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A multicentre case series of Raltegravir use in pregnancy

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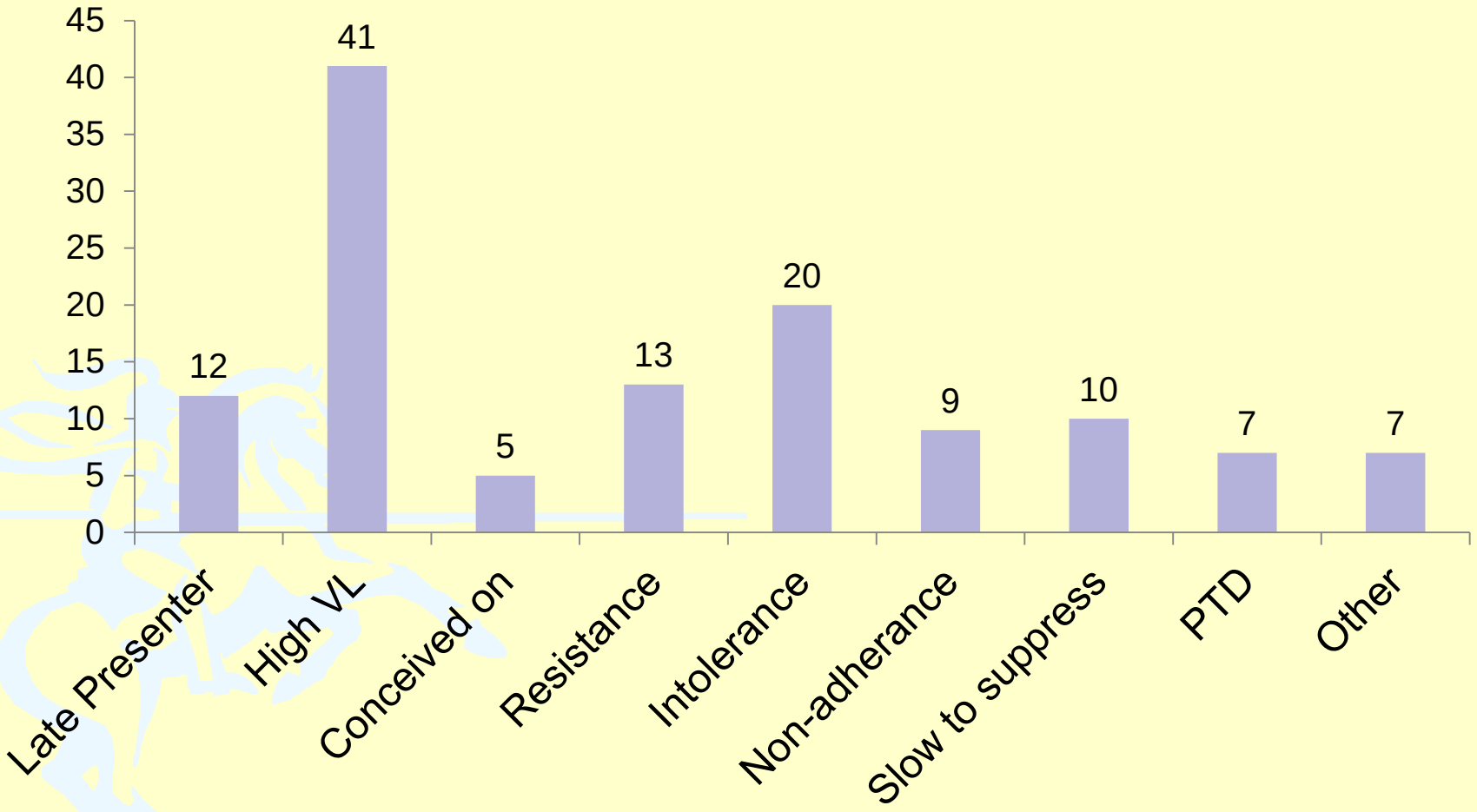
Aims / Methods:

- Aim: to describe the current use, efficacy and tolerability of RAL in pregnant women
- Retrospective case notes review
- 67 pregnancies
- 64 women
- 18 UK centres

Baseline Characteristics

Mean Age	31 years (17-44)
Black African	56 (84%)
Heterosexual transmission	60 (90%)
Hepatitis B/C co-infection	3 (4%)
Mean CD4 count	348 (13-1219)
Diagnosed in current pregnancy	22/67 (33%)
Need for continuous HAART	49 (73%)
Confirmed ARV resistance	25 (37%)

