POSTER 806

Raltegravir in Pregnancy: Patterns of Use and Birth Outcomes in the UK & Ireland

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BACKGROUND

Raltegravir (RAL) is an HIV-1 integrase inhibitor known to rapidly reduce HIV RNA viral load (VL).

RAL was first licensed by the European Medicines Agency (EMA) in 2007, with initial therapeutic indications for the treatment of HIV-1 infection in combination with other antiretroviral therapy (ART).

RAL is **often used in pregnancy to reduce risk of mother-to-child transmission**, particularly for women presenting and/or diagnosed late in pregnancy. However, **safety data have been limited.**

METHODS

The National Study of HIV in Pregnancy and Childhood (NSHPC) conducts **active surveillance of pregnancies in women living with HIV** in the UK and Ireland, infants born to diagnosed women living with HIV, and all children living with HIV.

We aimed to **describe trends and patterns of "real-world" RAL use in pregnancy** and **outcomes among live- or stillbirths in 2008-2016** (reported to the NSHPC by March 2017).

Trends were assessed using logistic regression. Differences among treatment groups were assessed using Kruskal-Wallis tests for medians and chi-squared tests for proportions.

RESULTS

RAL was used in 709 (7%) of 10,144 reported pregnancies in the period 2008-2016. The proportion of pregnancies with RAL use increased steadily over time from 0.5% (13/2605) of pregnancies in 2008-2009 to 14.4% (252/1747) in 2015-2016 (Figure 1, p<0.001).

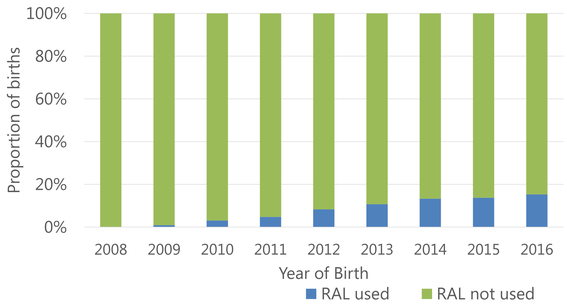


Figure 1. Births with antenatal RAL use, 2008-2016

Of RAL-exposed pregnancies, use at conception increased from 15% (2/13) in 2008-09 to 30% (76/252) in 2015-2016. Of 265 pregnancies with late ART start in pregnancy due to late antenatal booking (>27 weeks), 68 (26%) received RAL overall, reaching 52% (15/29) in 2015-2016.

Median maternal age at delivery was 33 years (IQR 29-37). Maternal and clinical characteristics of RAL-exposed pregnancies are presented in Table 1. Patterns of RAL use are displayed in Figure 2.

RESULTS

Table 1. Characteristics of RAL-exposed pregnancies

	n	(%)
Maternal ethnic origin (n=709)		
White	169	(23.8)
Black African	494	(69.7)
Other	46	(6.5)
Maternal region of birth (n=695)		
UK/Ireland	129	(18.6)
Africa	468	(67.3)
Elsewhere	98	(14.1)
Maternal HIV acquisition route (n=709)		
Heterosexual	614	(86.6)
Injecting drug use	15	(2.1)
Vertical	26	(3.7)
Other/Not known	54	(7.6)
Timing of maternal diagnosis (n=709)		
Before pregnancy	514	(72.5)
During pregnancy	195	(27.5)
Any ART at conception (n=705)		
No	407	(57.7)
Yes	298	(42.3)
Trimester of first RAL exposure (n=694)		
First	184	(26.5)
Second	191	(27.5)
Third	319	(45.9)
Late antenatal booking (>27 weeks) (n=664)		
Yes	76	(11.5)
Maternal VL within 30 days of delivery (n=555)		
Detectable (>50 copies/ml)	164	(29.5)

In 44 RAL-exposed pregnancies, HIV diagnosis occurred in pregnancy and booking for antenatal care and initiation of ART were late; in these cases, RAL was started at a median 34 gestational weeks (IQR 32-37).

