Kesho Bora Study

(A Better Future: Swahili)

May 2004

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Rationale

- Efficacy of MTCT prevention interventions in developing countries needs to be improved
- Health of HIV-infected mothers needs more attention
- Alternatives to replacement feeding for children born to HIV-infected mothers need to be identified

→ HAART during pregnancy and breastfeeding may achieve all 3 purposes

Goal

- To optimize the use of ARV drugs during the antepartum, intrapartum and postpartum periods to prevent MTCT of HIV and preserve the health of the mother in settings where the majority of HIV-positive women breastfeed

General Outline - Mothers

- Intervention according to disease status in late pregnancy (32-34 weeks)
  - CD4 count < 200 or HIV Stage 4 (prospective cohort)
    - ZDV+3TC+NVP during pregnancy, delivery and continued as long as required, potentially lifelong
  - CD4 count > 500 (prospective cohort)
    - ZDV from 34-36 wks until onset of labour and one dose NVP in labour
  - CD4 count 200 – 500 (randomised study)
    - *Triple-ARV MTCT prophylaxis*: ZDV+3TC+NVP from 34-36 wks until 6 mths post-partum
    - *Short-course MTCT prophylaxis* (see above)

Infants

- All infants receive single-dose NVP within 72h
- Standard WHO/UNICEF infant feeding counselling
- Study implemented in sites where majority of women choose to breastfeed
- Free formula offered to mother/children opting for replacement feeding
- All women choosing to breastfeed counselled to breastfeed exclusively for 5½ months, followed by weaning over a 2-week period

Primary objectives

Prospective cohort study

- Describe the rates and correlates of HIV-free child survival
- Describe the rates and correlates of AIDS-free maternal survival
- Assess the acceptability and tolerability of ARVs (women and children)

Randomized controlled trial

Compare efficacy and safety of triple-ARV and short-course MTCT-prophylaxis:

- HIV-free infant survival among all infants, irrespective of mode of infant feeding
- HIV-free infant survival among infants who received any breast milk
- AIDS-free survival of mothers
- Incidence of severe adverse events in mothers

Main study endpoints

- HIV-free infant survival at 6 weeks and 12 months
- AIDS-free survival among mothers by 12 months postpartum
- Incidence of severe adverse events in mothers

Sample size

N = 2,400 (1,200 randomised)

Secondary objectives (1)

- To estimate MTCT rates according to immuno, virological status and ARV regimen received
- To describe correlates of HIV-free survival in children
- To describe the correlates of HIV progression and survival of mothers
- To identify immuno. & viro. Determinants of residual transmission
- To describe the modifications of viral load in blood and breast milk and the incidence of emergence of viral resistance, particularly after HAART cessation
- To assess the acceptability, feasibility and safety of various – UN recommended - infant feeding methods, particularly exclusive breastfeeding followed by rapid weaning before 6-months of age

Secondary objectives (2)

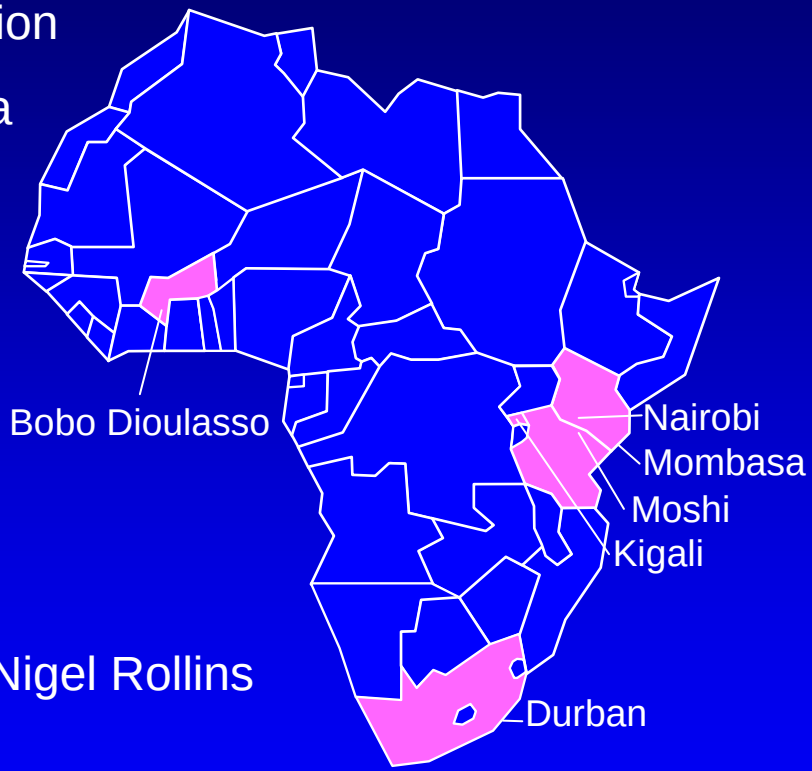
- To assess the feasibility/acceptability/adherence/safety of ZDV+3TC+NVP during late pregnancy and post-partum
- To analyse partner involvement, family planning choices, condom use and sexual practices
- To describe and analyse the social and cultural factors that may increase or reduce post-partum HIV transmission
- To describe family HIV-care needs
- To compare the cost-effectiveness of HAART and regimens currently recommended for PMTCT

Context

- All mothers and infants provided with ARV therapy when required for own health
- ARV therapy provided for (some) close household members
- Embedded in existing MTCT-prevention programme
- Continued ARV therapy and care available, or partnerships under development

Sites and partners

- **Bobo-Dioulaso, Burkina-Faso**: Centre Muraz, Nicolas Meda
  WHO, ANRS and GlaxoSmithKline Foundation
- **Kigali, Rwanda**: CHUK – J. Vyankandondera
  Funds being requested
- **Mombasa, Kenya**: ICRH - Mark Hawken
  Belgian cooperation and WHO core funds
- **Moshi, Tanzania**: KCMC - Olola Oneko
  WHO (LID and core funds)
- **Nairobi, Kenya:** KNH - Ruth Nduati
  CDC and NIH
- **Durban, South Africa: U. KwaZulu Natal** - Nigel Rollins
  Funds being requested



Coordination - Other partners

Coordination

- World Health Organization (WHO)

Other partners

- Laboratoire de Virologie, Hôpital de Montpellier
  Virology and immunology
- Institut de Recherche pour le Développement (IRD)
  Nutrition
- Laboratoire d'Écologie Humaine et d'Anthropologie (LEHA)
  Anthropology
- International Centre for Reproductive Health, Ghent (ICRH)
- CDC & NIH
- International Antiviral Therapy Evaluation Centre (IATEC)
  External monitoring

Status

Protocol

- Approved by the WHO Scientific and Ethical Review Groups
- Minor revisions requested by CDC Ethical Review Group
- Institutional and national approvals obtained in Burkina Faso, Kenya, Tanzania

Instruments under development

- Questionnaires pilot tested and finalised
- MOP and SOPs being finalised
- Translations pending

To start in June-July 2004 in two sites

Progressive expansion to other sites