State of the IMPAACT Network
June 27, 2012

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Specific Aims

1. Develop and evaluate safe, cost effective approaches to interrupt mother-to-child transmission (MTCT)

2. Evaluate treatments for HIV-infected children, adolescents, and pregnant women, including treatment and prevention of co-infections and co-morbidities

3. Evaluate vaccines for prevention of MTCT and sexual transmission among adolescents, and for therapeutic use
Primary Isoniazid Prophylaxis against Tuberculosis in HIV-Exposed Children

Shabir A. Madhi, M.D., Ph.D., Sharon Nachman, M.D., Avy Violari, M.D., Soyeon Kim, Sc.D., Mark F. Cotton, M.D., Ph.D., Raziya Bobat, M.D., Patrick Jean-Philippe, M.D., George McSherry, M.D., and Charles Mitchell, M.D., for the P1041 Study Team
P1041 Results

Results showed that primary isoniazid prophylaxis did not improve TB-disease–free survival among HIV-infected (TB or death 19.0% in INH group vs. 19.3% in placebo group; P=0.93) or among HIV-uninfected children (TB or death 10% in INH group vs. 11% in placebo group; P=0.44).

Study suggests that targeted programmatic improvement will be more important than a blanket policy of giving isoniazid to all HIV-exposed infants.
Efficacy and safety of an extended nevirapine regimen in infant children of breastfeeding mothers with HIV-1 infection for prevention of postnatal HIV-1 transmission (HPTN 046): a randomised, double-blind, placebo-controlled trial

Hoosen M Coovadia, Elizabeth R Brown, Mary Glenn Fowler, Tsungai Chipato, Dhayendre Moodley, Karim Manji, Philippa Musoke, Lynda Stranix-Chibanda, Vani Chetty, Wafaie Fawzi, Clemensia Nakabiito, Lindiwe Msweli, Roderick Kisenge, Laura Guay, Anthony Mwatha, Diana J Lynn, Susan H Eshleman, Paul Richardson, Kathleen George, Philip Andrew, Lynne M Mofenson, Sheryl Zwierski, Yvonne Maldonado, for the HPTN 046 protocol team
"Nevirapine prophylaxis can be safely used to provide protection from mother-to-child transmission of HIV-1 via breastfeeding for infants up to 6 months of age."

See Articles page 211
Results showed that extending daily infant NVP from 6 weeks to 6 months lowered the risk of transmission through breastfeeding at age 6 months (1.1% vs. 2.4% (p=0.048). The difference in transmission was most significant in mothers whose CD4 cell count was >350 mm$^3$ and not on HAART (0.7% vs. 2.8%, p=0.014). There was no significant difference between the arms in terms of deaths, or serious adverse events.
Three Postpartum Antiretroviral Regimens to Prevent Intrapartum HIV Infection

Karin Nielsen-Saines, M.D., D. Heather Watts, M.D., Valdilea G. Veloso, M.D., Yvonne J. Bryson, M.D., Esau C. Joao, M.D., Jose Henrique Pilotto, M.D., Glenda Gray, M.D., Gerhard Theron, M.D., Breno Santos, M.D., Rosana Fonseca, M.D., Regis Kreitchmann, M.D., Jorge Pinto, M.D., Marisa M. Mussi-Pinhata, M.D., Mariana Ceriotto, M.D., Daisy Machado, M.D., James Bethel, Ph.D., Marisa G. Morgado, Ph.D., Ruth Dickover, Ph.D., Margaret Camarca, M.P.H., Mark Mirochnick, M.D., George Siberry, M.D., Beatriz Grinsztejn, M.D., Ronaldo I. Moreira, M.Sc., Francisco I. Bastos, Ph.D., Jiahong Xu, M.P.H., Jack Meye, M.D., and Lynne M. Mofenson, M.D., for the NICHD HPTN 040/PACTG 1043 Protocol Team*
HPTN 040/P1043 Results

• Results showed that neonatal post-exposure prophylaxis with a 2 or 3 ARV drug regimen is superior to ZDV alone for the prevention of intrapartum transmission among infants born to women not receiving ARVs before labor.

• Of 1684 evaluable infants, the intrapartum transmission rates were 4.8% (ZDV alone arm); 2.2% (ZDV+NVP arm), p=0.045; and 2.4% (ZDV/NFV/3TC arm), p= 0.046).
Nevirapine versus Ritonavir-Boosted Lopinavir for HIV-Infected Children

P1060 Results

• Cohort 1 showed that LPV/r is superior to NVP in reducing viral load in sdNVP–exposed infants (N=164) (NEJM Oct 2010) and changes in WHO Pediatric Treatment Guidelines.

• Among 288 infants in Cohort 2 with no NVP exposure, the 24 week primary endpoint difference in virologic failure was 21.5% (p<0.001) in favor of LPV/r. Time to a protocol defined toxicity endpoint was shorter in the NVP group (P=0.04), as was the time to death (P=0.06).
P1066 evaluated safety, PK, and effectiveness of both the raltegravir tablet and a new chewable formulation for the 2 to <12 year age group

- Results provided the data for the recent FDA approval of the integrase inhibitor raltegravir (RAL) for children ages 2 to 18 yrs of age.
- The availability of this drug in a palatable, child-friendly formulation will likely transform the treatment landscape for young children.
PROMISE P1077

• All components of IMPAACT’s highest priority and largest protocol, P1077 PROMISE “Promoting Maternal and Infant Survival Everywhere” are now enrolling.
IMPAAACT 1077HS Cumulative Accrual by Country

through 31 May 2012

Cumulative Total
n = 659 women

Targeted Total
n = 2000 women

Argentina
Botswana
Brazil
China
Haiti
Peru
Thailand
USA
IMPAACT 1077BF Cumulative Accrual by Country
through 31 May 2012

Cumulative Total (all sites)
n = 1244 mother-infant pairs

Targeted Total
n = 5900 mother-infant pairs
All IMPAACT Sites

Number of Subjects on Interventional Studies
By Month From June 2011 through May 2012
The network has 28 protocols open to enrollment, 7 protocols closed to accrual and 20 protocols in development.

Eight new interventional protocols are planned to open by December 1, 2012 (P1049, P1082, P1109, P1104s, P1098, P1078, P1081 and P1091) requiring a total of 2,579 participants to be enrolled.
Priorities of Future Peds/Maternal Health Network

- Prevention of HIV acquisition
- Vaccines of high priority to these populations
- PK, safety of new drugs and formulations
- Co-infections, co-morbidities, and ART consequences
- Cure and/or functional cure
IMPAACT’s Scientific Committee Structure

Scientific Oversight Committee (SOC)

- HIV Prevention (Adolescent PREP, PMTCT)
  - P. Flynn
  - B. Chi

- HIV Treatment (PK, Safety, Formulations)
  - E. Abrams

- HIV/ARV Complications, Treatment of Co-infections and Co-morbidities
  - M. Levin

- Vaccines: Preventive and Therapeutic
  - C. Cunningham

- HIV Cure
  - D. Persaud

- Tuberculosis
  - A. Hesseling

- Hepatitis (HBV, HCV)
  - A. Kovacs
Purpose of Meeting

- Review recent findings and new potential interventions relevant to the IMPAACT scientific agenda
- Review, update, prioritize, and obtain input and feedback on the scientific agenda and Network operational/financial issues
- Provide a venue for training sessions, protocol team meetings, and joint HPTN/IMPAACT projects/protocol meetings
IMPAACT now needs to plan for the structure and scope of the scientific agenda for the future with an eye towards building an infectious disease center network centered around HIV.