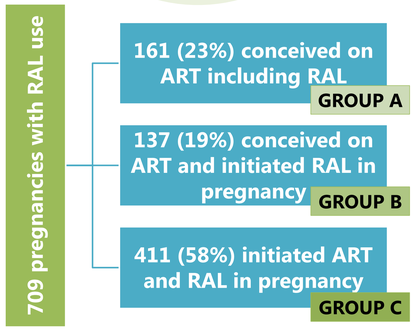
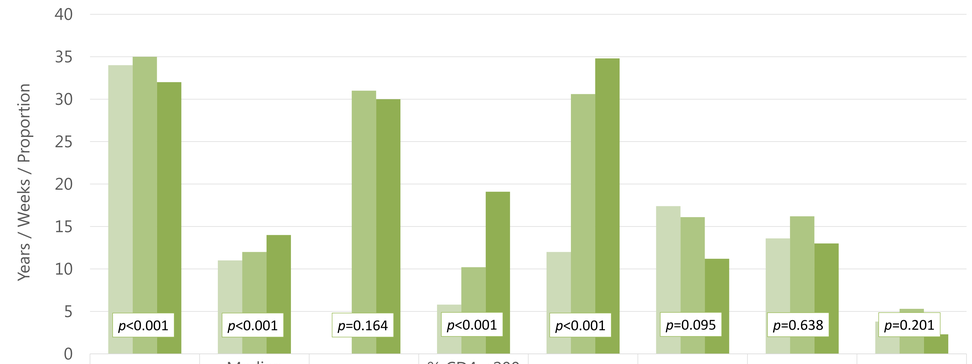


Figure 2. All RAL pregnancies, grouped by pattern of treatment

Characteristics and outcomes of pregnancies by treatment group are presented in Figure 3.

Six pregnancies ended in stillbirth and there were 728 live-born infants (50 twins).



	Median maternal age in years (N=708)	Median gestational weeks at booking (N=664)	Median gestational weeks at RAL start (N=533)	% CD4 <200 at latest count in pregnancy (N=680)	% detectable viral load at delivery (N=555)	% preterm delivery (<37 weeks) (N=709)	% low birthweight (<2.5 kg) (N=685)	% congenital abnormality (N=690)
Group A	34	11		5.8	12.0	17.4	13.6	3.8
Group B	35	12	31	10.2	30.6	16.1	16.2	5.3
Group C	32	14	30	19.1	34.8	11.2	13.0	2.3

Figure 3. Characteristics and outcomes of pregnancies receiving RAL by treatment group

RESULTS

Twenty-one (3.1%) of 678 singleton RAL-exposed liveborn infants had a reported congenital abnormality, with a similar rate seen in unexposed infants (2.7%); 4.0% (7/174) of infants exposed in the first trimester had an abnormality versus 2.7% (13/490) of those exposed in second/third trimester (14 missing RAL start date) (p=0.36).

A summary of reported congenital abnormalities is presented in Table 2. One infant had two abnormalities reported (Trisomy 21 and Atrioventricular Septal Defect). Three abnormalities did not meet EUROCAT definitions of congenital anomaly.

Table 2. Summary of congenital abnormalities by classification and earliest trimester of RAL exposure

Classification of abnormality	Earliest trimester of RAL exposure: First	Earliest trimester of RAL exposure: Second / Third	Total
Heart	2	2	4
Upper/lower gastrointestinal tract	1*	2	3
Renal/urinary		3	3
Limbs	1	2	3
Cleft lip and/or palate		1	1
Lung		1	1
Brain		1*	1
Chromosomal anomalies		1	1
Other anomalies / syndromes	2	2 + 1**	5
Total abnormalities	7	15	22

* Neonatal death; ** RAL start date unknown, estimated to second trimester from booking date & VL result

Reported abnormality meeting EUROCAT definitions | Reported abnormality not meeting EUROCAT definitions

CONCLUSIONS

RAL **use is steadily increasing in pregnancy in the UK/Ireland**, particularly from before conception.

The **group of pregnant women receiving RAL is heterogeneous**. Pregnancies in women with perinatal HIV accounted for nearly four percent of all pregnancies receiving RAL in 2008-2016, suggesting the importance of this drug for this emerging, highly treatment-experienced group.

Half of pregnancies with late (third trimester) ART initiation received RAL in 2015-2016, consistent with recommendations for RAL usage in pregnancy.

Data on infant outcomes, particularly congenital abnormalities, in RAL-exposed pregnancies are reassuring, but more work is needed to assess overall safety and rates of vertical transmission in exposed infants.

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