Challenges in Prevention of Mother to Child HIV Transmission

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Goal:
“Eliminate pediatric HIV infection”

but also

“Maximize HIV-free survival of infant”

And

“Maximize maternal health”

Sometimes Means of Achieving these Goals may be at Odds with Each Other (eg, early weaning and infant survival, stopping prolonged maternal HAART and mom health)
Don’t Forget Contraception as the Most Effective Intervention to Prevent MTCT And Prevention of HIV in Women
Four-Phase Strategy for Prevention of Mother to Child HIV Transmission

Wilcher R et al. Sex Trans Inf 2008;84 (Suppl2):ii54-60
Efficacy of PMTCT Programs is Related to More than Just the PMTCT Regimen Used

- To provide PMTCT, need to identify HIV-infected women during pregnancy.
  - In 2007, only 18% of pregnant women received HIV testing in RLC.

- Regardless of what PMTCT intervention, must get it to & accepted by the woman.
  - In 2007, only 33% of HIV-infected pregnant women received ARV for PMTCT in RLC.

Program efficacy is as much related to the PMTCT cascade as the specific PMTCT regimen
PMTCT Cascade: Most Critical Thing for PMTCT is Number of Women Completing Cascade

P. Barker, WHO Mtg Nov 2008

100 HIV+ mothers

- Attend ANC clinic 92%
- Counseled and tested for HIV, CD4 75%
- Get ARVs (pre-and perinatal) 50%
- Overall Program Effectiveness (early MTCT)
  - sdNVP: 19.5% tx
  - AZT/sdNVP: 17.5% tx
  - HAART: 17.1% tx

CD4 >200 / CD4 <200
sdNVP / HAART (8% MTCT): 3 infected
AZT+sdNVP/ HAART (3% MTCT): 1 infected
HAART all (2% MTCT): 0.6 infected

No ARV (25% MTCT): 16.5 infected
PMTCT Cascade: Most Critical Thing for PMTCT is Number of Women Completing Cascade

P. Barker, WHO Mtg Nov 2008

100 HIV+ mothers

Change cascade efficiency

Attend ANC clinic 95%
Counseled and tested for HIV, CD4 95%
Get ARVs (pre-and perinatal) 95%

Enter into program

Missed - no PMTCT

Overall Program Effectiveness (early MTCT)

sdNVP: 10.4% tx
AZT/sdNVP: 6.1% tx
HAART: 5.2% tx

CD4 >200 / CD4 <200
sdNVP / HAART (8% MTCT): 6.9 infected
AZT+sdNVP/ HAART (3% MTCT): 2.6 infected
HAART all (2% MTCT): 1.7 infected

No ARV (25% MTCT): 3.5 infected
To Maximize Effectiveness
Need to Prevent *In Utero* Transmission

Interventions Need to Start During Pregnancy – so Need **Early Identification** For **Early Intervention**

“Residual Transmission”: Even if Prevent All IP and PP Transmission, When Start ARV at 28 Weeks:

1-2% *In Utero* Infection
For Maximal Efficacy of Any Regimen, Need to Start Early in Pregnancy to Prevent *In Utero* Transmission


Even if intervention is 100% effective for IP/PP transmission, still have “residual infection” of 1.6% starting at 28 weeks.
A Key Issue:
ARV **Treatment** vs ARV **Prophylaxis**

What Should CD4 Threshold for ARV **Treatment** be in Pregnancy?

(Treatment = HAART Started in Pregnancy and **Continued** “Life-Long” Even After No Further MTCT Risk Exists)
Why CD4 Threshold of <350 for Treatment?
Includes Most Maternal Deaths and Postnatal Infections
ZEBS Study – L. Kuhn personal communication 2009

CD4 < 200: 55% of maternal deaths, 47% of postnatal infections
If assume all pregnant women with CD4 <350 should be initiated on antiretroviral treatment for life then remaining research questions revolve around what is optimal intervention used solely for PMTCT for women with CD4 >350?
IF ASSUME TREATMENT FOR ALL WITH PREGNANT WOMEN WITH CD4 <350

