DEBATE: HAART should be used for PMTCT in all pregnant women

The Pro side

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DEBATE: HAART should be used for PMTCT in all pregnant women

Universal antiretroviral therapy (ART)

Eliminating pediatric infections and saving lives
OUTLINE OF THE PRESENTATION

- Context

- Maternal universal ART prevents almost all pediatric HIV infections

- Maternal universal ART saves children lives

- Maternal universal ART saves mothers lives

- The road to B+
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2009-2010 WHO guidelines say it all!
Guiding principles

- Women (including pregnant women) in need of ARVs for their own health should get life-long ART

- **Antenatal CD4 is critical for decision-making about ART eligibility**

- Interventions should aim to maximize reduction of vertical transmission, minimize side effects for mothers and infants, and preserve future HIV treatment options

- Effective postpartum ARV-based interventions for all women will allow safer breastfeeding practices

- **Simple, unifying principles** needed for different country settings
Antiretroviral therapy (ART)

- Women with CD4 ≤350 regardless of clinical stage
- Women with clinical stage 3 or 4 (symptomatic) regardless of CD4
- Start ART as soon as feasible regardless of gestational age

Strong recommendation
Antiretroviral therapy (ART)

- Women with CD4 ≤350 regardless of clinical stage
- Women with clinical stage 3 or 4
- Start ART as soon as feasible regardless of gestational age

Strong recommendation

NO VOTE PLEASE!
ARV prophylaxis to prevent MTCT

For women not eligible for ART or unknown eligibility

• Beginning as early as 14 weeks of gestation (2\textsuperscript{nd} trimester) or as soon as possible thereafter

Strong recommendation
## Two prophylactic options

<table>
<thead>
<tr>
<th>Option A</th>
<th>Option B = Triple ARV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mother</strong></td>
<td><strong>Mother</strong></td>
</tr>
<tr>
<td>- Antepartum AZT (from 14 weeks)</td>
<td>- <strong>Triple ARV</strong> (<em>from 14 wks until 1 wk after all exposure to breast milk has ended</em>)</td>
</tr>
<tr>
<td>- sd-NVP at onset of labour*</td>
<td>- AZT + 3TC + LPV-r</td>
</tr>
<tr>
<td>- AZT + 3TC during labour &amp; delivery*</td>
<td>- AZT + 3TC + ABC</td>
</tr>
<tr>
<td>- AZT + 3TC for 7 days postpartum*</td>
<td>- AZT + 3TC + EFV</td>
</tr>
<tr>
<td></td>
<td>- TDF + XTC + EFV</td>
</tr>
<tr>
<td><strong>Infant</strong></td>
<td><strong>Infant</strong></td>
</tr>
<tr>
<td><strong>Breastfeeding population</strong></td>
<td><strong>Breastfeeding population</strong></td>
</tr>
<tr>
<td>- Daily NVP (from birth until one wk after all exposure to breast milk had ended)</td>
<td>- Daily NVP from birth to 6 weeks</td>
</tr>
<tr>
<td><strong>Non-breastfeeding population</strong></td>
<td><strong>Non-breastfeeding population</strong></td>
</tr>
<tr>
<td>- AZT for 6 weeks OR</td>
<td>- AZT for 6 weeks OR</td>
</tr>
<tr>
<td>- NVP for 6 weeks</td>
<td>- NVP for 6 weeks</td>
</tr>
</tbody>
</table>
Maternal Universal ART

Maternal ART + Maternal triple ARV prophylaxis
OUTLINE OF THE PRESENTATION

▪ Context

▪ Maternal universal ART prevents almost all pediatric HIV infections (Overall transmission rate < 5%)

▪ Maternal universal ART saves children lives

▪ Maternal universal ART saves mothers lives

▪ The road to B+
The best available triple ARV prophylactic regimens prevent most cases of MTCT in African populations

