IMPAACT Prevention Science Working Group:

PROMISE Update
June 14, 2016
PROMISE : Past, Present and Future

Its been a long Journey!
The Beginnings, 2009-2011

- 2009--Jerry Coovadia and Lynne Mofenson propose a comprehensive concept to address all remaining major PTMCT questions!
- 2009-2011 The PROMISE name is born over a glass of wine at the Double Tree Rockville.
  - Many meetings, Many hotels,
  - Lynne n wears out at least one computer
  - Protocol trainings par excellence per FHI
- March 2011, the first enrollment!
1077BF is Launched: 3 Components

**Antepartum**
(14 wks-term)

**Labor/ Delivery**

**Postpartum**
(for duration of BF)

**Maternal Health**
(after BF cessation)

**Maternal CD4 >350**

(Version 2.0)

<table>
<thead>
<tr>
<th>Infant NVP Prophylaxis</th>
<th>Triple ARV Prophylaxis</th>
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<tbody>
<tr>
<td>ZDV</td>
<td>ZDV + sdNVP + TRV</td>
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**Late Presenters**

- Continue Triple ARV Regimen
- Stop All ARVs

- Infant uninfected at birth
- Mother

- Mother
- Infant NVP Prophylaxis
- Triple ARV Prophylaxis
1077FF is Launched: 2 Components

**Antepartum**
(14 wks-term)

- **Labor/ Delivery**

**Maternal Health**

- **Maternal CD4 > 350**

- **Babies Formula Fed**

**Triple RV Prophylaxis**
- Randomized
- ZDV + sdNVP+

**Mothers on ART Antepartum Randomized to**

- Continue Triple ARV Regimen
- Stop All ARVs

(Version 2.0)
IMPAACT 1077BF

Designed for settings in which the standard of care for PMTCT involves maternal use of zidovudine (ZDV) or other non-triple antiretroviral (ARV) regimens during pregnancy and the standard method of infant feeding is breastfeeding.

Sites in:
- India*
- Malawi
- South Africa*
- Tanzania
- Uganda
- Zambia
- Zimbabwe

* Also FF sites
PROMISE 2011-2015

- 2011-2014 Ongoing Enrollment
- Semi Annual DSMB meetings
- NIAID Convened Ethics meeting May 2012
- HPTN 052 results IAS Vienna 2012
- 2013 WHO Harmonized Guidelines Announced
- 2014 PROMISE Enrollment Halts—
  - July Late presenters and 1077FF
  - Oct 1, Antepartum, Post partum, Mat Health
- March 2015, last PROMISE baby is born!
- June 2015, START results announced;
- PROMISE randomized data ends July, 2015
PROMISE Substudies

Hepatitis B Substudy

- 139 Hepatitis B co-infected mothers enrolled
- Estimated Hepatitis B prevalence = 3.9%

P1084s Substudy

- 400 pairs enrolled in the Postpartum Part
- 479 pairs enrolled in Antepartum Part
- Antepartum analyses presented CROI
- Postpartum analyses to be presented Durban

Other Substudies:

- Resistance
- Inflammatory Markers
- Hair ARV levels
- Adherence
- and other planned Studies
1077BA and 1077FA
Final Accrual by Country

- South Africa (5) 31%
- Malawi (2) 32%
- Zimbabwe (3) 16%
- Zambia (1) 2%
- Uganda (1) 14%
- Tanzania (1) 2%
- India (1) 3%

n = 3543 mother-infant pairs
Data and Safety Monitoring Board (DSMB) Reviews and Recommendations

- Nov 2014 interim review, DSMB reported pre-specified efficacy boundary for 1077 Antepartum Component was crossed and safety differences by arm. Disseminate

- START results announced June 2015

- Offering of ART to all women in PROMISE begins July 2015.