For Women with CD4 >350
Antepartum/Intrapartum PMTCT

AZT/sdNVP + “tail”
vs
Maternal HAART

May Have Comparative Efficacy in Women with Higher CD4 Counts
AZT + sdNVP results in MTCT Rates of 1% in Women with CD4 >200, Thailand


Comparing Difference in Transmission Rates Between AZT/Placebo-Placebo and AZT/NVP-NVP by CD4

AZT + sdNVP results in MTCT Rates of 1% in Women with CD4 >200, Thailand


Comparing Difference in Transmission Rates Between AZT/Placebo-Placebo and AZT/NVP-NVP by CD4
HIV+ pregnant women with CD4>200 are given AZT from 28 weeks through labor, and sdNVP at onset of labor.

Women with CD4 ≤200 are given HAART.

PMTCT uptake stood at 90% in 2007.

Most women formula feed.

PMTCT program data analyzed from October 2006- November 2007 on records of HIV test results of 10,516 children born to HIV-infected women from all health districts.
MTCT at Age 6 Weeks by ARV Regimen
Tlale J et al. IAS Mexico City Aug 2008 (Abs ThAC04)

Most Women Formula Feed Their Infants

- HAART pre-preg: 0.7%
- HAART during preg: 2.3%
- AZT >4 wk + sdNVP: 3.3%
- AZT >4 wk alone: 3.1%
- AZT <4 wk + sdNVP: 4.7%
- AZT <4 wk alone: 5.5%
- sdNVP: 7.0%
- No ART: 12.3%
MTCT at Age 6 Weeks by ARV Regimen
Tlale J et al.  IAS Mexico City Aug 2008 (Abs ThAC04)

HAART most effective if started prior to pregnancy in women with low CD4

0%  5%  10%  15%

HAART pre-preg     HAART during preg

AZT >4 wk sdNVP   AZT <4 wk sdNVP
0.7%  2.3%  3.3%  3.1%  4.7%  5.5%  7.0%  12.3%  No ART
MTCT at Age 6 Weeks by ARV Regimen
Tlale J et al.  IAS Mexico City Aug 2008 (Abs ThAC04)

Starting HAART during pregnancy if CD4 <200 and AZT+sdNVP if CD4 >200 results in similar MTCT rates (CI likely overlap)
MTCT at Age 6 Weeks by ARV Regimen
Tlale J et al. IAS Mexico City Aug 2008 (Abs ThAC04)

Longer AP duration is more effective than shorter (<4 wks) AP drug

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Pre-preg</th>
<th>During preg</th>
<th>&gt;4 wk AZT</th>
<th>&gt;4 wk AZT +sdNVP</th>
<th>&lt;4 wk AZT</th>
<th>&lt;4 wk AZT +sdNVP</th>
<th>sdNVP</th>
<th>No ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAART</td>
<td>0.7%</td>
<td>2.3%</td>
<td>3.3%</td>
<td>3.1%</td>
<td>4.7%</td>
<td>5.5%</td>
<td>7.0%</td>
<td>12.3%</td>
</tr>
<tr>
<td>No ART</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
sdNVP reduces MTCT by 43% implemented in a National Program
### Mother to Child Transmission, 2000-2006, 5,930 Births to HIV+ Women, UK/Ireland


<table>
<thead>
<tr>
<th>Prophylaxis</th>
<th>MTCT</th>
<th>Adjusted Odds Ratio (for mode delivery, sex, viral load)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>1.2%</td>
<td></td>
</tr>
<tr>
<td>ART &gt;14 days</td>
<td>0.8%</td>
<td></td>
</tr>
<tr>
<td>HAART with NNRTI</td>
<td>0.9%</td>
<td>1.31 (0.6-2.8) p=0.48</td>
</tr>
<tr>
<td>HAART with PI</td>
<td>1.1%</td>
<td></td>
</tr>
<tr>
<td>HAART at conception</td>
<td>0.1%</td>
<td>0.18 (.02-1.3) p=0.09</td>
</tr>
<tr>
<td>HAART during pregnancy</td>
<td>1.3%</td>
<td></td>
</tr>
<tr>
<td>HAART Elective CS</td>
<td>0.7%</td>
<td></td>
</tr>
<tr>
<td>HAART Planned vaginal</td>
<td>0.7%</td>
<td>p=0.15</td>
</tr>
<tr>
<td>AZT Elective CS (N=464)</td>
<td>0%</td>
<td></td>
</tr>
</tbody>
</table>