Reasons for RAL use



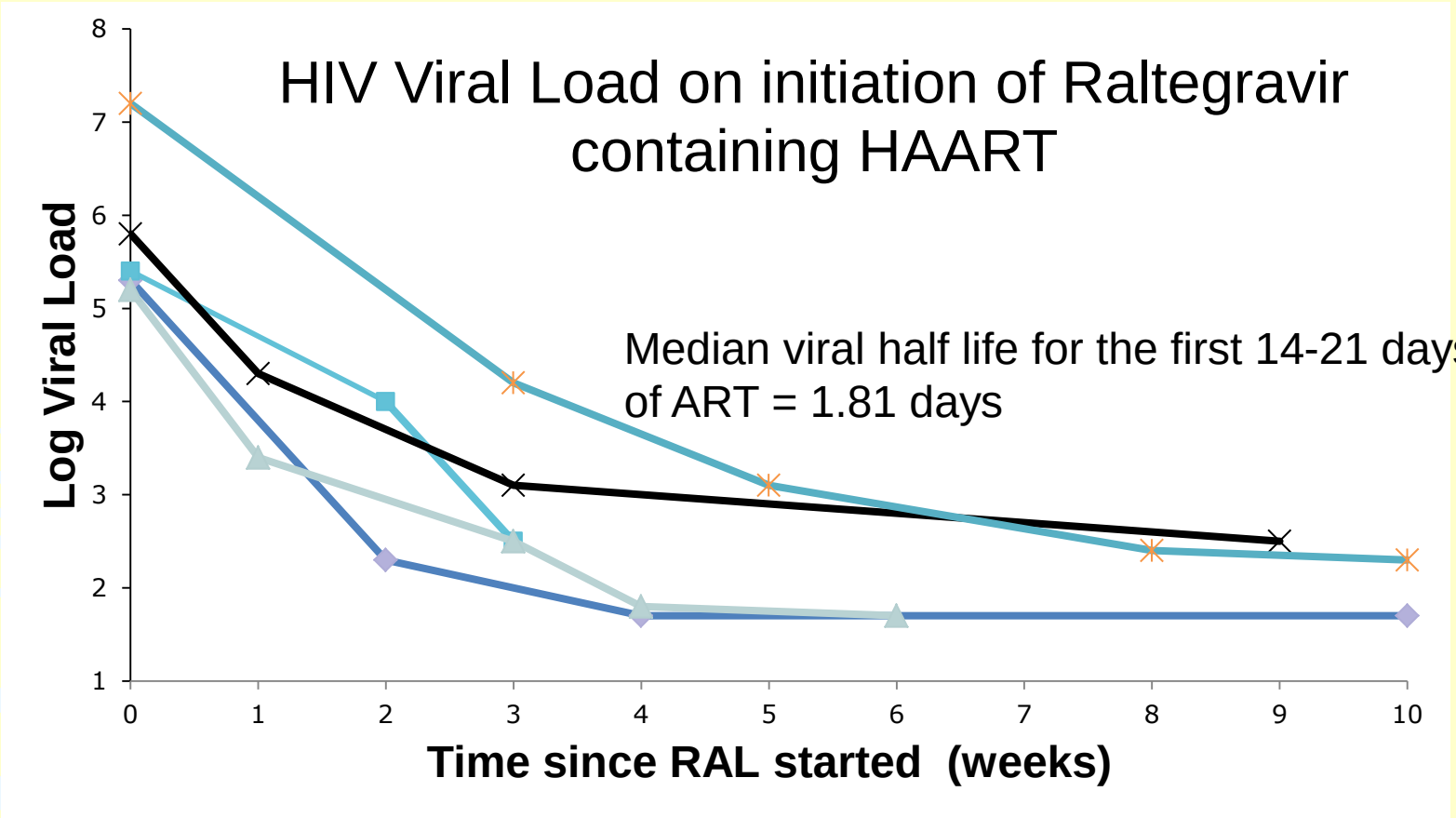
Indication: hepatotoxicity

- 7 on PI-based regimens
- No Hepatitis B/C co-infection
- Median Grade 3 hepatotoxicity
- Resolved in all

Indication: late presentation

Late Presentation	N=12
Median pre-RAL VL (copies/ml)	105k (125-17.4 million)
Proportion with VL <400 copies/ml pre-RAL	2/12 (17%)
Median length of time on RAL pre delivery	4 weeks (1-17)
Proportion with VL <50 copies/ml at birth	4/12 (33%)
Proportion with VL <400 copies/ml at birth	11/12 (92%)

Naive patients (n=5)



Kay N et al (2012) Showed a median viral half life of 2.05 days for Nevirapine and 2.65 days for Lopinavir/Rit after 14 days ART[1]

