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BACKGROUND

- In 2018, the **Tsepamo Study, Botswana** reported significant increased risk of NTD in women conceiving on DTG (0.94%)¹ leading to a safety alert
- Updated analysis of NTD prevalence (08/2014 - 03/2019)²
 - 5 NTDs/1,683 deliveries in women on DTG at conception (**0.30%**, 95% CI 0.13-0.69 vs **0.10%**, 95% CI 0.06-0.17 for non-DTG ART at conception)
- The **Antiretroviral Pregnancy Registry** recently reported 1 NTD in 312 periconception DTG exposures (**0.3%**)³
- The **Dolomite Study** was set up in 2017 to address use & safety of DTG in pregnancy and exposed infants in Europe and Canada; conducted within the NEAT-ID network and EPPICC (the European Pregnancy and Paediatric Infections Cohort Collaboration)

AIM

- To assess pregnancy and neonatal outcomes following DTG use during pregnancy in real-world European settings
- Objectives were to describe:
 - characteristics of pregnant women receiving DTG-based regimens
 - frequency of adverse pregnancy and birth outcomes, by earliest timing of DTG exposure

METHODS

- Dolomite-EPPICC** involves pooled analyses of prospectively collected individual patient data on DTG-exposed pregnancies from participating studies
- Data specification based on a modified HIV Data Exchange Protocol (www.hicdep.org)
- Data merger included
 - All pregnancies with any prenatal DTG exposure
 - With birth outcomes reported by Feb 2019
- Periconception DTG exposure was defined as initial exposure at ≤6 weeks of estimated gestational age (EGA)

RESULTS

- 453 pregnancies in 428 women included (Figure)
- Pregnancies reported from **six countries**
 - 347 (76.6%) UK and Ireland, 45 (9.9%) Spain, 29 (6.4%) Switzerland, 29 (6.4%) Italy, 3 (0.7%) Romania

Maternal characteristics

- 229/428 (53.5%) women were of Black African ethnicity
- 326 (82.7%) acquired HIV heterosexually
- 24 (6.1%) were HCV seropositive and 14 (3.6%) HBsAg+

¹Zash et al, NEJM 2018; ²Zash et al, NEJM 2019; ³Vannappagari et al EACS 2019

Dolomite-EPPICC study found 70% of enrolled pregnancies had periconception DTG exposure, with no NTDs and an overall 4.1% prevalence of birth defects

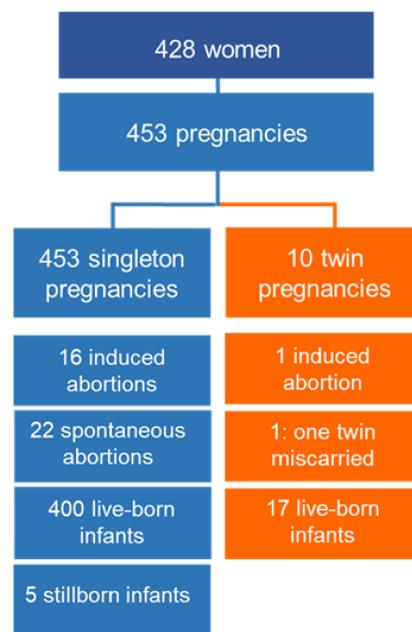


Table 1 Outcomes, by earliest DTG exposure

	Total DTG exposed	Earliest exposure to DTG		
		Periconception	Later T1	T2/T3
Total outcomes, N	463*	325	31	106
Live births	417 (90.1%)	280 (86.1%)	30 (96.8%)	106 (100%)
Stillbirths	5 (1.1%)	5 (1.5%)	0	0
Spontaneous abortions	23 (5.0%)	23 (7.2%)	0	0
Induced abortions	18 (3.8%)	17 (5.2%)	1 (3.2%)	0

*includes outcomes from 10 twin pregnancies

- Timing of earliest DTG exposure in **453 pregnancies**

- periconception: 317 (70.0%)
- later T1: 31 (6.8%)
- T2/T3: 105 (23.2%)

- Among 417 live-born infants, there were **17 reported with birth defects** (4.1%, 95% CI 2.4, 6.5)
- One infant had two defects
- No defects in stillborn infants
- One neonatal death in infant born at 23 weeks gestation (no defects)

Table 2 Neonatal Outcomes: 400 singleton, live births

	Total DTG exposed	Earliest exposure to DTG		
		Periconception	Later T1	T2/T3
Total, N	400	266	30	104
Gestational age				
<34 weeks	12 (3.1%)	8 (3.0%)	1 (3.3%)	3 (2.8%)
34-36 weeks	39 (9.7%)	24 (9.0%)	2 (6.7%)	13 (12.5%)
≥ 37 weeks	334 (83.5%)	222 (83.5%)	26 (86.7%)	86 (82.7%)
missing	15 (3.7%)	12 (4.5%)	1 (3.3%)	2 (1.9%)
Birth weight				
<1500g	12 (3.0%)	8 (3.1%)	1 (3.3%)	3 (2.9%)
1500-2499g	36 (9.0%)	23 (8.6%)	2 (6.7%)	11 (10.6%)
≥2500g	342 (85.5%)	230 (86.5%)	26 (86.7%)	86 (82.7%)
missing	10 (2.5%)	5 (1.8%)	1 (3.3%)	4 (3.8%)

BIRTH DEFECTS

- % infants with birth defects by earliest exposure to DTG:**

Periconception	12/266	4.5%	(95% CI 3.9, 5.1)
Later T1	1/30	3.3%	(95% CI 0.08, 17.2)
T2/T3	4/104	3.8%	(95% CI 1.1, 9.6)
- 18 outcomes of induced abortion – one due to identified birth defects (at 29 weeks, neuronal migration disorder & severe microcephaly)

Table 3 Details of birth defects in live-born infants

Organ system	Exposure	Birth defect	EUroCAT?
Heart N=3	PC	Patent Foramen Ovale	No
	PC	Interatrial communication – ostium secundum	Yes
	PC	Septal defect	Yes
Genitourinary N=7	PC	Congenital hydronephrosis x2	Yes
	PC	Ectopic Kidney	Yes
	PC	Hypospadias* x3	Yes
	T2/3	Hypospadias	Yes
Gastrointestinal N=2	T2/3	Duodenal atresia and stenosis	Yes
	PC	Gastroschisis	Yes
Limb N=3	PC	2 x Polydactyly*	Yes
Other N=3	Later T1	Ankyloglossia	No
	T2/3	Hyperpigmentation on back	No
	PC	Naevus flammeus	No

*1 infant had hypospadias and polydactyly PC= periconception

CONCLUSIONS

- This is the largest study to date of DTG use in pregnancy in Europe, in which **70%** of 453 pregnancies had **periconception DTG exposure**
- Overall, **4.1% prevalence of birth defects** (3.1% for EuroCAT)
- No NTDs were reported, but 2000 exposures would be needed to rule out a 3-fold increase for these rare events (≈0.1% birth prevalence)
- The birth defect rate and pattern add to the current evidence base on periconception DTG use and safety
- Study is ongoing, in order to provide additional data from European settings