*Note: ART = Antiretroviral Therapy, HAART = Highly Active Antiretroviral Therapy, NNRTI = Non-Nucleoside Reverse Transcriptase Inhibitors, PI = Protease Inhibitors, AZT = zidovudine, CS = Caesarean Section.*
In Breastfeeding Settings, ~40% of All Mother to Child Transmission Can be Attributed to Breastfeeding

10-15% of Infants with Prolonged Breastfeeding Become Infected
Prevention of Breast Milk HIV Transmission

- Hypothesized that “safer” breastfeeding, through giving antiretroviral prophylaxis during period when breast milk is most beneficial, with early weaning might reduce postnatal transmission.

- Ongoing studies are evaluating the safety and efficacy of:
  - Infant antiretroviral prophylaxis + early weaning
  - Maternal HAART during lactation + early weaning.

- However, increasing data indicate early cessation of breastfeeding at 6 months is not safe in some poor countries.
Potential Problems with Universal HAART Solely for PMTCT in Developing Countries

- **Complexity** – implementation issues; postnatal adherence issues (= resistance risk).

- **Limited resources and cost** – can’t provide ART even to patients who need for own health.

- **Limited regimen choice**, limited by toxicity with NVP with CD4 >250 cells/uL; EFV teratogenicity; PI expense.

- **Pregnancy outcome/long-term infant outcome**

- **Maternal health** (issues of start-stop HAART).

- **Differential penetration of ARV drugs into milk** could result in resistant virus in milk.
If Choose to Use HAART
In Women with CD4 >350 for PMTCT:

Drug choice problematic:

- NVP toxicity
- EFV okay 3\textsuperscript{rd} trimester but PP repeat pregnancy risk if prolonged?
- PI cost
NVP Liver Toxicity More Common in Pregnant than Non-Pregnant Thai Women and Women Receiving ART for PMTCT than for Treatment

*Phanuaphak N et al. HIV Med 2007;8:357-66*

<table>
<thead>
<tr>
<th></th>
<th>Non-Preg (N=87)</th>
<th>Preg (N=244)</th>
<th>P value</th>
<th>ART for RX (N=102)</th>
<th>ART for PMTCT (N=142)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median CD4</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>152</td>
<td>277</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sx hepatitis</strong></td>
<td>1.5</td>
<td>7.5</td>
<td>0.02</td>
<td>2.5</td>
<td>16.0</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Rash+liver</strong></td>
<td>0.8</td>
<td>4.3</td>
<td>0.05</td>
<td>0.8</td>
<td>10.2</td>
<td>0.0003</td>
</tr>
<tr>
<td><strong>Gr 1/2 liver</strong></td>
<td>0.8</td>
<td>4.8</td>
<td>0.04</td>
<td>0.8</td>
<td>5.8</td>
<td>0.02</td>
</tr>
<tr>
<td><strong>Gr 3/4 Rash</strong></td>
<td>5.5</td>
<td>5.8</td>
<td>0.42</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>
First Trimester Efavirenz Use and Central Nervous System Defects

- Antiretroviral Pregnancy Registry prospective data do not indicate an increase in overall birth defects (10/364, overall 2.7%, 95% CI 1.3-5.0%).

- However, with *in utero* exposure in primates at doses resulting in drug levels similar to human exposure, 3/20 infant monkeys had severe central nervous system (CNS) defects (e.g., anencephaly, anophthalmia, cleft palate).

- 5 retrospective and 1 prospective human cases of CNS defects (e.g., meningomyelocele) with first trimester efavirenz exposure.

