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

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Background

DTG shows high penetration across the placenta, suggesting protection against infant HIV infection, but potential increased adverse birth outcomes.

This analyses assessed real-world outcomes, during pregnancy and birth, from women living with HIV on DTG based regimen during pregnancy according to exposure trimester, using data from clinical sites participating in DOLOMITE - NEAT ID Network study, sponsored by ViiV.

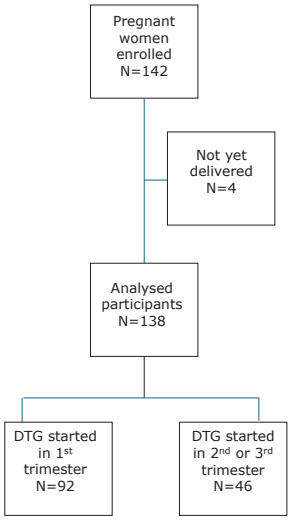
Methods

Design

Data were included from women in **Belgium, France, Italy, Poland, Portugal, Spain, UK, Ukraine** and **Canada** 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.

Study Flowchart



Statistical Methods

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 women with a VL value at delivery were included in the HIV RNA VL evaluation (first primary endpoint analysis). *Women with spontaneous or induced abortion were excluded as depicted in Table 2.

No adjusted analyses were performed due to the small number of events observed except maternal VL at delivery and birth weight.

Results

The analysis included 138 DTG exposed pregnancies with 120 pregnancies resulting in 131 live neonates (8 multiples), 2 still births and 16 miscarriages or abortions. At baseline 109 (79.0%) women were on treatment experienced and 91 had undetectable VL (<50 copies/ml), **Table 1**.

Of 92 (66.7%) women exposed to DTG during 1st trimester, 77 conceived while on DTG, four within the first six weeks after conception and ten after 6 weeks (one with missing information), **Table 2**.

In 5 cases of live births, a birth defect was recorded; no birth defects were seen in stillbirths, (**Table 3**). There were 3 TORCH infections (1 in 1st trimester, 2 in 2nd/3rd trimester). There were no reports of HIV infected infants (17.6% unknown), neural tube defects, maternal SARs or deaths.

Conclusions

- **no significant difference in frequency of birth defects was observed for first trimester exposures compared to 2nd/3rd trimester exposures**
- **no neural tube defects in either group**
- **most achieved viral suppression at delivery**

Table 1: Baseline Characteristics

Characteristics at DTG first exposure in pregnancy	Any trimester N=138	1st Trimester, N=92 (66.7%)	2nd or 3rd trimester N= 46 (33.3%)	P-value
Age, years, median (IQR)	32 (27-37)	33 (28-37)	30 (26-36)	0.229
Ethnicity, n (%): White; Black; Other/Unknown.	56 (40.6); 55 (39.9); 27 (19.6)	33 (35.9); 40 (43.5); 19 (20.7)	23 (50.0); 15 (32.6); 8 (17.4)	0.275
Time since HIV diagnosis, years, median (IQR)	9.1 (4.3-15)	9.4 (5.2-15.5)	5.2 (2.2-10.8)	0.003
Prior AIDS defining illness, n (%)	23 (16.8)	17 (18.5)	6 (13.3)	0.438
CD4 count, median (IQR) cells/mm³	545 (327-782)	537 (328-777)	564 (294-786)	0.933
Plasma HIV RNA, copies/mL prior pregnancy confirmation, median (IQR)	40 (20-293)	40 (20-50)	40 (40-7370)	0.023
Maternal VL at date of DTG exposure, n/N (%) a) <50 copies/ml b) <200 copies/ml	a) 91/138(65.9) b) 95/138(68.8)	a) 68/92 (73.9) b) 70/92 (76.1)	a) 23/46 (50.0) b) 25/46 (54.3)	a)0.019 b)0.032
Presence of any drug resistance mutations in those with resistance test, N= 78, (56.5%), n (%)	46/78 (59.0)	33/61 (54.1)	13/17 (76.5)	0.162
Cumulative exposure to DTG during pregnancy in days, median (IQR)	96 (55-198)	98 (54-256)	91 (56-119)	0.162

Table 2: Pregnancy Outcomes

	DTG started			
	Any trimester N=138	1st trimester N=92	2nd or 3rd trimester N=46	P-value
Type of delivery; n (%)				**0.006**
Vaginal birth	75 (54.3)	41 (44.6)	34 (73.9)	
Vaginal forceps	1 (0.7)	1 (1.1)	0 (0.0)	
Cesarean section	46 (33.3)	34 (37.0)	12 (26.1)	
Events; n (%)				
Induced abortion	7 (5.1)	7 (7.6)	0 (0.0)	0.095
Spontaneous abortion	9 (6.5)	9 (9.8)	0 (0.0)	**0.029**
Gestational age at delivery, median (IQR)	38 (37-39)	38 (37-39)	39 (37-40)	0.407
Smoking, alcohol, or drug abuse during current pregnancy; n (%)	30 (21.7)	14 (15.2)	16 (34.8)	**0.027**
Number of live births per woman, medianę (IQR)	1 (1-1)	1 (1-1)	1 (1-1)	0.824
0	18 (13)	18 (19.6)	0 (0.0)	**0.019**
1	112 (81.2)	68 (73.9)	44 (95.7)	
2	6 (4.3)	4 (4.3)	2 (4.3)	
3	1 (0.7)	1 (1.1)	0 (0.0)	
4	1 (0.7)	1 (1.1)	0 (0.0)	
HIV RNA VL at delivery, n (%)				
N-MISS (spontaneous or induced abortion)*	16	16	0	
<50 copies/mL	104 (85.2)	68 (89.5)	36 (78.3)	0.116
≥50 copies/mL	18 (14.8)	8 (10.5)	10 (21.7)	
<200 copies/mL	111 (91.0)	74 (97.4)	37 (80.4)	**0.002**
≥200 copies/mL	11 (9.0)	2 (2.6)	9 (19.6)	

Table 3: All Birth Outcomes (Still and Live)

	DTG started			
	Any trimester N=133	1st trimester N=85	2nd or 3rd trimester N=48	P-value
Number of stillbirths, n (%)				0.535
0	131 (98.5)	83 (97.6)	48 (100)	
1	2 (1.5)	2 (2.4)	0 (0.0)	
Birthweight (kg), median (IQR)	3.1 (2.7-3.5)	3.1 (2.7-3.5)	3 (2.6-3.5)	0.489
APGAR Score, median (IQR)	9 (8-10)	9 (9-10)	9 (8-9)	**0.005**
Incidence of events, n (%)				
Low birth weight (<2500g)	20/116 (17.2)	10/69 (14.5)	10/47 (21.3)	0.453
Very low birth weight (<1500g)	5/116 (4.3)	2/69 (2.9)	3/47 (6.4)	0.394
Extremely low birth weight (<1000g)	1/116 (0.9)	0/69 (0.0)	1/47 (2.1)	0.405
Preterm birth (<37 weeks gestation)	20/116 (17.2)	10/69 (14.5)	10/47 (21.3)	0.453
Severely preterm birth (<32 weeks gestation)	5/116 (4.3)	2/69 (2.9)	3/47 (6.4)	0.394
Stillbirth (death ≥22 weeks GA or where GA N/A, weight ≥500g)	2 (1.5)	2 (2.4)	0 (0.0)	0.535
Birth defects in live birth, n (%)	5/131 (3.8)	4/83 (4.8)	1/48 (2.1)	0.652
flat cutaneous haemangioma in occipital region	1	1		
Left hydronephrosis and megaurether. Enlargement of right calico-pelvis system	1	1		
suspicion of pelvicalyceal system enlargement	1	1		
small umbilical hernia	1	1		
Atrial Septal Defect	1		1	
Birth defects in stillbirth, n (%)	0/2 (0.0)	0/2 (0.0)	0/0 (0.0)	
Neonatal HIV status, n (%)				0.129
Infected	0 (0.0)	0 (0.0)	0 (0.0)	
Uninfected	108 (82.4)	64 (77.1)	44 (91.7)	
Unknown	23 (17.6)	19 (22.9)	4 (8.3)	

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