Changes in Dolutegravir Use Following the NTD Safety Signal in Botswana

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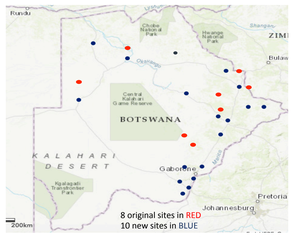
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BACKGROUND

- **This study evaluates patterns of dolutegravir (DTG) use in pregnant women in Botswana before and after report of a preliminary safety signal for neural tube defects (NTDs) associated with DTG in May 2018**
- In 2016, Botswana was the first country to roll out DTG as first line for all adults, including pregnant women
- In May 2018, following a preliminary safety signal associating DTG and NTDs, in-country guidance supported:
  - *Individualized counseling for pregnant women who had already conceived, and for those desiring pregnancy*
  - *Continued use of DTG-based ART for new ART starts, without specific mention of ART starts in pregnancy*
- It is unknown how this guidance impacted clinical practice or use of DTG during the NTD risk period (first 6 weeks of pregnancy)

METHODS

- We performed a secondary analysis of data abstracted from Aug 2016-Sept 2019 in the Tsepamo study
- Data were collected from 8 government maternity wards until mid-2018, when 10 new sites were added, increasing coverage to over 70% of births in the country (see map)
- HIV diagnosis date, ART regimens taken before or during pregnancy, and dates of ART initiation and discontinuation were collected from all women living with HIV who delivered at study sites



STUDY POPULATION

- Between Aug 15, 2016 and Aug 31, 2019:
  - 20,245 HIV+ women delivered at study sites
    - 13,205 (65.2%) on ART prior to conception
    - 5,718 (28%) started on ART during pregnancy
    - 904 (4.5%) received no ART during pregnancy
    - 427 (2.1%) had unknown timing of ART start

After the NTD signal, the strategy of individualized ART counseling
-did not change DTG exposure at conception (28% vs. 27%)
-but more than HALF of pregnant women presenting after the NTD risk period (>6wks GA) were started on non-DTG ART.

Figure 1a. ART regimen at conception by month of delivery before and after release of DTG safety warning in Botswana

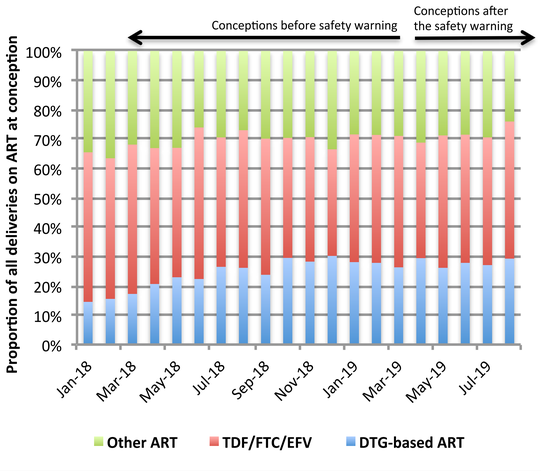
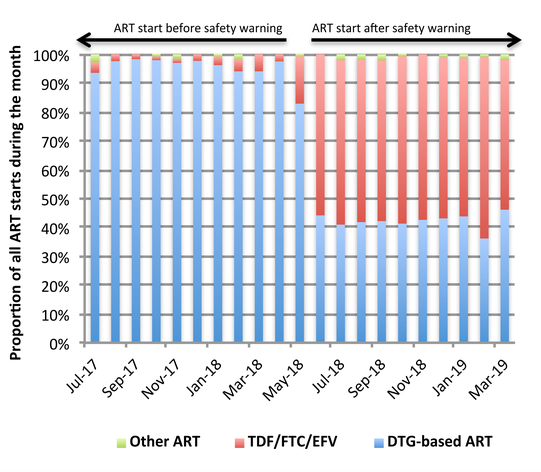


Figure 1b. ART regimen started during pregnancy before and after release of DTG safety warning in Botswana



RESULTS

- **DTG at CONCEPTION**
- The proportion of deliveries with DTG conception exposure increased steadily during the study period to a maximum of 30% in October 2018 (Figure 1a)
- Among women who likely conceived in the 5 months after the May 2018 guidance, 27% of conceptions were on DTG-based ART, which was unchanged from 28% in the 5 months prior to the guidance

- **DTG started DURING PREGNANCY**
- Before May 2018, 97% of women initiating ART in pregnancy started DTG-based ART (Figure 1b)
  - 1.7% started < 6 weeks gestational age
- After May 2018, 43% of starts in pregnancy were DTG-based ART, and 56% were EFV-based ART
  - 1.6% started < 6 weeks gestational age

- **ART SWITCHES and TERMINATIONS**
- Among 441 who changed ARVs during pregnancy, 177 (40%) switched from DTG-based ART to EFV-based ART (99% after May 2018)
- Only 71 (0.4%) women discontinued ART during pregnancy, including 35 women on DTG and 24 on EFV

CONCLUSIONS

- Program guidance based on individual counselling regarding pregnancy intention had no apparent impact on DTG exposures in the periconception NTD risk period
- Pregnant women frequently initiated non-DTG ART, but did so beyond the NTD risk period
- Individualized counseling without clear public health guidance may be insufficient to address ART treatment decisions in the event of new safety concerns.

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