- FDA Class D (+ animal & potential human risk).
### Maternal Antenatal HAART and Pregnancy Outcome

<table>
<thead>
<tr>
<th>Published data</th>
<th>Low Birth Weight</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HAART pre-conception</td>
<td>HAART start during Pregnancy</td>
<td></td>
</tr>
<tr>
<td>Machado Sex Tx Dis 2008 (Brazil) N=696</td>
<td>33.3%</td>
<td>16.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ekouevi AIDS 2008 (Cote d’Ivoire) N=326</td>
<td>12.4%</td>
<td>22.3%</td>
<td></td>
</tr>
</tbody>
</table>

**Ekouevi AIDS 2008 (Cote d’Ivoire) N=326**: Low birth weight compared to HAART pre-conception and start during pregnancy, with a statistically significant difference (p=0.02).
Mitochondrial Dysfunction in Infants and In Utero ARV Exposure

- *In utero* ARV exposure has been reported to be associated with:
  - Mostly aSx transient neonatal lactic acid elevations in 50-95% (some transient neuro sx)
  - Mild, clinically aSx but persistent hematologic abnormalities
  - Rarely with clinically Sx of mitochondrial dysfunction – primarily neurologic Sx

- Combination ARV exposure may be associated with greater risk than single drug exposure.
# Antiretroviral Drug Penetration into Human Breast Milk

## Maternal Plasma/Breast Milk Ratio

<table>
<thead>
<tr>
<th>Category</th>
<th>Drug</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRTI</td>
<td>AZT</td>
<td>0.44-1.86</td>
</tr>
<tr>
<td></td>
<td>3TC</td>
<td>1.8-5.57</td>
</tr>
<tr>
<td></td>
<td>TDF</td>
<td>Low levels (non-bioavailable form - TFV, not TDF?)</td>
</tr>
<tr>
<td>NNRTI</td>
<td>EFV</td>
<td>0.54</td>
</tr>
<tr>
<td></td>
<td>NVP</td>
<td>0.60-0.75</td>
</tr>
<tr>
<td>PI</td>
<td>ATV</td>
<td>0.04-0.11</td>
</tr>
<tr>
<td></td>
<td>LPV/r</td>
<td>0.11</td>
</tr>
<tr>
<td></td>
<td>NFV</td>
<td>0.06-0.24</td>
</tr>
</tbody>
</table>

Shapiro R. JID 2005;192:720 (3TC, NVP)  
Giuliano M. JAIDS 2007;44:286 (AZT, 3TC, NVP)  
Mirochnick M. AAC 2009;53:1170 (AZT, 3TC, NVP)  
Colebunders R. AIDS 2005;19:1912 (NVP, NFV, IDV)  
Schneider S. JAIDS 2008;48:450 (EFV)  
Mirochnick M. CROI 2009 Abs 940 (TDF)  
Spenser L. CROI 2009 Abs 942 (AZT, 3TC, ATV)  
Corbett A. CROI 2009 Abs 947 (AZT, 3TC, LPV/r)
Maternal Health: Are There Long-Term Consequences in Healthy Women of Receiving HAART During Pregnancy for Prophylaxis of MTCT and then Stopping HAART?
<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Interrupted ART # pt (rate 100pt-yr)</th>
<th>Continuous ART # pt (rate 100pt-yr)</th>
<th>Hazard Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline CD4</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>350-449</td>
<td>24 (3.2)</td>
<td>18 (2.2)</td>
<td>1.5</td>
</tr>
<tr>
<td>450-549</td>
<td>27 (3.7)</td>
<td>7 (0.9)</td>
<td>4.1</td>
</tr>
<tr>
<td>550-649</td>
<td>19 (3.5)</td>
<td>7 (1.3)</td>
<td>2.8</td>
</tr>
<tr>
<td>&gt;650</td>
<td>50 (3.2)</td>
<td>15 (2.0)</td>
<td>3.2</td>
</tr>
<tr>
<td><strong>Duration ART</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-&lt;3 yrs</td>
<td>23 (2.8)</td>
<td>7 (0.8)</td>
<td>1.6</td>
</tr>
<tr>
<td>3-5 yrs</td>
<td>30 (2.7)</td>
<td>8 (1.1)</td>
<td>1.5</td>
</tr>
<tr>
<td>5-&lt;7 yrs</td>
<td>27 (3.3)</td>
<td>15 (1.7)</td>
<td>1.8</td>
</tr>
<tr>
<td>&gt;7 yrs</td>
<td>40 (3.6)</td>
<td>17 (1.5)</td>
<td>2.5</td>
</tr>
<tr>
<td><strong>Hx ART baseline</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4 (2.7)</td>
<td>1 (0.5)</td>
<td>5.2</td>
</tr>
<tr>
<td>Yes</td>
<td>22 (4.4)</td>
<td>9 (1.7)</td>
<td>2.6</td>
</tr>
</tbody>
</table>
Lack of Long-Term Adverse Effects of AZT Prophylaxis in Women in PACTG 076


No significant differences between AZT and Placebo Groups (overall progression/death, p=0.28)
Among ART-naïve women entering pregnancy with a CD4 > 350 and initiating ARV for PMTCT, change in CD4 and HIV RNA were similar over the 1st year postpartum among women stopping or continuing therapy PP.

No women in either group progressed to AIDS or death during the 1st year postpartum.

However, a non-significant trend to increased risk CDC Class B events (RR 2.9, 0.6-13.4) and significant increase in activated CD8 cells (CD38+, DR+) was observed among women stopping compared to continuing ART PP.
For Women with CD4 >350
Postnatal PMTCT via Breastfeeding

Infant ARV Prophylaxis
Vs
Maternal HAART

May Have Comparative Efficacy in Women with Higher CD4 Counts
14 Week Extended ARV Prophylaxis Significantly Reduces Postnatal HIV Infection: PEPI Malawi

Maternal Antiretroviral Prophylaxis of Breast Milk HIV Transmission

- Observational suggest maternal HAART during lactation may reduce transmission.
- For women who require therapy for their own health, the benefit of HAART for maternal health outweighs potential risks.
- These women are at highest risk for postnatal transmission and HAART may reduce this risk.
- NVP toxicity not a concern in women with low CD4.
- Research needed for women with high CD4.
MITRA (Infant ARV) vs MITRA-PLUS (Maternal HAART) to Prevent Postnatal MTCT, Tanzania

*Kilewo et al. 4th IAS Sydney Australia 2007 Abs. TuAX101*

<table>
<thead>
<tr>
<th></th>
<th>MITRA (Infant ART, N=398)</th>
<th>MITRA-Plus (Maternal ART, N=440)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6 Weeks</strong></td>
<td>3.8% (2.0-5.6%)</td>
<td>4.1% (2.1-6.0%)</td>
</tr>
<tr>
<td><strong>6 Months</strong></td>
<td>4.9% (2.7-7.1%)</td>
<td>5.0% (3.2-7.0%)</td>
</tr>
<tr>
<td><strong>Increment MTCT</strong>&lt;br&gt;6 weeks-6 months</td>
<td>1.1%</td>
<td>0.9%</td>
</tr>
</tbody>
</table>

No significant difference in terms of postnatal transmission between maternal or infant prophylaxis strategies.
<table>
<thead>
<tr>
<th></th>
<th>0-7 Days</th>
<th>6 Wks</th>
<th>3 Mos</th>
<th>6 Mos</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall MTCT</td>
<td>2.4%</td>
<td>3.9%</td>
<td>4.1%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Postnatal Tx</td>
<td>+1.5%</td>
<td>+1.7%</td>
<td>+2.6%</td>
<td></td>
</tr>
<tr>
<td>By CD4 count:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 &lt;250</td>
<td>3.4%</td>
<td>4.3%</td>
<td>5.2%</td>
<td>5.2%</td>
</tr>
<tr>
<td>CD4 &gt;250</td>
<td>2.1%</td>
<td>3.8%</td>
<td>3.8%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>
For Women with CD4 >350
No Significant Difference in Postnatal MTCT: KiBS (Maternal HAART) vs PEPI (Infant ARV)
(infants uninfected at birth)

