of continents.

As the "Berlin patient" present at CROI celebrates his 12th anniversary of **getting cured** of HIV, two similarly cured persons – now "UK patient", also "Dusseldorf patient" are being announced to the audience. Actually, these are just specific HIV remission cases from successful stem cell transplantations *(oral 29LB).*

Anyway, the fact that we do not see a cure today does not mean that it will not come! The same, even *AZT*, CART, now– long-acting injectables were not expected at their time…

End of life HIV cure- related research provides a novel approach to study HIV reservoirs and promising research interventions. Terminally ill HIV patients expressed great motivation to get involved in cure research, as revealed by the *LAST GIFT clinical research study (poster 405).*

Still, there are ethical issues for cure-related studies - the most difficult of them – the need for treatment interruptions that are contradicting HIV treatment guidelines. Anyway, there is currently no other option to measure interventions of VL suppression without the need for ART *(pre-CROI Community HIV Cure workshop).*

The previously mentioned *(info-sheet #34)* **new medications** are continuously showing good results:

Fostemsavir (FTR) has comparable rates of virologic suppression to *ATV/r* throughout 192 weeks. These results support the ongoing *Phase 3* evaluation of *FTR* in heavily treatment- experienced adults with limited therapeutic options *(p. 483).*

The regimen of monthly injections of long-acting *Cabotegravir (CAB)* + *rilpivirine (RPV)* was non-inferior to continued 3-drug oral ART at week fourty eight. 98% of *ATLAS study* participants were more satisfied with *CAB + RPV* compared with their daily oral treatment at study entry *(p. 139).*

Ibalizumab (IBA) is an effective, safe and durable treatment for multi-drug resistant HIV-1 infected patients *(p. 485).*

There are other medications of new classes in development *(e.g., p. 141; 356).*

TREATMENT SIMPLIFICTION

2 Drug Regimens (**dual therapy**) are becoming a key strategy in maintenance therapy to spare ART classes, decrease toxicities and minimize drug-drug interactions. They show a high efficacy as a switch strategy with a low rate of virologic failure *(p. 493).*

GEMINI 1&2 studies compared dual *DTG + 3TC* vs *DTG + FTC/TDF*, concluding that dual therapy works as good as triple, with CD4 recovery exactly the same. *DTG+ 3TC* is one of the preferred combinations *(as referred to during a post-conference webinar).*

CD4 cell count recovery is an important predictor of AIDS-related morbidity and mortality, especially among those who start ART with lower counts. After an analysis in *Brazil*, *DTG* led to a higher CD4 cell recovery after the 1st year of ART than did *EFV (p. 503).* Similar results showed the *RESPOND cohort (p. 504).*

ARV TOXICITIES

Adverse drug reactions have been reported with all drugs and have been a major cause for non-compliance with ART.

Treatment-naïve PLWH starting INSTI *(especially DTG and RAL)* are at higher risk of **weight gain** compared to older NNRTI-class regimens. E.g., by year 2, PLWH starting *DTG* or *RAL* gained 5,5kg compared to 3,3kg for NNRTI *(p. 670; 672; 675).*

On Tenofovir

Lipid parameters of patients on *TAF (tenofovir alafenamide)* are worsening *(OPERA study).* The actual reason for it is not the presence of *TAF*, but the absence of *TDF (the webinar)*.

Alopecia (**hair loss**) is a rare but known side effect of some ARTherapies. An *academic outpatient HIV practice in Detroit* reported 5 cases of alopecia in HIV-infected African American female patients that started after switching *TDF* to *TAF* containing regimens. Hair loss was severe. Time-to-onset of alopecia after switching to *TAF* ranged between 2 months and 1 year, but 4 out of 5 patients reported hair loss after 2-3 months. All patients had sustained VL and had no clinical evidence of active infections. Concomitant use of other medications could not explain the alopecia *(p. 696).*

