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A multicentre case series of Raltegravir use in pregnancy

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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Age</td>
<td>31 years (17-44)</td>
</tr>
<tr>
<td>Black African</td>
<td>56 (84%)</td>
</tr>
<tr>
<td>Heterosexual transmission</td>
<td>60 (90%)</td>
</tr>
<tr>
<td>Hepatitis B/C co-infection</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Mean CD4 count</td>
<td>348 (13-1219)</td>
</tr>
<tr>
<td>Diagnosed in current pregnancy</td>
<td>22/67 (33%)</td>
</tr>
<tr>
<td>Need for continuous HAART</td>
<td>49 (73%)</td>
</tr>
<tr>
<td>Confirmed ARV resistance</td>
<td>25 (37%)</td>
</tr>
</tbody>
</table>
Reasons for RAL use

- Late Presenter: 12
- High VL: 41
- Conceived on: 5
- Resistance: 13
- Intolerance: 20
- Non-adherence: 9
- Slow to suppress: 10
- PTD: 7
- Other: 7
Indication: hepatotoxicity

- 7 on PI-based regimens
- No Hepatitis B/C co-infection
- Median Grade 3 hepatotoxicity
- Resolved in all
<table>
<thead>
<tr>
<th>Late Presentation</th>
<th>N=12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median pre-RAL VL (copies/ml)</td>
<td>105k (125-17.4 million)</td>
</tr>
<tr>
<td>Proportion with VL &lt;400 copies/ml pre-RAL</td>
<td>2/12 (17%)</td>
</tr>
<tr>
<td>Median length of time on RAL pre delivery</td>
<td>4 weeks (1-17)</td>
</tr>
<tr>
<td>Proportion with VL &lt;50 copies/ml at birth</td>
<td>4/12 (33%)</td>
</tr>
<tr>
<td>Proportion with VL &lt;400 copies/ml at birth</td>
<td>11/12 (92%)</td>
</tr>
</tbody>
</table>
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.
**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
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

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