- Continue Safety Follow up in 1077HS thru Aug 2016; and 1077BF/FF through Sept 2016

- Nov 2015: Disseminate PROMISE Postpartum and Maternal Health
PROMISE 1077
Durban Presentations
2016 Durban Abstracts

- Pediatric International Workshop-
  - Post partum efficacy/safety results
  - 1084s Maternal DXA results
  - 1084s Growth results
  - Maternal Uptake post START Results
  - Neurodevelopmental and Growth results, Malawi and Uganda compared to controls

- IAS
  - 1077BP Post Partum Results
  - 1077HS results
  - Maternal Uptake ART post START results—HS and BF
PROMISE 1077
Publication Updates
PROMISE Publications

- **Antepartum**
  - Efficacy and Safety—submitted NEJM
  - Risk Factors for LBW and PTD—in prep
  - Risk Factors for Transmission
  - 1084s newborn growth results—presented CROI—manuscript in prep

- **Cross Cutting**
  - Hepatitis B
  - Resistance
PROMISE Publications: Primary and Secondary Objectives

- Post Partum
  - Efficacy and Safety—in prep
  - Risk Factors for Transmission
  - 1084s postnatal growth results—
  - Maternal DXA results by treatment arm
  - Infant infection—RF
  - Late Presenters

- Maternal Health
  - Efficacy and safety—in prep
  - Maternal adherence—in prep

- DACS and investigator initiated using PROMISE data and specimens
PROMISE Grants: Submitted and Planned

- Resistance – Lisa Frenkel/Susan Fiscus
- Inflammatory Markers – Risa Hoffman/Judy Currier, Adrianna Weinberg
- Hair ARV measures—Monica Gandhi
- Breast Milk antibody responses – Sallie Permar
Life after PROMISE

What’s next?
Extended Follow up of Safety at High Enrolling PROMISE Sites: PROMOTE

- PEPFAR funded
- 7 sites in Zimbabwe, S. Africa, Uganda and Malawi
- Focus on follow up of safety including
  - Repeat pregnancy outcomes
  - Safety outcomes by specific regimens
  - Maternal DXA follow up
  - Long term maternal adherence
  - Development of resistance over time
  - Child growth and Developmental Follow up
- Mentor/Mentee implementation science
Summary and Conclusions

- PROMISE has achieved many of its goals in providing important safety and efficacy
- All ART regimens appear effective as do simpler regimens
- Longer Term Follow up for Safety of ART will be important for maternal complications including resistance, child growth and development
- PK and safety of new drugs is needed in pregnancy and neonates
- Maternal lifetime adherence remains a major challenge for HIV infected mothers
PROMISE Team Acknowledgements

- All the Women and their Children who gave their time and participated in the PROMISE study
- The investigators and PROMISE staff at all the PROMISE sites
- IMPAACT Leadership
- FSTRF – Michal Basar/ FSTRF PROMISE staff
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- FHI 360—Anne Coletti, Katie McCarthy, Megan Valentine
- NIH staff – Lynne Mofenson, Devasena G, Karin Klingman, Renee Browning, George Siberry
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The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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1077HS is Launched: 1 Component

Antepartum Labor/ (14 wks-term) Delivery

Maternal Health

Maternal
CD4 > 400

Babies Formula Fed

Mothers on Triple ARVs
Antepartum as SOC
Randomized at Delivery to

Continue Triple ARV Regimen

Stop All ARVs
Conducted in settings where the standard of care for PMTCT for involves use of triple antiretroviral regimens throughout pregnancy and the standard method of infant feeding is formula feeding.

Sites in:
- Argentina
- Botswana
- Brazil
- China
- Haiti
- Peru
- Thailand
- US
Accrual into all components closed on or before 1 October 2014

- 3259 mother-infant pairs 1077BA
- 284 pairs in 1077FA
  (3543 pairs in Antepartum total)
- 204 pairs in 1077BL
- 2431 pairs in 1077BP
- 799 women in 1077BM
- 76 women in 1077FM (875 in MH total)
Thanks to everyone for all the hard work and dedication to carry out PROMISE!