Infosheet #37 *from the series* ***"For a Better QL of PLWHA"***

NO BAD ANTIRETROVIRALS LEFT ANYMORE?

(the **XV** International Congress
"**HIV Drug Therapy**",
X 2020, virtual, ex-Glasgow)

Eventually, the Glasgow Congress's change to an online regimen, and COVID pandemy's impact has reduced the volume of scientific HIV information in it compared to the previous congress *(2018):* the amount of its abstracts has reduced almost twice.

Main feature this year was the announcement of the **new** version 10.1 of the **EACS Guidelines**, with small alterations in their contents.

The first keynote lecture of the Congress was on **obesity**. Overweight as such results in an increased risk of death and multiple morbidities. Weight gain has been noted in more PLWH over the last 3 years. Most integrase inhibitors are associated with weight gain, as is tenofovir alafenamide TAF *(not tenofovir disoproxil fumarate TDF and efavirenz EFV) (KL1).* Integrase strand transfer inhibitors *(INSTI)* do not cause large effects on human adipose cells, while dolutegravir *(DTG)* and raltegravir *(RAL)* show alterations in adiponectin expression *(not bictegravir BIC) (poster P075).*

HIV SCREENING

Hospital de Cascais *(Portugal)* provided **routine**, universal screening of HIV infection in its Emergency Department *(ED).* Screening was offered by nursing staff *(with "opt-out" strategy applied).* In the first 3 years, 18072 of 21487 individuals were tested *(opt-out rate: 6,3%):* 44 patients were newly diagnosed with HIV. Late stage diagnosis *(CD4<350)* in this ED dropped from 90% in the 16 months prior to study implementation to 42%; average CD4 count at diagnosis went from 198 to 388 cells/mm³. This screening project bypassed common barriers to testing: lack of time, staff concerns over test offering, issues with confidentiality and privacy *(P128).*

ANTIRETROVIRALS *(ARVs)*

Lot of studies have already shown the effectiveness and non-inferiority of INSTI- or protease inhibitors- *(PI)* based **two-drug regimens** *(oral O411).* The same regards to **long-acting injectables** cabotegravir *(CAB)* in combination with rilpivirine *(RIL) (both their nano- formulations are at the very late stages of clinical development) (O412).* The most advanced novel compounds islatravir and lenacapavir are in the pipeline *(O413).*

TREATMENT STARTEGIES

Combination	Study/site	Some	references	#
DTG/ lamivu-dine/abacavir: DTG/3TC/ABC single tablet	Multicentre cohort study, Italy	11% of early discon-tinuations, especi-ally in the over- 60s & in those coming from regimens withoutABC		P040

Bictegravir/ TAF/ emtricitabine: BIC/TAF/FTC single tablet	_,,_	5% of early discontinuations		_,,_
DTG/3TC single tablet	GEMINI studies	Non- inferior to DTG+TDF/FTC	First- line option	P018
_,,_	STAT study	Feasible, safe		P020
_,,_ multi/ single tablet	Prospective non- inter-ventional URBAN coh	Significant improve-ments in symptom distress & treatment satisfaction	High acceptance in patients	P044
DTG/RIL single tablet	JUNGLE cohort study, Germany	Discontinuation due to adverse drug reactions *(ADRs):* 10%; viral failures: 0	High virolo-gical sup-pression rate *(>1 yr)*	P039
RAL *(elvitegra-vir)[RAL(EVG)]* based combinations	EuroSIDA study	50% higher dis-continuation rates compared to DTG-containing regimens		P049
RAL- based dual therapies	Multicentre ARCA cohort, Italy	Substantial treatment discontinuation rate, particularly RAL+PI		P027
Darunavir/ cobicistat//FTC //TAF *(DRVcob)* single tablet	Retrospect. prospective observation DIAMANTE study, Italy	Improvement in **immunological** aspect Reduced pill burden	Effective & well tolerated in clinical practice	P043
Single tablets FTC/RIL/TAF; FTC/EVGcob/ TAF; **multitabl** FTC + TAF-based combin.	Prospective TAFNES cohort study	4% discontinuations; 2 year persistence: 80% *(87% for single tablet FTC/EVGcob/ TAF)*	Effective, safe	P050
FTC/BIC/TAF single tablet *(biktarvy)*	Retrospect. cohort, Scotland	May have compa-rable incidence of neuro-psychiatric side-effects to DTG-based regimens	Non-inferior to dual NRTI regimens	P041
_,,_	singlecentre study, Spain	Only 0,4% of viral failures *(VF)*	High safety, tolerability	P013
_,,_	BICSTaR cohort	Weight gain…	Highly effective	P046
Fostemsavir FTR	Phase IIb, III: **functional mono-therapy**	First-in-class attach-ment inhibitor for hea-vily ART- experienced patients with multidrug resistant HIV-1	Higher re-duction in HIV-1 RNA from Day 1 to 8 with 600mg BID *(twice daily)*	P021