KiBS intervention

PEPI intervention

Thomas T, Fowler M, and KiBS study team, unpublished

Taha T, Kumwenda N, Hoover D, and PEPI study team, unpublished
Postpartum Prophylaxis of Breast Milk MTCT

Issue of ARV Drug Resistance in Infants:

Problem with Infant NVP Prophylaxis but also with Maternal HAART
NVP Resistance More Frequent in Infants Infected While Receiving Extended NVP but Not in Infants Infected After Extended NVP was Stopped


92%

38%

15% 15%

P=0.002

P=1.0

Infants Diagnosed with HIV *Within the First 6 Weeks of Life*

Infants Diagnosed with HIV *After Age 6 Weeks (Late BF MTCT)*
## Resistance in BF Infected Infants in KIBS (Maternal HAART Prophylaxis)

*Zeh C et al. 15th CROI, 2008, Boston, MA Abs 45aLB*

<table>
<thead>
<tr>
<th>Week Postpartum</th>
<th>N</th>
<th>Not Amplified</th>
<th>First Positive Viral (PCR) Test</th>
<th>Wk 14 + 24 Specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery</td>
<td>12</td>
<td>3</td>
<td>0/9</td>
<td>11/12</td>
</tr>
<tr>
<td>2 Wks</td>
<td>2</td>
<td>1</td>
<td>0/1</td>
<td>1/2</td>
</tr>
<tr>
<td>6 Wks</td>
<td>6</td>
<td>0</td>
<td>1/6</td>
<td>1/6</td>
</tr>
<tr>
<td>14 Wks</td>
<td>2</td>
<td>0</td>
<td>2/2</td>
<td>2/2</td>
</tr>
<tr>
<td>24 Wks</td>
<td>2</td>
<td>0</td>
<td>1/2</td>
<td>1/2</td>
</tr>
<tr>
<td>36 - 72 Wks</td>
<td>5</td>
<td>1</td>
<td>0/4</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>29</td>
<td>10</td>
<td><strong>3/19 (16%)</strong></td>
<td><strong>16/24 (67%)</strong></td>
</tr>
</tbody>
</table>

Resistance not seen on first viral test but rather appears to have emerged during breastfeeding period.
Summary: Breastfeeding and HIV Transmission

- ARV prophylaxis of infant or the mother during breastfeeding will likely both reduce postnatal MTCT, possibly to a similar extent.
- Infants who become infected in both scenarios are likely to have resistant virus.
- Women who require treatment should receive HAART, which will likely decrease PP MTCT.
- However, the risks and benefits of infant vs maternal prophylaxis need to be compared for women with higher CD4.
- Longer interventions to permit safe prolonged breastfeeding need to be assessed.
PROMISE
Promoting Maternal Infant Survival Everywhere
PROMISE General Overview: Sequential Randomized 2x2 Factorial Trial

Women with CD4 >350

AP 28-term

IP

PP for Duration BF

HAART

Infant uninfected at birth

Mother

HAART

Stop All ARVs

Continue HAART

Infant daily NVP

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

Maternal Health

After Weaning

Antepartum

Postpartum

Infant Health

HAART

AZT + SD NVP + 7d TRV

Maternal AZT + SD NVP + 7d TRV

No ARV

Late presenters

CTX to 18 months

No CTX

Infant uninfected at birth

Continue HAART

Stop All ARVs

Infant daily NVP

Infant (if uninfected and <12 mos old at time of weaning)
Antiretroviral Regimens in PROMISE and Renal and Bone Safety Study of TDF

Antepartum

- AZT/sdNVP (TRV 1 week tail)
- HAART AZT/3TC/LPV-r
- TRV/LPV-r

If HBsAg+

AZT/3TC/LPV-r

Postpartum

- Infant NVP
- HAART TRV/LPV-r (all regardless HBV status)

TDF Substudy:
- Dexa scans mothers and infants
- Infant growth
- Ca, P, creatinine
- Renal tubular function
- Markers of bone growth
- Inflammatory cytokines
- TDF levels in breast milk, infant
Thank You For Your Attention