



UGANDAN CLINIC EXPERIENCE FOLLOWING POTENTIAL TERATOGENICITY ALERT FOR DOLUTEGRAVIR



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Background

In 2017, the Infectious Disease Institute (IDI) introduced dolutegravir (DTG)-based regimens in its Kampala clinic in Uganda. See Image 1

In May 2018, the WHO and international regulators released warnings on a possible increased risk of neural tube defects in infants born to women on DTG at the time of conception^{1,2}.

In response, IDI implemented a process to inform and support women already on DTG to make informed treatment choices.

Objective:

To share the Ugandan clinical experience following the potential teratogenicity alert for dolutegravir in the middle of the roll out.

Image 1: Infectious Diseases Institute - Mulago



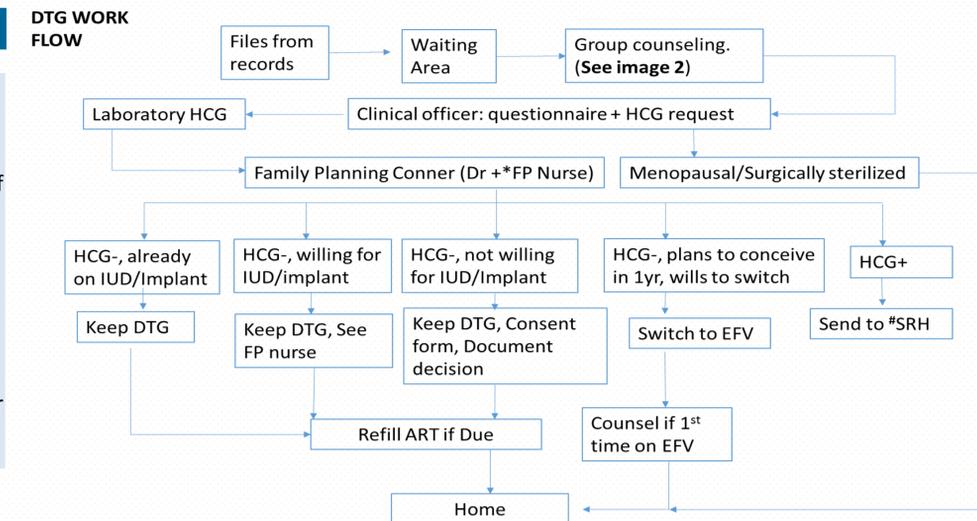
Methods

- A clinic response plan was developed in the first week following the alert and clinic staff were trained on safety guidance.
- All women <55 years on DTG were identified from the clinic database and contacted by phone for earlier appointments.
- From May-June, group counselling sessions (<15 women/ group) were held
- Non-menopausal and non-surgically sterilized women were referred for urine pregnancy testing, evaluation of pregnancy intentions in next 12 months and effective family planning was offered (preferably condoms plus implants, IUDs, Depo-Provera or pills).
- Pregnancies were confirmed by ultrasound and obstetrician review.
- Women intending to conceive were offered efavirenz (EFV)-based regimens.
- Women that chose to remain on DTG without effective family planning signed a declaration of informed choice.

Statistical Analysis:

We used modified Poisson regression to determine factors associated with switching off DTG.

Results



*Family Planning, #Sexual Reproductive Health

Image 2: Group counseling



9% (692/7963) were identified to be on DTG and 95% (658/692) were reviewed by September 2018. 22% (146/658) were menopausal or surgically sterilized. 510 women were of reproductive potential with median age (IQR); 37 (30 - 42) and mean duration (SD) on DTG of 4.26 months (1.63). 5% (23/510) were HCG positive and all initial ultrasound reports revealed no deformities. 21% (108/510) had intentions to conceive and opted to be switched off DTG with 90% (97/108) switched to EFV. 79% (402/510) opted to stay on DTG. However only, 40% (160/402) chose effective contraceptives methods and 60% (242/402) opted for condoms only/no contraceptive method.

