Infosheet #34 *from the series* ***"For a Better QL of PLWHA"***

LATVIA – THE NEXT RICHEST COUNTRY TO THE U.S.A.!?

(the **XIV** International Congress
"**HIV Drug Therapy**",
X, 2018, Glasgow)

(translated from Latvian)

Glasgow congress still remains the most welcoming one to community educators.
The congress exhibition hall is not crowded as less companies are still in the AIDS field – with only *"Gilead", "ViiV", "MSD"* and *"Janssen"* presented.
AIDS geography has not yet changed with **HIV rates still rising in E Europe *(including Baltics)*** and C Asia. As the president of IAS Linda G. Bekker *(S. Africa)* has put it: "...This is sub- Saharan Africa happening all over again...a whole region where the virus is actually on the increase...**The leadership is missing here. The political will is missing here**".
Statistically: virally suppressed are 92%, 78% and 74% of patients in Western, Central and E Europe respectively *(keynote lecture KL2)*.

Anyway, this congress is on **HIV drugs**. So, about the novel ones:
There are two ongoing Phase III trials, investigating the efficacy of the following ones for heavily treatment- experienced, multi- drug resistant and difficult-to-treat populations:
1) ***Fostemsavir (FTR)*** in a combination therapy was well tolerated, demonstrated durability of virological response and a notable improvement in CD4+ counts! *(oral O344);*
2) ***Ibalizumab (IBA)*** *(intravenous injections fortnightly with an optimized background regimen)* was also well tolerated and led to substantial viral load *(VL)* reductions. It is already approved by the U.S. FDAdministration *(O345)*;
And one more Phase III trial:
3) ***Bictegravir (B)*** – a novel, potent integrase strand transfer inhibitor *(in a single- tablet combination)* showed a good tolerability and safety profile, with no emergent resistance, and led to VL<50 in 100% of cases. CD4+ counts rose by 11% *(similar to Dolutegravir arm in this trial)*. *Bictegravir* single- tablet combination is licensed by the U.S. and European regulators *(O211)*.

Treatment simplification

Triple therapy *(TT)* is still a standard in all the main guidelines.
Though, some **two drug combinations *(DT*** – *dual therapy)* are now recommended as alternative in guidelines for use in specific contexts *(poster P068)*.
For example, 42,5% of 1526 HIV patients older than 65 years in Italy were taking DT in 2017 *[combinations with Dolutegravir (DTG) being the most popular] (P155).*
Dolutegravir was approved for triple combinations. However, very early physicians started to use *DTG* within different regimens, including DT *(P098)*.
This time I shall not draw any tables comparing DT to TT – the table would be too long. Enough to say that around 16 oral and poster presentations on cohorts, studies and a meta- analysis showed non- inferiority of DT compared to TT, with less adverse events and saving toxicity and future options, as stressed in several presentations *(O144, O145, O213; P021, P071, P094, P096, P098, P101, P104, P113, P155, P297, P311, P313).*
Even a cohort study *(Nobel Prize Laureate C. Katlama, Pitié- Salpêtrière Hospital)* of *DTG* mono- therapy *(not recommended by any guidelines)* at week 96 showed viral suppression in 95% of patients, reducing drug exposure and long- term toxicity *(P095)*.
There were only two poster presentations in which TT was prioritized:
A cohort analysis has shown that TT *(in a single tablet)* has a greater treatment

persistence *(while adherence is much lower)* compared to DT *(P087)*.
Anyway, there is no need for a switch unless there is a good reason for that, as dr P. Cahn *(Buenos Aires)* quoted during a post- congress webinar.

Tenofovir switch

As some clinical cohorts and a study have shown – while switching from *TDF (tenofovir disoproxil fumarate)* to *TAF (tenofovir alfenamide)* worsens the lipid profile, it improves renal parameters *(P206, P187, P188)*.

Cure research

was covered in a couple of presentations.
Most experts agree that a remission *(preventing HIV replication in the absence of any therapy)* could be easier to achieve. Recent advances in using novel immunotherapies to reduce and control cancer cells gives inspiration to investigators *(O216)*.

Poly- pharmacy

- considered as an intake of ≥5 non- ARV medications – is still an issue. E.g., in Madrid area it was observed in 32% of HIV- positives and only in 22% of HIV- negatives *(P211)*.

STI's

incidence, both bacterial *(Chlamydia, gonorrhea etc.)* and viral *(hepC, hepA and human papillomaviruses)* is increasing worldwide, especially in MSM: due to less consistent use of condoms *(O131)*.
E.g., syphilis co- infection has dramatically increased in Germany's HIV population, especially in younger MSM. Regular screening is extremely important as >1/2 of syphilis cases miss symptoms of infection. Decrease of absolute CD4 cell count could serve as one of the indicators *(P214)*.

Dose reductions

Lowering the dose of *Efavirenz (EFV)* has benefits in terms of side- effects and cost. The ENCORE1 study showed that *EFV400mg* was non- inferior to *EFV600mg (see info-sheets #27/2013, #28/2014).*
EFV400 was finally recommended as an alternative option for first- line treatment by WHO in 2016.
The NAMSAL ANRS 12313 study compared *EFV400* and *DTG* based regimens.
It showed that both are equally effective, with less resistance in *DTG* regimen *(O342)*.

But what about Dolutegravir price?

And here we come to the guess of this info- sheet's title.
Latvia is the next in the list of *DTG* price worldwide after the U.S.A., leaving behind Norway, Switzerland, U.K., Australia, Canada, Japan and the rest of countries where *DTG* is cheaper!
In the SINGLE trial, *DTG* showed fewer adverse events than *EFV* as first- line treatment, but no difference in virological suppression, quality of life or survival.
In switching studies *(NEAT 022, SWORD, STRIIVING), DTG* led to significantly higher rates of adverse events and no virological benefit. Yet, in upper- income countries, e.g., U.K., *DTG* costs £ 6068/year compared to £108 for *EFV (P275)*.
Disregarding the similar efficacy profile *(with moderate improvements in tolerability of DTG vs EFV)*, clinical guidelines from several high income countries *(HICs)* have downgraded *EFV* from a preferred option to an alternative treatment option.
While the patent of *EFV* has expired, *DTG* is sold at high prices due to ongoing patent restrictions. The prices of *DTG* seen in HICs and upper- middle ICs are likely set by pharma to gain substantial profits from a wealthier subset of the global population.
The higher prices of *DTG* may be a result of confidential agreements or ineffective price negotiations due to incomplete information of policymakers. Countries should use reported prices from other countries as a benchmark to negotiate lower prices of *DTG ("Journal of Virus Eradication", #4/2018, pages 230-237).*

Sorry for being over-serious - Unrevocably yours - A. Kalnins, AGIHAS