CAB+ RIL long acting injectabl	ATLAS & FLAIR	High efficacy, non-inferior to oral ART	Safe	Oral 442
_,,_	_,,_	Increased treatment satisfaction	*(phase III clinic. trials)*	P012
_,,_	Phase III randomised FLAIR study	Monthly injectable, non- inferior to DTG/ 3TC/ABC	Well tolerated, effective	Oral 414
_,,_	Phase III multicentre, open- label study ATLAS	Virological suppression in majority of participants, no VFs or safety signals	HIV-1 main-tenance the-rapy, non-inferior to 3-drug orals	P006
Islatravir + doravirine: ISL + DOR	Doubleblind dose ranging trial	ISL - the first NRTTI in development	Efficient, well tolerated	Oral 415
Elsulfavirine- *(Elpida®)* based combinations	Open- label, safety study PASS, Russia/USA	A novel,potent NNRTI in combination with two NRTIs. High viral suppression,adheren	Firstline ther . Significant **immunolog ical** efficacy	P007

SWITCH STUDIES

From	**To**	**Study**	**Some results**		**#**
TAF-based regimen	DTG/3TC	Phase III randomized open- label non-inferior. TANGO st.	Good safety & tolerability, high barrier to resistance with zero VF	Non-inferior . Robust switch optio with durable efficacy	Oral 441
boostedPI-based regimen	BIC/FTC/ TAF single tablet	Phase III non-inferiority study	Safe & well tolerated; no emergent resistance	High rates of virologic suppression	P036
Two NRTIs +boostedPI **or** boosted EVG **or** NNRTI	DOR/3TC/ TDF single tablet	Phase III non-inferior. open- label DRIVE-SHIFT trial	Well-tolerated	An option for maintaining viral suppression	P037
…	BIC/FTC/ TAF single tablet	Phase IIIb open- label international trial	Data support the switch in virologically suppressed pts ≥65years	High rates of virologic suppression	P038

DE- SIMPLIFICATION OF SINGLE TABLET REGIMENS *(STRs)*

As some ARVs lose their patents, generic ARVs have become available that allow for **affordable** and effective drugs. However, just 20% hospitals in Spain de- simplified combinations in single tablets, while the generic STR

(EFV/TDF/FTC) were introduced in 88% of the centres *(P051).*

SINGLE- vs MULTI- TABLET REGIMENS (STR vs MTR)

There are calls to reintroduce *(generic)* components as multi- tablet regimens *(MTRs)* because of cost savings. A Belgian longitudinal study showed that **more** people on a **STR reported neurocognitive complaints** *(NCC)* over time to the MTR group. Contrarily, treatment satisfaction in the STR group increased significantly. Thus, higher treatment satisfaction was however, not translated into better health- related quality of life or adherence *(P112).*

MALIGNANCIES

CANCER

Dr J. Ph. Spano informed the web- audience that cancers have become the **leading cause of death** among PLWH in France. The advent of the highly active ART has led to a significant decrease in the incidence of AIDS- related cancers. However, there is currently a resurgence of Kaposi's disease among PLWH on ART despite suppressed HIV viremia, and the relative risk for PLWH of developing non- Hodkin lymphoma *(NHL)* remains 10 times higher. Non- AIDS- related cancers also are much more frequent among PLWH. Thus, specific organised cancer **screening campaigns should be offered** to this population such as annual clinical skin examination and proctological exam without ignoring screening tests for general population *(in France: breast, cervical and colorectal cancers) (O123).*

In the large RESPOND cohort both **smoking** and poor CD4/VL outcomes predicted increased cancer rates *(O124).*

CO- MORBIDITIES

CARDIOVASCULAR

In the era of effective ART, ischaemic **stroke** *(iSk)* is one of the important causes of morbidity in PLWH. Investigators from Portugal have confirmed the association of a low CD4/CD8 ratio with the anticipation of iSk in PLWH with CD4/CD8<0,4 ~nine years earlier compared to PLWH with normalised CD4/CD8≥1 *(or 18 years earlier compared to uninfected population) (P069).*

In their turn, doctors from Croatia are warning that HIV positives have **peripheral artery disease** *(PAD)* more frequently than HIV negative renal patients, and chronic kidney disease *(CKD)* worsens the findings *(P068).*

COVID-19

The SARS-CoV2 infection responsible for Covid-19 challenges the most at- risk populations *(including the elderly, obese and those with cardiovascular or pulmonary chronic conditions) (KL2).*

Anyway, as Italian and Portuguese studies show, there is no statistically significant difference in SARS-CoV2 sero- prevalence between HIV positive and HIV negative people *(P134, P145),* and the outcomes are similar *(P147).*

AOB

Investigators from Istanbul are warning on a dramatic **increase in** the incidence of **HIV** infection **in Turkey** *(P108).*

Overall, the Congress seemed to have stressed the characteristics of all the available HIV medications.

Anyway, a virtual "gathering" is not an inspiring event at all.

Let’s have a brighter sight into the future!-Irresistibly yours-A. Kalnins-AGIHAS