« HIV-1 drug resistance patterns of maternal HAART cohort to prevent post-partum HIV mother-to-child transmission in Rwanda »

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HIV mother to child transmission worldwide

• 400 000 new HIV infections among infant in Sub-Saharan Africa in 2009

✓ 90 % through mother-to-child transmission (MTCT)

• In some African countries, 1 pregnant woman out of 5 is HIV-infected.
HIV mother-to-child transmission

Prevention of unwanted pregnancies (Family Planning)

Primary HIV prevention in parents.

Prevention of Mother to Child Transmission (PMTCT)
- during late pregnancy
- peri-partum
- post-partum

Jeff Stringer, CROI 2009
PMTCT and HIV drug resistance

• Peri-partum Prevention (6-8 weeks)
  - NVP: 12%
  - AZT
  - 3TC: 6-9%
  Conor et al, 1994 PACTG076
  Guay et al, 1999 HIVNET 012
  Saba et al, 1999, PETRA

• HIV drug resistance in PMTCT
  - NVPsd resistance: 14-69%
  - HAART: 43-63% (minority variants)
    Roger Paredes et al, AIDS 2010

HAART for PMTCT and FF is a standard of care in developed countries: HIV MTCT< 2%
  - Safety of FF is difficult for Africa
  - Increased infant mortality

Maternal HAART and Breastfeeding in PMTCT an option for Africa: ???

KIBS study, MITRA-Plus, AMATA…
Main goal: evaluate breastfeeding with maternal HAART or formula feeding to prevent HIV MTCT in post-partum period.

- **Primary objectives:**
  - assess cumulative infant mortality
  - assess cumulative incidence of HIV-free survival: HIV infection or death (whichever came first)

- **Secondary objectives:**
  evaluate HIV drug resistance within two arms
  - Arm 1: women who received HAART for PMTCT
  - Arm 2: women who received HAART before/for PMTCT and continue treatment for lifelong according to nationa HIV guidelines.

*Peltier et al AIDS 2009, 23:2415-2423*
AMATA STUDY: DESIGN

AMATA ENROLMENT (562)

Non eligible for HAART:
CD4 > 350 and WHO clinical stage 1-3
AZT+3TC+EFV from 28 weeks of pregnancy

Eligible for HAART: CD4 < 350 or/
and stage 4 WHO
D4T+3TC+NVP
Choose feeding option before delivery

Breastfeeding (BF) group:
Exclusively until 6 months
and stop 1 month after weaning
(240 women)

Formula feeding (FF) group:
Stop HAART after delivery
(322 women)
Baseline and delivery characteristics of mothers

<table>
<thead>
<tr>
<th></th>
<th>Breastfeeding (N 240)</th>
<th>Formula feeding (N 322)</th>
<th>P (≤ 0.005)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Median in years)</td>
<td>28</td>
<td>29</td>
<td>0.000</td>
</tr>
<tr>
<td>WHO clinical stage</td>
<td></td>
<td></td>
<td>0.345</td>
</tr>
<tr>
<td>1 and 2</td>
<td>204</td>
<td>266</td>
<td></td>
</tr>
<tr>
<td>3 and 4</td>
<td>23</td>
<td>39</td>
<td></td>
</tr>
<tr>
<td>Maternal CD4 (Mean)</td>
<td>498</td>
<td>434</td>
<td>0.005</td>
</tr>
<tr>
<td>Viral Load (VL) at delivery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 40 copie/ml</td>
<td>94</td>
<td>126</td>
<td>0.898</td>
</tr>
<tr>
<td>&lt; 1 000 copies/ml</td>
<td>160</td>
<td>225</td>
<td>0.168</td>
</tr>
<tr>
<td>Duration of HAART (Mean in weeks)</td>
<td>16.4</td>
<td>21.8</td>
<td></td>
</tr>
<tr>
<td>Eligible for HAART</td>
<td></td>
<td></td>
<td>0.007</td>
</tr>
<tr>
<td>Started at enrolment</td>
<td>36</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Started before enrolment</td>
<td>56</td>
<td>122</td>
<td></td>
</tr>
</tbody>
</table>
AMATA STUDY: vertical transmission results