Figure 1: Regimen Choice after counseling

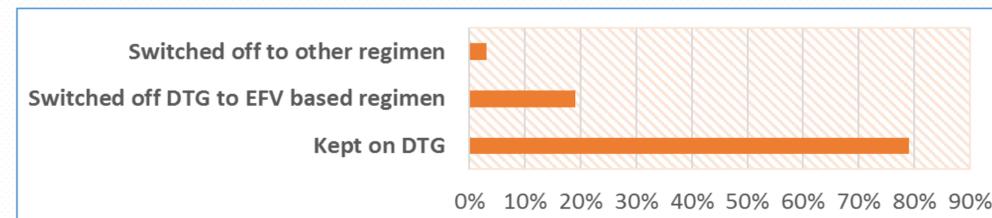
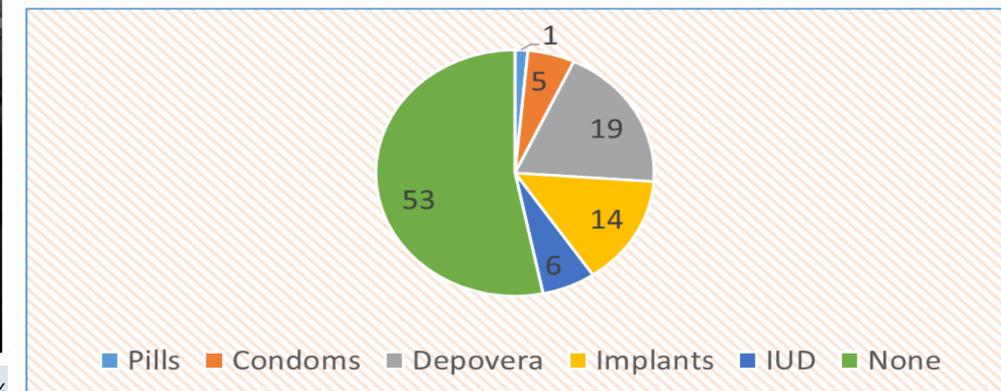


Table 1: Risk factors associated with switching off Dolutegravir

Characteristics	Freq [N=510 (%)]	Unadjusted IRR (95% CI)	P-value	Adjusted IRR (95% CI)	P-value
Age; median (IQR)	37 (30 - 42)	0.97 (0.95 - 1.00)	0.023	0.96 (0.94 - 0.99)	0.002
Duration in care, years; mean (st.d)	6.74 (4.44)	0.99 (0.94 - 1.04)	0.581	1.01 (0.96 - 1.06)	0.704
Duration on DTG, months; mean (st.d)	4.26 (1.63)	0.92 (0.81 - 1.04)	0.180	0.94 (0.86 - 1.04)	0.252
Pregnant					
No	486 (95.48)	1.00		1.00	
Yes	23 (4.52)	1.92 (0.97 - 3.80)	0.061	1.05 (0.61 - 1.81)	0.852
HCG					
No	86 (17.73)	1.00		1.00	
Yes	399 (82.27)	1.39 (0.79 - 2.43)	0.256	1.07 (0.65 - 1.78)	0.791
Effective contraceptive					
No	345 (67.65)	1.00		1.00	
Yes	165 (32.35)	0.10 (0.04 - 0.25)	<0.001	0.04 (0.01 - 0.15)	<0.001
FP method before DTG					
No FP before	312 (61.18)	1.00		1.00	
Had FP	198 (38.82)	0.60 (0.39 - 0.92)	0.018	1.31 (0.91 - 1.89)	0.141
Regimen before DTG					
Nevirapine	115 (22.68)	1.00		1.00	
Efavirenz	318 (62.72)	0.97 (0.61 - 1.53)	0.894	0.96 (0.64 - 1.45)	0.853
Naïve	74 (14.60)	0.99 (0.53 - 1.86)	0.986	0.78 (0.40 - 1.51)	0.460

IRR - Incidence Rate Ratio; st.d – standard deviation; FP- family planning; DTG- Dolutegravir; missing – Pregnant 1(0.20%), HCG 25(4.90%), Regimen before DTG 3 (0.59%)

Figure 2: Contraceptive choices for women who stayed on DTG



Conclusions

A rapid well-coordinated response ensured prompt communication of the DTG safety warning. Women made informed decisions with most opting to stay on DTG however effective contraception uptake was low. Age was associated with switching off DTG.

While a patient-centered approach was feasible in this clinic, ongoing monitoring for DTG pregnancy exposures is needed.

References:

- World Health Organization. Potential safety issue affecting women living with HIV using dolutegravir at the time of conception. Geneva, Switzerland. May 18, 2018.
- <https://www.fda.gov/Drugs/DrugSafety/ucm608112.htm>