Overall tolerability of RAL

- 53/67 (80%) no documented side effects
- 7/67 (10%) nausea
- 6/67 (9%) new hepatotoxicity (G1-4):
  - 3 improved on stopping other meds
  - 2 thought obstetric cholestasis: 1 stopped RAL

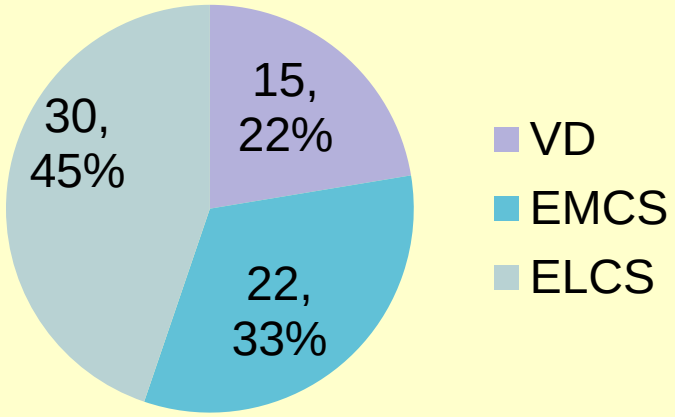
Overall outcomes of RAL

- 43/67 (64%) VL <50 copies/ml at birth
- 59/67 (88%) VL <400 copies/ml at birth
- 5/67 (7%) stopped RAL in pregnancy:
  - 3 no longer needed it
  - 1 virological failure and resistance
  - 1 Grade 3 hepatoxicity

Obstetric Outcomes

- 2/21 started RAL <28 wks had PTD
- Mean weight 3.1 kg (0.6-4.9kg)
- 11/67 (16%) neonatal adverse events not related to RAL

Mode of Delivery:



Neonatal screening results

- No in utero transmissions
- 12 weeks: 52/53 HIV DNA PCR negative
- 1 intrapartum transmission: PCR detected at 9 wks
  - Started Truvada, Raltegravir at 21/40
  - VL undetectable by 28/40
  - VL ‘blip’ of 91 copies/ml at ELCS
  - Neonatal AZT and maternal Cabergoline

Maternal & Neonatal RAL TDM

Case	One	Two	Three	Four	Five	Six	Seven
When RAL initiated pre-birth	14 hrs	22.5 hrs	1 wk	4wks	4 wks	11 wks	11 wks
Delivery gestation	30 wks	29 wks	40 wks	39 wks	40 wks	33 wks	39 wks
Maternal RAL level (ng/ml)	64	300	50	316	22	2318	493
Time post mat dose	3 hrs	10.5 hrs	12 hrs	1 hr	13 hrs	6 hrs	7 hrs
Time post birth	1 hr	0 hr	9 hrs	0 hr	1 hr	0 hr	3 hrs
Neonatal RAL level (ng/ml)	120	602	776	640	209	3781	3634
Time post mat dose	4 hrs	11 hrs	5.5 hrs	2 hrs	13 hrs	7 hrs	7 hrs
Time post birth	2 hr	0.5 hrs	2.5 hrs	1 hr	1 hr	1 hr	3 hrs
Neonatal RAL level (ng/ml)	67	-	5	608	-	312	-
Time post birth	2.6 days	-	3 days	2 days	-	3.8 days	-
Neonatal RAL level (ng/ml)	-	-	-	15.5	-	-	-
Time post birth	-	-	-	6 days	-	-	-

Conclusions

- RAL appears to be well tolerated in pregnancy
- Reasonable ‘switch’ option for those with toxicities on other regimens
- May have a role in women who need a rapid reduction in VL
- Demonstrates effective placental transfer

Acknowledgments

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- Chelsea and Westminster, NHS Foundation Trust
- Brighton and Sussex University Hospitals NHS Trust
- Portsmouth Hospitals NHS Trust
- Barts and the London, NHS Trust
- Homerton University Hospitals, NHS Foundation Trust
- Mortimer Market Centre, Camden PCT
- The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust
- Royal Free London NHS Foundation Trust
- Epsom and St Helier University Hospitals NHS Trust
- University Hospitals of Leicester NHS Trust
- St George's Medical School, University of London

References

(1) Kay, N et al. (2012) The Impact of Highly Active Antiretroviral Therapy (HAART) on HIV RNA Decay within the first 2 weeks of therapy among HIV-infected pregnant women. Paper 1020, 19th Conference on Retroviruses and Opportunistic Infections, 5-8 March 2012, Seattle, USA.