A multicentre observational study to determine the safety and effectiveness of dolutegravir (DTG) use during pregnancy: Data from DOLOMITE-NEAT ID Network study

P008

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Key Takeaways

- **The birth defect rate and pattern add to the current evidence base on DTG use and safety in pregnancy**
- **DTG continues to be an effective treatment for prevention of vertical transmission**

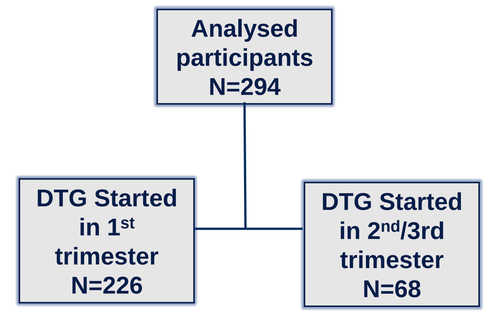
Introduction

- Dolutegravir (DTG) is an integrase inhibitor used in combination with other antiretrovirals (ARVs) and is widely recommended during pregnancy for maternal viral suppression and prevention of vertical HIV transmission
- This analysis assessed pregnancy and neonatal outcomes of pregnancies in individuals living with HIV using DTG based regimens (DBRs) by trimester of earliest exposure, using data from clinical sites participating in DOLOMITE - NEAT ID Network study

Methods

- Data were included from individuals in Belgium, France, Italy, Poland, Portugal, Spain, UK, and Ukraine who were exposed to DTG based regimen during pregnancy for at least one day
- Exposure was categorised by trimester, overall days and days per trimester
- Outcomes assessed include birth defects, live births, stillbirths, birth weight and gestational age at birth
- HIV RNA VL at delivery was defined by HIV RNA VL measured at or after 34 weeks of gestation or at partum ± 6 weeks if delivery before 34 weeks of gestation
- All enrolled pregnant individuals with a VL value at delivery were included in the HIV RNA VL evaluation (first primary endpoint analysis)

Figure 1. Study Flowchart



Results

- 294 DTG exposed pregnancies resulted in 281 live neonates (including 10 sets of twins and 1 set of triplets), 2 stillbirths, 8 induced abortions, 13 spontaneous abortions and 2 with unknown pregnancy outcome (Table1) The median age of pregnant individuals was 33 (IQR 27-37)
- Viral load at delivery was undetectable (<50 copies/ml) among 86.4% of individuals and there were no reported vertical transmissions
- One fetus with trisomy 13 and 6 drug related adverse events [headache (2), hepatitis, high blood pressure, and elevated aspartate aminotransferase (AST) and elevated alanine aminotransferase (ALT)] were reported
- Among 261 live births with gestational age available, 40 (15.3%) were preterm (<37 weeks of gestation) and 7 (2.7%) were severely preterm (<32 weeks of gestation, Table 2)
- Among 259 live births with birth weight available, 46 (17.8%) had low birth weight (<2500 grams) and 8 (3.1%) had very low birth weight (<1500 grams)
- A total of 21 birth defects were seen in 18 live births with a defect prevalence of 7.2% but no neural tube defects (NTDs) were reported

Table 1. Pregnancy Outcomes

	Earliest exposure to DTG			
	Any trimester N=294	1st trimester N=226	2nd/3rd trimester N=68	P-value
Pregnancy outcome, n (% of enrolled pregnant individuals)				
Live birth (at least one)	269 (91)	203 (90)	66 (97)	0.061
Stillbirth	2 (1)	2 (1)	0	0.436
Induced abortion	13 (4)	13 (6)	0	0.043
Spontaneous abortion	8 (3)	7 (3)	1 (1)	0.470
Unknown	2 (1)	1 (0)	1 (1)	
HIV RNA VL at delivery (±6 weeks); n/N (%)[a] *				
N (HIV RNA VL at delivery available within timeframe)	*228/271 (84.1)*	*174/205 (84.9)*	*54/66 (81.8)*	
<50 copies/mL	197/228 (86.4)	155/174 (89.1)	42/54 (77.8)	0.034
≥50 copies/mL	31/228 (13.6)	19/174 (10.9)	12/54 (22.2)	
<200 copies/mL	216/228 (94.7)	169/174 (97.1)	47/54 (87.0)	0.004
≥200 copies/mL	12/228 (5.3)	5/174 (2.9)	7/54 (13.0)	
Drug related AEs and SAEs (n, %; no. of SARs)	6/294 (2.7)	2/226 (1.6); 1 SAR	4/68 (5.0); 0 SAR	

The analysis population consists of all enrolled pregnant individuals unless otherwise stated
P-values are for the event vs all other events (dichotomous)
*Includes all enrolled pregnant individuals with at least 22 weeks gestation (ie, excluding induced and spontaneous abortions)
[a]HIV RNA VL at delivery (±6 weeks) defined by HIV RNA VL measured within partum ±6 weeks. Individuals without a measurement in this timeframe were excluded. Where multiple HIV RNA VL were recorded, the result closest to delivery is considered

Table 2. Infant Outcomes

	Earliest exposure to DTG			
	Any trimester N=281	1st trimester N=212	2nd/3rd trimester N=69	P-value
No. live births with outcomes available	261/281 (92.9)	195/212 (92.0)	66/69 (95.7)	
Gestational age at delivery, median (IQR)	38 (37-39)	39 (38-39)	38 (37-49)	0.425
Birthweight, median (IQR), kg	3.1 (2.7-3.4)	3.1 (2.7-3.4)	3.0 (2.7-3.4)	0.931
Incidence of events, n (%)				
Low birth weight (<2500 grams)	46/259 (17.8)	35/194 (18.0)	11/65 (16.9)	0.838
Very low birth weight (<1500 grams)	8/259 (3.1)	6/194 (3.1)	2/65 (3.1)	0.995
Preterm birth (<37 weeks gestation)	40/261 (15.3)	28/195 (14.4)	12/66 (18.2)	0.456
Severely preterm birth (<32 weeks gestation)	7/153 (2.7)	5/195 (2.6)	2/66 (3.0)	0.839
Birth defects in live births, n (% of live birth with non-missing result, 95% CI) [Total N birth defects]	18/249 (7.2, 4.3-11.2) [21]	16/184 (8.7) [19]	2/65 (3.1) [2]	0.133
Neonatal HIV status, n (%)				
Infected	0/245 (0.0)	0/245 (0.0)		
Uninfected	245/245 (100.0)	182/182 (100.0)		

The analysis population consists of all live births (including multiple births) unless otherwise stated. Significance tests exclude unknown/missing observations.

Conclusions

- No significant difference in frequency of birth defects was observed for infants with earliest exposure in the 1st compared to the 2nd/3rd trimester; no NTDs were reported
- The results highlight the importance of starting ARV regimen early in pregnancy in order to achieve viral suppression

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