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Botswana-Baylor ANtiretroviral Assessment: A study comparing the management of human immunodeficiency virus (HIV) in children using continuous or structured interrupted antiretroviral treatment

Submission date
20/08/2013

Recruitment status
No longer recruiting

Registration date
18/09/2013

Overall study status
Completed

Last Edited
18/09/2013

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Highly active treatment for human immunodeficiency virus (HIV) (highly active antiretroviral therapy - HAART) has markedly reduced death and illness in children. However, its effectiveness is limited by the need for lifelong adherence to medication, the risk of medication burnout, medication side effects, cost and the risk of the virus becoming resistant to the treatment. This study evaluates whether the strategy of treating children until their immune cells have recovered, stopping the treatment and only restarting it when the immune cells fall below normal levels, works as well as continuous treatment.

Who can participate?
Children aged 6 months up to 12 complete years can participate if they have been proved to have the HIV virus in their body and if their parents or guardians give informed consent. Children aged 6 years or more must also agree to be included in the study.

What does the study involve?
Children will be randomly allocated to one of the two groups. One group of children will be treated continuously with HAART while children in the second group will be treated only when the number of immune cells in their body drops below the normal level. During the study blood will be drawn during monthly visits to the clinic to check the amount of virus in the body, the level of immune cells, and whether the main organs of the body are working well.

What are the possible benefits and risks of participating?
The risks and discomforts of participating include frequent clinic visits, pain during blood draws, side effects from the medicines used and the possibility that on and off treatment may not work

well. To minimize these risks and discomforts blood will be drawn only when necessary and the children will be closely monitored by qualified nurses and doctors. Participants and their parents or guardians are free to withdraw from the study at any time without penalty.

Where is the study run from?
The study is being is run from the Botswana-Baylor Childrens Clinical Centre of Excellence, Gaborone, Botswana.

When is the study starting and how long is it expected to run for?
The study started in February 2004 and is expected to run until February 2014.

Who is funding the study?
The study is funded by Botswana-Baylor Children's Clinical Centre of Excellence with support from the Botswana Government Ministry of Health and the Bristol-Myers Squibb Secure the Future Programme.

Who is the main contact?
Professor Gabriel Anabwani
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
RES227-01

Study information

Scientific Title
A randomized, CD4+ cell guided, Kaletra-based, structured interrupted antiretroviral treatment in HIV infected infants and children in Botswana

Acronym
BANA2

Study objectives
CD4+ cell guided structured interrupted antiretroviral therapy has the same efficacy as continuous therapy in HIV infected children.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Health Research and Development Committee of the Botswana Ministry of Health, approval 22 February 2013 until 21 February 2014
Baylor College of Medicine IRB, approval 28 February 2013 until 27 February 2014.

Study design
Randomized un-blinded clinical trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
GP practice

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
HIV in children

Interventions
Those randomized to the continuous arm are treated continuously while those randomized to the treatment interruption arm (STI) are treated initially for a minimum of six months and until the CDC immunologic category improves to category 1 for at least three months. At that time, treatment is interrupted until the CDC immunologic category deteriorated to 2 or 3. This cycle of interruption and resumption of therapy is repeated if the child recovers to CDC immunologic category 1 for 3 months or deteriorated to category 2 or 3. Participants are treated with stavudine(d4T)/lamivudine(3TC)/Kaletra(ritonavir-boosted lopinavir) or received zidovudine (ZDV)/3TC/Kaletra. Dosing is as follows: d4T at 1 mg/kg twice a day (bid) (up a maximum of 80

mg per day) until (yr) when the maximum dosing of d4T was reduced to 60mg/day in accordance with the Botswana HIV treatment guidelines; 3TC at 4 mg/kg bid (up to a maximum of 300 mg per day); ZDV at 180 mg/m2 bid (up to a maximum of 600 mg per day); and Kaletra in accordance with the package insert dosing table up to a maximum of 800 mg lopinavir daily. Interim analyses of study data are conducted at such intervals as was determined by the Data Safety and Monitoring Board.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Stavudine/lamivudine/Kaletra(ritonavir-boosted lopinavir), zidovudine

Primary outcome measure
1. Drug associated toxicity or intolerance
2. Disease progression [growth failure, neuropsychological / neurological deterioration, opportunistic infections or conditions) or death]
3. Development of major genotypic resistance mutations

The study was not designed to have a fixed end point in time. Rather it was designed to generate a working database with oversight by a Data and Safety Monitoring Board. The primary outcomes (death, growth failure; change in neurodevelopment status and major reverse transcriptase or protease resistance mutations) are measured by events (rates/1000 person yrs). Patients have been followed up for >2000 person years.

Secondary outcome measures
Cost of treatment

Overall study start date
11/02/2004

Completion date
27/02/2014

Eligibility

Key inclusion criteria
1. Children between 6 months up to the 13th birthday who weigh >7kg at the time of enrolment are invited to participate if they have documented laboratory evidence of HIV-1 infection, have received <6 weeks of antiretroviral therapy and are Center for Disease Control and Prevention (CDC) immunologic category 2 or 3.
2. Children aged <18 months of age are considered infected if they have two positive PCR tests - qualitative DNA or quantitative RNA, or combination of both. For those aged >18 months, a positive HIV antibody test [(enzyme-linked immunosorbent assay (ELISA) or enzyme immunoassay (EIA)] can substitute for one of the PCR-based tests. Children who were enrolled in the BANA1 study are eligible after a one-week washout period.
BANA1 was the first trial that started in 2001 to show that antiretrovirals (ARVs) would work in

African as well as in western children, as the prevailing view at that time was not so. The study was stopped after one year when the standard of care in Botswana changed. BANA2, this study, is the sequential successor of BANA1.
3. Written informed consent is obtained from all participant's legal guardians. Assent is obtained from children aged 6 years or more.

Participant type(s)
Patient

Age group
Child

Lower age limit
6 Months

Upper age limit
12 Years

Sex
Both

Target number of participants
600 (300 per arm)

Key exclusion criteria
1. Liver function test values >5x above the upper limit of normal and documented or suspected acute hepatitis within 30 days prior to study entry, irrespective of [aspartate transaminase (serum glutamic oxaloacetic transaminase) (AST(SGOT)] and alanine transaminase (serum glutamic pyruvate transaminase) ALT(SGPT) values
2. Any grade 3 or greater toxicity
3. Known intolerance to study drug and current use of medications likely to interact with study drug (including rifampicin)

Date of first enrolment
11/02/2004

Date of final enrolment
27/02/2014

Locations

Countries of recruitment
Botswana

Study participating centre
Botswana-Baylor Children's Clinical Centre of Excellence
Gaborone
Botswana
-

Sponsor information

Organisation
Botswana-Baylor Children's Clinical Centre of Excellence (Botswana)

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Sponsor type
Charity

Website
http://www.bipai.org/botswana/

ROR
https://ror.org/053gd2580

Funder(s)

Funder type
Government

Funder Name
The Botswana-Baylor Children's Clinical Centre of Excellence (Botswana)

Funder Name
The Ministry of Health, Government of Botswana (Botswana)

Funder Name
Bristol-Myers Squibb - provides study products and other support free of charge but was not involved in the initiation or conduct of the study

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration