AFROCAB

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Statement by the African Community Advisory Board (AfroCAB) on Dolutegravir and neural tube defects in women living with HIV of child bearing age

Since information has been shared from a cohort of women living with HIV in Botswana indicating a potential link between neural tube defects (NTD) and dolutegravir (DTG) use at the time of conception, many statements have been released by various stakeholders. Some of the statements have been helpful, others alarmist and misleading. But they all have one thread in common: no community consultation.

What we know

In preparation for the review of WHO guidelines, an unplanned interim analysis of data from a cohort of pregnant women living with HIV in Botswana was conducted at WHO's request to help inform the guidelines review process. This interim analysis identified 4 cases of neural tube defects among 426 infants born to women who were taking DTG at the time they became pregnant. This is in comparison to 14 infants out of a total of more than 11,000 deliveries to women receiving antiretroviral therapy that did not contain DTG. This difference of 0.9% compared to 0.1% was considered statistically significant. lIt should also be noted that the overall adverse pregnancy outcomes among women who started taking DTG after they became pregnant were identical to the outcomes among women taking efavirenz (EFV), and lower than those among women taking a protease inhibitor.

NTD are a severe birth defect that can have many different causes, including dietary folate deficiency, genetics, and drug exposures. Since the neural tube develops very early in a pregnancy, exposures resulting in NTD occur within the first few weeks following conception.

Previously, several human cases as well as laboratory animal data suggested that EFV could also be associated with NTD, although years of routine use in pregnant women have shown that this fear was unfounded. Studies of DTG in laboratory animals have shown no evidence for NTD, despite being administered in extremely high doses (27x higher than the adult human dose). Furthermore, contrary to EFV, DTG has been shown to have no drug-drug interaction with hormonal birth control methods.

What we don't know

Because this information from Botswana came to light as a result of an unplanned interim analysis, a more thorough analysis of other potential causes for NTD in these 4 cases is lacking.

The absolute number of cases is smalls, and if another plausible explanation for these cases could be identified the association with DTG could be coincidental. As yet this analysis has not been conducted, although further investigation of the cases is understood to be underway.

Other countries have also been providing DTG to both pregnant and non-pregnant women, with other women giving birth after conceiving on DTG, but no other reports of NTD have been made from other countries or cohorts. More detailed analysis from other areas is being conducted but as yet these results are not publicly available. There are an additional 600 women in Botswana who were taking DTG at the time of conception that have yet to deliver. The outcomes of these additional cases are not yet known.

No plausible causative mechanism has been identified to explain why DTG might be associated with NTD.

While we appreciate the concern created by the recent description of the possible teratogenic effects of DTG, we are concerned that the statements were released without allowing PLHIV especially affected women being consulted or included in any appropriate course of action. We strongly urge WHO and various stakeholders – especially our governments – to respect the voices of those actually affected. At no point have we, or any actual women living with HIV, been consulted in the guidance offered by Ministries of Health especially now in light of the potential early NTD signal with DTG. We know women fall pregnant frequently and unexpectedly on ARVs, but we feel it is patronising to not give women the choice in this. We were shocked to learn of the potential harm to babies, but we do think it is critical to not just see the pregnant mother, and indeed all women of childbearing potential, as vessels of babies, but as individuals in their own right, who deserve access to the very best, evidence-based treatment available and the right to choose what they feel is best for them. We therefore think that to deny all women (and we believe, possibly men, as well) this new drug and fixed-dose formulation, should not be an option especially in the absence of any consultation with the community. We do not think that women are getting enough credit to be able to make conception decisions, and we hear this rhetoric as the same rhetoric that denied Africans treatment in the past.

Women living with HIV must be applauded for achieving and maintaining high levels of viral suppression, surpassing many developed countries. We see it as imperative that an education and information dissemination process is put in place so that women fully understand the risks, and a training programme is made available for healthcare workers to be able to appropriately counsel women on these risks and enable them to make an informed decision on their choice of treatment and conception decisions. Ministries of Health and other stakeholders should improve access to hormonal family planning methods rather than deny better treatment options to women who do

not wish to conceive, especially that DTG can be used with many effective contraceptives currently in use, with less drug interactions than alternative regimens.

We want to know when is TLD coming?

Why we have not been consulted?

We understand that moving to TLD, while maintaining tenofovir-lamivudine-efavirenz/tenofovir-emtricitabine-efavirenz (TLE/TEE) in the system is complex and will be somewhat more complicated for government supply chains, but we do not believe that this complexity is impossible to deal with. We have multiple other regimens in the system for second-line and toxicity. And truthfully, we always knew that TB and pregnancy could be an issue, possibly requiring other regimens to be included.

We are calling for TLD to be made available urgently across the continent with everyone having access, and with appropriate education and support with regard to pregnancy (and the option of using TLE), and TB, for all stakeholders.

What we need is honest and open communication and consultation with all stakeholders, including Civil Society.

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About AFROCAB

AfroCAB is a regional access to treatment network focusing primarily on Sub-Sahara Africa. The network prioritises optimised treatment - drugs and diagnostics, to ensure innovative high quality and effective health products and commodities are quickly accessible to all Africans at affordable prices.

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