



Update in infection related meetings 2017

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Highlights from 9th Conference on HIV Science from International AIDS Society

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INTRODUCTION

This congress is one of the main forums to raise awareness of the latest advances and developments in the field of HIV infection. It is difficult to summarize the amount of information presented, but we believe the most relevant pieces could be categorized in three sections: epidemiological aspects of infection in Africa, safety of antiretroviral treatment during pregnancy, and data on new drugs and antiretroviral treatment strategies.

Epidemiological data on the HIV situation in Africa.

In the study published by Nkambule et al. [1] the prevalence, incidence and degree of viral suppression in a national representative sample of people older than 15 years in Swaziland was analyzed. This is one of the countries with the worst HIV epidemic in sub-Saharan Africa. The study included 10,934 subjects. Since 2011, there has been an important improvement in the collection of epidemiological data, getting close to the 90-90-90 UNAIDS objectives, which means 90% of people with HIV are diagnosed, 90% are on antiretroviral treatment and 90% are under viral suppression. Published data from 2016 show that in Swaziland, 84.7% are diagnosed, 87.4% are in treatment and 91.9% are suppressed. The HIV prevalence infection over this period of time has changed in this country from 32.1% to 30.5% (without significant differences); the incidence has decreased from 2.5% to 1.4% (reduction of 44%, $p < 0.012$); and patients with viral suppression following treatment has increased from 34.8% to 71.3% (increase above 100%, $p < 0.001$). These data are extraordinarily positive and suggest that with the generalization of treatment, the HIV epidemic in this area of the world can be partially controlled.

Data on maternal-fetal transmission and safety of antiretroviral treatment during pregnancy.

Almost everywhere in the world, drugs included in the first treatment lines are a combination of two nucleoside reverse transcriptase inhibitors (lamivudine [3TC] or emtricitabine [FTC] plus tenofovir [TDF], mainly), together with a third drug that in most cases is a non-nucleoside reverse transcriptase inhibitor (especially nevirapine or efavirenz). Efavirenz (EFV) is a very safe and effective drug, whose main toxicity relates to the central nervous system (dizziness and insomnia during the first weeks of treatment). In animal experimental studies, the use of EFV is associated with the development of congenital defects [2]. However, these data have not been confirmed in registries of women with HIV who continued taking this drug during pregnancy. In general, EFV is the most widely used drug in pregnant women but data of potential toxicity make it reasonable to look for better tolerated regimens. In this IAS congress the results of the Tsepamo [3] study have been presented; this is a prospective observational study carried out in Botswana which included 5,438 pregnant women, and which analyzed the risks of toxicity associated with the use of EFV / FTC / TDF and dolutegravir (DTG) together with FTC/TDF. In the study the complications related to treatment were low, quite similar to those observed in general population (around 10% of pregnancies) and there were no differences between both types of treatment in adverse effects during pregnancy (adjusted relative risk [aRR] 1.0 (95% CI 0.9-1.1), neonatal death (aRR 0.9 IC95% 0.6-1.5), prematurity (aRR 1.0, IC95% 0.8-1.1) or low birth weight (aRR 1.0 95% CI 0.9-1.2). These results suggest that EFV neonatal toxicity is very low, which reinforces that it is a safe drug in these circumstances. DTG, however, has the same low toxicity and is well tolerated in this situation, so it can be considered an alternative drug to the EFV, when circumstances do not allow for it to be used.

New antiretroviral drugs. Bictegravir (BIC) is a new integrase inhibitor that has been studied in combination with

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New antiretroviral drugs: data from IAS 2017 BIC/FTC/TAF vs DTG-Containing Regimens

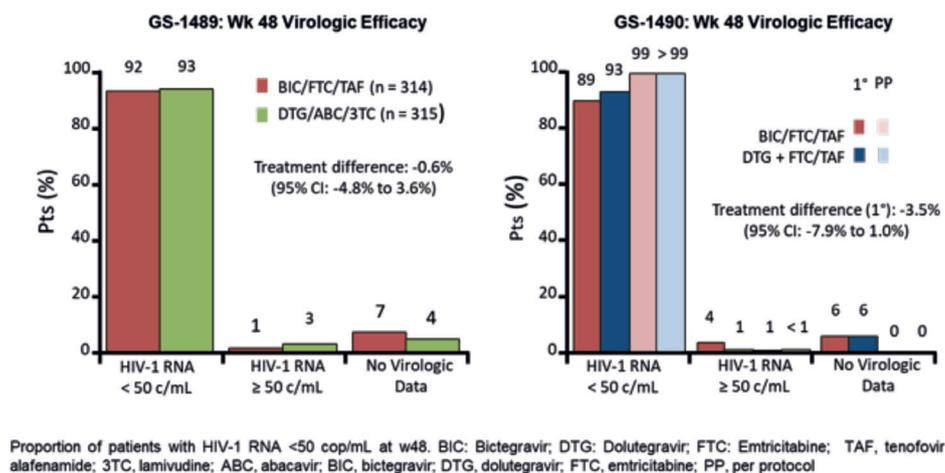


Figura 1 | New antiretroviral drugs. Data from IAS 2017. Bictegravir/TAF/FTC vs Dolutegravir-containing regimens. Adapted from Gallant J et al [4] and Sax PE. et al [5]

tenofovir alafenamide (TAF) and FTC, in a single pill. It has the advantage of having a high genetic barrier to resistance. Its favorable pharmacokinetics allows once a day administration, and it does not require an enhancer. In this congress the results of two trials comparing BIC / TAF / FTC to DTG, which is the most modern inhibitor of integrase with very similar characteristics to BIC, have been presented. The GS-US1489 [4] trial is a double-blind study comparing BIC / TAF / FTC against DTG / abacavir (ABC) / 3TC in 630 naive patients; after 48 weeks of treatment there were no significant differences in the patients with undetectable viral load (<50 copies). The double-blind trial GS-US 1490 [5], (BIC / TAF / FTC compared to DTG plus TAF / FTC in 640 naive patients) confirmed that there were no significant differences between both arms. In both studies, the viral response rates were higher than 90% of the patients, and no viral failures or resistance mutations were detected. In the protocol analysis, more than 99% of the patients presented viral suppression at week 48 (figure 1). These magnificent results of BIC / TAF / FTC combination anticipate a very promising future for this treatment.

Darunavir/cobicistat/TAF/FTC. Darunavir (DRV) is a protease inhibitor (PI) that has been combined in a single pill along with cobicistat (COBI), TAF and FTC. Clinical trials results about this switching strategy with very good results were published. The Emerald study [6] is an open-label study that included 11.459 patients on PI treatment, who were randomized to continue with the same regimen or switch to DRV/COBI/TAF/FTC in a single pill. At 48 weeks, 95% of patients had viral suppression <50 copies, with no differences between the two

arms; virological failures were below 1% with no differences between the two arms of the study and resistance mutations were not detected. In the TAF arm, patients developed an improvement in bone mineral density and a reduction in tubular toxicity markers compared to patients in the control arm. This new unique tablet composed of protease inhibitors has very positive levels of efficacy and safety.

Long-acting therapies cabotegravir/rilpivirine (CBG/RPV). Long-term treatments offer advantages over oral treatment that may be relevant for some patients. The most important is the improvement in compliance, since an intramuscular dose (IM) applied every 2 months could cover the whole treatment during this period. CBG/RPV is a drug combination administered parenterally that has been studied for a short time offering promising results. In the Latte-2 study [7], two doses of CBG / RPV were compared by IM route (every month and every 2 months) versus CBG + ABC / 3TC orally. In IAS 2017, the data for week 96 were published, showing the non-inferiority of both parental branches, compared to the VO; specifically, 87% of those assigned to CBG / RPV IM each month had HIV-1 RNA < 50 copies /ml in week 96, compared to 94% of those treated with CBG / RPV IM every 2 months and 84% of those treated with CBG + ABC / 3TC orally. 30% of the patients who received IM treatment had adverse effects related to the injection, mostly mild. 88% of the patients assigned to IM treatments were very satisfied with this medication compared to 43% of those who received oral treatment. The results of the phase III trials are expected because these therapeutic strategies can be very interesting for many patients.

Dual therapies (dolutegravir/rilpivirine) as a simplification strategy. Treatments based on two drugs may be useful in some patients as a simplification to diminish drug toxicity. At IAS 2017 the results of the Sword Clinical Trial [8] (combination of dolutegravir and rilpivirine, DTG/RPV) have been published. It included 1,024 patients with HIV infection who had suppressed viral load and who were randomized to receive either DTG/RPV or to continue with their basic treatment. At 48 weeks, 95% of the patients continued to be under viral suppression. Significant improvement in bone mineral density was observed, since 73% of patients received TDF at the time of study inclusion.

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