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Impact of highly active anti-retroviral therapy (HAART) during pregnancy and breastfeeding on mother-to-child transmission (MTCT) and mother's health

Submission date
22/03/2004

Recruitment status
No longer recruiting

Registration date
01/04/2004

Overall study status
Completed

Last Edited
24/02/2015

Condition category
Infections and Infestations

[X] Prospectively registered

[_] Protocol

[_] Statistical analysis plan

[X] Results

[_] Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Protocol serial number
WHO/ HRP ID A25035

Study information

Scientific Title
Impact of highly active anti-retroviral therapy (HAART) during pregnancy and breastfeeding on mother-to-child transmission (MTCT) and mother's health

Study objectives
The overall goal of the study is to optimise the use of anti-retroviral (ARV) drugs during the antepartum, intrapartum and postpartum periods to prevent mother-to-child transmission (MTCT) of human immunodeficiency virus (HIV) type-1 and preserve the health of the mother in settings where the majority of HIV-positive women breastfeed. The primary objectives of the prospective cohort study are to describe the rates and correlates of acquired immune deficiency syndrome (AIDS)-free maternal survival and HIV-free child survival among HIV-positive pregnant women and their children receiving care at participating clinical centres, and to assess the acceptability and safety of ARVs offered to these women and children according to World Health Organization (WHO) guidelines. The primary objective of the randomised controlled trial (RCT) is to assess the efficacy and safety of the triple-ARV MTCT-prophylaxis regimen compared with the short-course MTCT-prophylaxis regimen among eligible women enrolled in the prospective cohort study with CD4+ cell counts between 200 and 500 cells/mm^3.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Initial ethics approval received from the Ethics Committees of:
1. World Health Organization (WHO) Gender Advisory Panel on the 24th January 2002
2. WHO Specialist Panel on Epidemiological Research on the 13th March 2002
3. WHO Scientific and Ethical Review Group on the 26th April 2002
4. WHO Secretariat Committee on Research Involving Human Subjects on the 1st May 2003
5. Centre Muraz Ethics Committee on the 25th October 2002
6. Ministry of Health (Burkina-Faso)
7. Kenyatta National Hospital Ethics and Research Committee on the 7th April 2003
8. Ministry of education, science and technology (Kenya) on the 5th July 2005
9. Tumaini University, Kilimandjaro Christian Medical College Ethics committee on the 16th April 2003
10. University of Kwazulu-Natal 20 July 2007

All subsequent version and protocol amendments have been reviewed and approved by the above ethics committees.

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS)

Interventions

In the prospective cohort study (Part I), there will be two groups of women:

Group A: Women who meet WHO criteria for HAART, i.e. CD4+ cell counts below 200 cells/mm^3 or with stage four HIV disease, who have no contraindications to HAART, and who accept HAART. They will be offered a HAART regimen, consisting of zidovudine (ZDV), lamivudine (3TC), and nevirapine (NVP), to be initiated at 34 to 36 weeks gestation and then continued as long as required for the woman's own health.

Group B: Women who do not meet WHO criteria for HAART, or, although meeting criteria, have one or more contraindications to HAART and/or refuse HAART. These women will be offered short-course mother-to-child transmission (MTCT) prophylaxis (see below).

Please note that as of 03/10/2007 enrolment in part I of this trial has stopped.

In Part II of the study, those women enrolled in the prospective cohort study with CD4+ cell counts between 200 and 500 cells/mm^3 with no contraindication and willing to be randomised will receive one of two different regimens for the prevention of MTCT of HIV:
1. A triple-ARV regimen (ZDV, 3TC and NVP) beginning at 34 to 36 weeks gestation, through delivery, until six months postpartum, or
2. A short-course regimen consisting of ZDV beginning at 34 to 36 weeks gestation until labour, plus one dose of ZDV and one dose of NVP at the onset of labour

Intervention Type
Drug

Phase
Not Applicable

Primary outcome(s)
1. HIV-free infant survival at 6 weeks and 12 months
2. AIDS-free survival among mothers by 12 months postpartum
3. Incidence of severe adverse events in mothers

Key secondary outcome(s))
The secondary objectives of the RCT are to:
1. Assess HIV-free survival at birth, 2 weeks, 6 weeks, 6 months, 9 months (a point when all breast feeding is likely to have ceased) and 12 months of age among all enrolled children
2. Estimate the rates of early and late postpartum transmission in ever breastfed infants, according to maternal HIV status and treatment received
3. Describe the correlates of infant HIV-free survival including stage of maternal HIV disease (clinical, immunological and virological factors), ARV prophylaxis and/or therapy given to the mother, and mode of infant feeding
4. Describe the correlates of mother's HIV disease progression and survival including socio-demographic characteristics, disease and nutritional status at enrolment, ARV prophylaxis and /or therapy given to the mother, and mode of infant feeding
5. Identify immunological and virological determinants of residual HIV-1 transmission during breastfeeding (coordinated by P. Van de Perre through ANRS1271 programme)
6. Describe and compare the feasibility, acceptability, safety, tolerability of and adherence to the maternal ARV prophylaxis
7. Describe the feasibility and acceptability of current UNAIDS/UNICEF/WHO recommendations on HIV and infant feeding (coordinated by K. Simondon through ANRS1271 programme)