<table>
<thead>
<tr>
<th>Trial (Publication)</th>
<th>ARV regimen</th>
<th>Time of measurement</th>
<th>Transmission rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mma Bana Bostwana NEJM 2010</td>
<td>3 NRTI ZDV + 3TC + ABC vs ZDV + 3TC + LP/r &gt; 200 CD4</td>
<td>M6</td>
<td>2.1%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.4%</td>
</tr>
<tr>
<td>Kesho Bora Burkina Faso, Kenya, SA Lancet Infect Dis 2011</td>
<td>ZDV + 3TC + LP/r 200 – 500 CD4</td>
<td>M6</td>
<td>4.9%</td>
</tr>
<tr>
<td>KiBS Kenya PLOS Med 2011</td>
<td>ZDV + 3TC + NVP or NFV 350 – 500 CD4 ≥ 500 CD4</td>
<td>M6</td>
<td>3.8%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3.3%</td>
</tr>
</tbody>
</table>
PROMISE NIH: Sequential Randomized 2x2 Factorial Trial

Women with CD4 >350

AP 28-term

WHO - B

HAART

HAART

AZT

AZT + SD NVP + 7d TRV

WHO - A

Maternal AZT + SD NVP + 7d TRV

Late presenters

Antepartum

No ARV

IP

Infant uninfected at birth

Infant daily NVP

Infant

(if uninfected and <12 mos old at time of weaning)

Infant Health

Postpartum

Infant daily NVP

Infant SD NVP + AZT x1 wk

HAART

Mother

HAART

Infant SD NVP + AZT x1 wk

Infant uninfected at birth

Maternal Health

Continue HAART

Stop All ARVs

Continued HAART

CTX to 18 months

No CTX

Presented at the 3rd HIV Pediatrics Workshop, 15 - 16 July 2011, Rome, Italy
PRESENTED AT THE 3RD HIV PEDIATRICS WORKSHOP, 15 - 16 JULY 2011, ROME, ITALY

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Findings:

35.2% of infected children died <1 year and 52.7% by the age of 2.

Maternal death was the strongest predictor of death among infected children.

aOR: 2.0 (95% CI: 1.3 – 3.1)
Orphanhood remains a risk factor for infant and child death in the HAART era even if children are on treatment themselves
OUTLINE OF THE PRESENTATION

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Mortality among HIV-positive postpartum women with high CD4 cell counts in Zimbabwe

John W. Hargrove\textsuperscript{a}, Jean H. Humphrey\textsuperscript{b,c},
for the ZVITAMBO Study Group

\textbf{Fig. 1.} Hazard ratios for mortality between delivery and 24 months postpartum among HIV-positive compared with HIV-negative mothers according to CD4 cell count soon after delivery. Hazard ratios are taken from Cox models.
HPTN* 052

- Myron Cohen et al: Randomised study to evaluate HAART in preventing sexual transmission in sero-discordant couples
- 1,800 couples (3,600 individuals)
- CD4 = 350-550 cells/mm$^3$
- One partner HIV+, the other HIV-

* HPTN: Health Prevention and Treatment Network
HPTN 052 – Intermediate results
12 May 2011 (and Monday July 18)

1. Transmissions: 1 vs 27 cases (96% reduction) after >2 years of follow-up

1. Extra-pulmonary tuberculosis: 3 vs 17 cases
2. Severe morbidity and mortality: 40 vs 65 events (41% reduction)

« HPTN 052 provides compelling evidence for a new HIV prevention approach that links prevention and care efforts »
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- Maternal universal ART as per WHO-B will save mothers lives in the short-term, but …

- The road to B+
... but Kesho-Bora - Vienna, July 2011
Rates of Progression to Stage 3 or CD4<350
Women with CD4>=350 at entry

Rate of progression from delivery

<table>
<thead>
<tr>
<th>Time since delivery (weeks)</th>
<th>Proportion not progressed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-ARV</td>
<td>(182) 12.0%</td>
</tr>
<tr>
<td>Tripe-ARV</td>
<td>(151) 15.7%</td>
</tr>
<tr>
<td></td>
<td>(129) 24.1%</td>
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</tbody>
</table>

P=0.002

Rate of progression from stopping ARV-prophylaxis

<table>
<thead>
<tr>
<th>Time since end of ARV-prophylaxis (weeks)</th>
<th>Proportion not progressed</th>
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<tr>
<td>Short-ARV</td>
<td>(168) 3.7%</td>
</tr>
<tr>
<td>Tripe-ARV</td>
<td>(152) 8.2%</td>
</tr>
<tr>
<td></td>
<td>(98) 9.5%</td>
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P=0.013

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Prevention of mother-to-child transmission of HIV and the health-related Millennium Development Goals: time for a public health approach

Erik J Schouten, Andreas Jahn, Dalitso Midiani, Simon D Makombe, Austin Mnthambala, Zengani Chirwa, Anthony D Harries, Joep J van Oosterhout, Tarek Meguid, Anne Ben-Smith, Rony Zachariah, Lutgarde Lynen, Maria Zolfo, Wim Van Damme, Charles F Gilks, Rifat Atun, Mary Shawa, Frank Chimbwandira


courtesy of Tony Harries (CROI 2011, Boston)

Presented at the 3rd HIV Pediatrics Workshop, 15 - 16 July 2011, Rome, Italy
Malawi Policy 2011

TDF + 3TC + EFV

to all HIV-infected pregnant women

for life

regardless of CD4 count

↓

“BORN HIV FREE”

Presented at the 3rd HIV Pediatrics Workshop, 15 - 16 July 2011, Rome, Italy
Malawi’s New PMTCT Policy

Advantages

• Simple to implement
• Minimizes vertical transmission
• Protects for the next pregnancy
• Improves maternal health and survival
• Reduces sexual transmission
• Reduces risk of tuberculosis
• Treats hepatitis B co-infection
Malawi’s New PMTCT Policy

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Careful monitoring of acceptability, feasibility, outcomes and safety
WHO Regimen B is now chosen by 20 + 4 = 24 African countries
Regimen B+ is no longer a theoretical option

<table>
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<th>Number of countries (list)</th>
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<tr>
<td>A</td>
<td>15</td>
</tr>
<tr>
<td>B</td>
<td>Angola, Benin, Botswana, Burundi, Chad, Comoros, Congo, Côte d’Ivoire, Erythrea, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea Bissau, Madagascar, Mali, Rwanda, Senegal, Seychelle, Togo</td>
</tr>
<tr>
<td>B+</td>
<td>Malawi South Africa?</td>
</tr>
<tr>
<td>A and B</td>
<td>Guinea, Niger, Nigeria, Sierra Leone</td>
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# Conclusion

Many benefits to move from universal maternal ART as per WHO - B to the B+ approach

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<th>Maternal triple ARV prophylaxis (option B)</th>
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<td>• Low rate of adverse events in infants.</td>
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<td>• May be easier to implement: both eligible and ineligible women receiving the same triple ARV regimen (note: NVP-containing regimens should not be used for women with CD4 &gt;350 cells/mm³).</td>
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<td>• No change in regimen between antepartum and postpartum periods.</td>
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Conclusion
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Maternal triple ARV prophylaxis (option B)

- Significant reduction of the MTCT risk.
- Low rate of adverse events in infants.
- May be easier to implement: both eligible and ineligible women receiving the same triple ARV regimen (note: NVP-containing regimens should not be used for women with CD4 >350 cells/mm$^3$).
- No change in regimen between antepartum and postpartum periods.
- Strategy may improve maternal health during the period woman is receiving the regimen.

+++
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<td>And beyond</td>
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Acknowledgements

Abidjan: Didier Koumavi Ekouevi, Patrick Coffié
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Universal Antiretroviral Therapy for Pregnant and Breast-Feeding HIV-1–Infected Women: Towards the Elimination of Mother-to-Child Transmission of HIV-1 in Resource-Limited Settings

Renaud Becquet,12 Didier K. Ekouevi,12 Elise Arrive,12 Jeffrey S. A. Stringer,9 Nicolas Meda,10 Marie-Laure Chaix,14 Jean-Marc Treluyer,35 Valérie Leroy,12 Christine Rouzioux,34 Stéphane Blanche,35 and François Dabis12