CO-MORBIDITIES

As HIV+ people are living longer, premature morbidity and mortality from age-associated comorbidities are more common. A *Canadian retrospective cohort study* shows that yearly **prevalence of**
kidney, liver, lung diseases and diabetes
were significantly higher among PLWH, while
non-AIDS-defining cancers, osteoarthritis, hypertension and cardiovascular diseases
were significantly higher among HIV-negative individuals.
PLWH experienced all comorbidities at a significantly younger age than their counterparts *(ranging between 8 years earlier for hypertension and 22 years for kidney diseases) (p. 1067).*

Lung cancer often does not cause symptoms at early stages and many people are diagnosed late, when it is more difficult to treat. *NLSTrial (U.S.A.)* found that people who received annual low-dose computerized tomography *(CT)* scans had a 20% lower risk of lung cancer death. *USPSTF* recommends annual CT screening for people age 55-80 with a cumulative smoking history of ≥30 pack-years *(1 pack-year=20 cigarettes daily/year)* who still smoke or have quit within the past 15 years. *NLST* researchers concluded that these

guidelines performed poorly in PLWH, as <25% of lung cancer cases met criteria and alternative thresholds for younger age, and decreased pack-year history and quit date are needed *(oral 15).*

Researcher from *University of Washington (CNICS cohort)* reported that PLWH who had chronic obstructive pulmonary disease *(COPD)* were associated with a 2-fold higher risk of **myocardial infarction** *(MI).* In those with COPD and no MI, 66% were on any type of inhaler, but 3/4 of these were short-acting inhalers. The speaker raised a question – people had ~3 years between when COPD criteria were met and a MI event, but in that time, they were continued on short-acting therapies *(o. 31).*

Deaths caused **by sudden cardiac arrest** are significantly more common in PLWH than the general population and were more likely to be associated with overdose or kidney failure in PLWH, as well as low CD4 count or detectable VL. *Veterans Aging Cohort Study (California)* participants had a mean age of 50. HIV+ veterans had a 14% higher risk of sudden *(excluded for care institutions)* cardiac death *(SCD)* compared to uninfected veterans. Another *countywide post-mortem study* showed an increased risk of sudden arrhythmic death *(SAD)* in HIV compared to the uninfected population. Development of criteria and evaluation for implantable defibrillators should be carefully considered in HIV as a means to prevent SAD in this high-risk population *(o. 32; 33).*

Most scientists agree that **cognitive** impairment is not HIV-status specific and cognitive functions remain largely stable in HIV+ persons on therapy *(p. 413; 414; 420).*

Anyway, **gait speed declines** more in PLWH compared to uninfected persons. *American observational cohort study (HAILO)* defined slowness as gait speed of >4 seconds on 4m walk. The study shows that the association between baseline haemoglobin A1C and development of slow gait speed highlights an intervenable target to prevent progression of physical function limitations *(p. 703).*

HIV, ART and aging have been associated with **mitochondrial dysfunction** in skeletal muscle. Scientists from *Colorado University* found improved physical function with exercise *(moderate to high intensity)* training among older PLWH *(p. 701).*

LIVING ALONE

In the context of SIV and HIV, **stress** has previously been demonstrated to result in lower CD4 counts, higher VL and increased mortality. Singly housed macaques had a greater drop in CD4 and CD8 counts and higher VL in a *J. Hopkins University's study* that questioned whether a similar effect might be found in HIV+ people *(p. 212).*

A SIDE THOUGHT

While with every conference new and perspective HIV drugs are appearing, there are no signs of even a single successful **vaccine**. What is the use of billions of $ spent on them through all these years?

Finally, **Latvia** has been mentioned at an AIDS conference. Alas, researchers from *INSERM institute in France* have "discovered" that contrary to Latvia, Estonia *"has started turning the tide of its epidemic"* – a fact that anyone interested could find in European statistics. Reasons lying in the positive influence of the *Global Fund* investments in Estonia have been beyond their scope of interests… *(p. 865).*

Wrapping up the conference: with all the promising therapies - as put in a *"Positively Aware"* editorial – the future is indeed looking bright!

Unretractably yours – A.Kalnins, AGIHAS, Latvia