AMATA ENROLMENT (562)

265 BF and 322 FF
10 lost to follow up

552 deliveries
432 children alive (follow up)
7 children infected with HIV, six un utero

3/227 children were infected at birth
1 infected through BF
7 (3.1%) died in the BF arm

3/305 children were infected at birth
0 infected through FF
17 (5.6%) died within FF arm

Presented at the 8th European HIV Drug Resistance Workshop, March 17-19 2010, Sorrento, Italy
Viral load 7 months after delivery for mothers

Inclusion population 562 women

HAART for PMTCT
282 women

HAART for PMTCT
Viral load at 7 months:
VL>1000 copies/ml: 30% (86)

BF (135):
VL>1000: 8% (11)

FF (147):
VL>1000: 50% (74)

HAART for lifelong
256 women

HAART for lifelong
Viral load at 7 months:
VL>1000 copies/ml: 9% (24)

BF (97):
VL>1000: 5% (5)

FF (168):
VL>1000: 30% (19)
AMATA: HIV DRUG RESISTANCE

Inclusion population 562 women

HAART for PMTCT
282 women

HAART for PMTCT
(46/86) seq. available
13% drug resist. mutations
(NNRTI)

BF (5/11):
2/5 with mutations

FF 41/75):
4/41 with mutations

HAART for lifelong
256 women

HAART for lifelong
(15/24). seq available
40% drug resist. mutations
66% dual class resistance

BF (3/5):
0/3 with mutations

FF (12/19):
6/12 with mutations
# HIV-1 Drug Resistance Mutations

<table>
<thead>
<tr>
<th>HAART for PMTCT</th>
<th>HAART for Lifelong</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM-G-M140</td>
<td>K103N</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>AM-G-M192</td>
<td>K103N</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>AM-K-M071</td>
<td>K103N, K219R</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>AM-M-M038</td>
<td>K103N</td>
<td>AZT+NVP</td>
</tr>
<tr>
<td>AM-M-M161</td>
<td>K103N, V106I, Y181I</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>AM-R-M002</td>
<td>K103N</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>AM-M-M141</td>
<td>A98G, K103N, M184V, P225H</td>
<td>AZT+3TC+EFV</td>
</tr>
<tr>
<td>AM-K-M064</td>
<td>V118I, M184V</td>
<td>AZT+3TC+NVP</td>
</tr>
<tr>
<td>AM-M-M076</td>
<td>T69N, K103N</td>
<td>AZT+3TC+NVP</td>
</tr>
<tr>
<td>AM-M-M151</td>
<td>E44D, K70R, V106I, V179I</td>
<td>AZT+3TC+NVP</td>
</tr>
<tr>
<td>AM-M-M119</td>
<td>Y181C, K103N</td>
<td>AZT+3TC+NVP</td>
</tr>
<tr>
<td>AM-M-M182</td>
<td>K103N, M184V</td>
<td>D4T+3TC+NVP</td>
</tr>
</tbody>
</table>
Conclusions (1)

- Maternal HAART was effective in preventing post-partum HIV mother-to-child transmission

- Breastfeeding when combined with maternal HAART was associated with a minimal risk of post-partum transmission

- Only 8% of women had viral load >1000 copies/ml after 10 months of PMTCT with HAART.
Maternal HAART for PMTCT minimized acquired drug resistance in pregnant women.

- All women receiving HAART for PMTCT showed low frequency of NNRTI mutations (13% of K103N) and absence of resistance to 3TC (M184V mutation)
- However, M184V mutations may have been underestimated because genotyping was performed 7 months after the end of HAART in the FF group
- Analysis of these samples by ultra-deep sequencing is ongoing
- Our data are consistent with few reported studies who reported 16% (Durant et al, AIDS 2007) or 13% (Lyons et al, AIDS 2005) drug resistance mutations after HAART for PMTCT.
Réduction de la transmission du VIH-1 par le lait maternel en donnant une prophylaxie à la mère allaitante comparée à l’allaitement artificiel

THANK YOU to the Rwandese mothers
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Thank you for your attention