8. Assess the feasibility and safety of rapid weaning over a two week period with complete cessation of breastfeeding by 6 months of age, and assess nutritional status and growth of children up to two years of age (coordinated by K. Simondon through ANRS1271 programme)
9. Describe changes in viral load and emergence of viral resistance in blood and breast milk according to the maternal ARV prophylaxis and therapy regimens and immunological and virological status at enrolment
10. Describe the extent of partner involvement, family planning practices, condom use and sexual activity of couples
11. Describe and analyse the social and cultural factors that may increase or reduce HIV rates of transmission through breastfeeding (coordinated by A. Desclaux through ANRS1271 programme)
12. Describe family HIV-care needs and accessibility of HIV-care services
13. Assess the cost-effectiveness of the ARV prophylaxis and therapy regimens in preventing MTCT

Completion date
31/03/2008

Eligibility

Key inclusion criteria
1. Pregnant, with a gestational age of 28 - 34 weeks (or between 16 and 32 weeks gestation if the woman is referred with medically-documented HIV stage four [clinical AIDS] or CD4+ cell count below 200 cells/mm^3 diagnosed before study screening)
2. No evidence of clinically-significant conditions likely to require specific care arrangements and which may interfere with study interventions (obstetric, cardiac, respiratory [including active tuberculosis], hepatic, gastrointestinal, endocrine, renal, haematologic, psychiatric, neurologic, or allergic) as assessed by the study site Principal Investigator
3. Confirmation of HIV infection at the study site
4. Not having received an HIV vaccine (never enrolled in an HIV-vaccine trial)
5. Willingness to receive, and no contraindication to receive, the short MTCT-prophylaxis regimen as a minimum
6. No previous enrolment in the Kesho Bora study
7. Capacity and willingness to participate in all follow-up visits, including participating in all clinical examinations, having blood drawn, as well as willingness for their infant to be clinically and physically examined and have blood drawn
8. Residing, and planning to continue to reside, within a predefined, site-specific catchment area until two years after delivery
9. Ability and willingness to give informed consent for enrolment in the study
10. Not currently taking Anti-RetroViral drugs (ARV) drugs

Women who meet the above eligibility criteria will be invited to enrol in the study (Part I). Those who, in addition, meet WHO criteria for initiating HAART, have no contraindications to HAART and accept HAART will be enrolled in Part IA and will receive HAART. All other women will be enrolled in Part IB and will receive the short-course MTCT prophylaxis. This includes women not meeting WHO criteria for treatment, having a contraindication to HAART, or refusing HAART. Additional eligibility criteria for women in Part IB to be enrolled in the randomised controlled trial (Part II) are:
1. Not meeting WHO clinical criteria for treatment
2. Having CD4+ cell count between 200 and 500 cells/mm^3
3. Having no contraindication to the triple-ARV MTCT-prophylaxis regimen
4. Willing to be randomised to receive the triple-ARV or short-course MTCT-prophylaxis regimen

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
Female

Key exclusion criteria
Does not comply with the inclusion criteria above.

Date of first enrolment
01/04/2004

Date of final enrolment
31/03/2008

Locations

Countries of recruitment
Burkina Faso

Kenya

South Africa

Switzerland

Study participating centre
World Health Organization
Geneva
Switzerland
CH-1211

Sponsor information

Organisation
World Health Organization (WHO) (Switzerland)

ROR
https://ror.org/01f80g185

Funder(s)

Funder type
Research organisation

Funder Name
World Health Organization (WHO) (Switzerland)

Alternative Name(s)
, , Всемирная организация здравоохранения, Organisation mondiale de la Santé, Organización Mundial de la Salud, WHO, , BO3, OMS

Funding Body Type
Government organisation

Funding Body Subtype
International organizations

Location
Switzerland

Funder Name
Agence Nationale de Recherches sur le Sida et les Hepatites Virales

Alternative Name(s)
National Agency for AIDS Research, National Agency for Research on AIDS and Viral Hepatitis, National Agency of Research on AIDS and Viral Hepatitis, ANRS | Maladies infectieuses émergentes, ANRS MIE, ANRS

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
France

Funder Name
Centers for Disease Control and Prevention

Alternative Name(s)

United States Centers for Disease Control and Prevention, Centers for Disease Control, U.S. Centers for Disease Control and Prevention, US Centers for Disease Control and Prevention, Centros para el Control y la Prevención de Enfermedades, CDC, U.S. CDC, USCDC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Funder Name
National Institutes of Health

Alternative Name(s)
US National Institutes of Health, Institutos Nacionales de la Salud, NIH, USNIH

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United States of America

Funder Name
Belgium Cooperation (Belgium)

Funder Name
Department for International Development

Alternative Name(s)
Department for International Development, UK, DFID

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Funder Name
European and Developing Countries Clinical Trials Partnership (EDCTP) (The Netherlands)

Alternative Name(s)
Le partenariat Europe-Pays en développement pour les essais cliniques, A Parceria entre a Europa e os Países em Desenvolvimento para a Realização de Ensaios Clínicos, The European & Developing Countries Clinical Trials Partnership (EDCTP), The European & Developing Countries Clinical Trials Partnership, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	safety and effectiveness results	01/01/2011		Yes	No
Results article	triple antiretroviral results	01/03/2011		Yes	No
Results article	results	01/08/2012		Yes	No
Results article	results	06/11/2013		Yes	No
Results article	results	01/12/2014		Yes	No