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Children with human immunodeficiency virus (HIV) in Africa - pharmacokinetics and acceptability/adherence of simple antiretroviral regimens (CHAPAS-3 trial)

Submission date
31/03/2010

Registration date
15/04/2010

Last Edited
15/11/2019

Recruitment status
No longer recruiting

Overall study status
Completed

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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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Version 1.0

Study information

Scientific Title
A randomised trial to compare the toxicity and pharmacokinetics of three fixed-dose combination based antiretroviral regimens for treatment of human immunodeficiency virus (HIV) infected children in Africa

Acronym
CHAPAS-3

Study objectives
The overall hypothesis to be tested is that new paediatric fixed dose combination (FDC) baby and junior tablets which contain abacavir (ABC) or zidovudine (ZDV) rather than stavudine (d4T) will provide superior toxicity and/or adherence/acceptability profiles, whilst maintaining adequate pharmacokinetics and similar cost-effectiveness and viral load suppression in human immunodeficiency virus (HIV)-infected children taking combination antiretroviral therapy (ART).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval sought from (pending as of 31/03/2010):
1. University College London (UCL) (UK)
2. Ugandan National Council for Science and Technology (UNCST) (Uganda)
3. Joint Clinical Research Centre IRB (Uganda)
4. Baylor College of Medicine (Uganda)
5. University of Zambia (Zambia)

Study design
Three-arm phase II/III open-label randomised trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

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
Human immunodeficiency virus (HIV)

Interventions
Participants will be randomised in a 1:1:1 ratio at trial entry to start or continue antiretroviral therapy with either stavudine (d4T), abacavir (ABC) or zidovudine (ZDV) in combination with lamivudine (3TC) and a non-nucleoside reverse transcriptase inhibitor, NNRTI (nevirapine (NVP) or efavirenz (EFV)). All arms will use either triple fixed dose combination tablets or dual FDCs with separate NNRTI, as below:
1. Arm d4T: d4T/3TC/NVP or d4T/3TC + EFV
2. Arm ABC: ABC/3TC/NVP or ABC/3TC + EFV
3. Arm ZDV: ZDV/3TC/NVP or ZDV/3TC + EFV

Children will be enrolled over 12 - 18 months and followed for 96 weeks after the last child is enrolled. Treatment will continue throughout the trial.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Stavudine (d4T), abacavir (ABC), zidovudine (ZDV), lamivudine (3TC), nevirapine (NVP), efavirenz (EFV)

Primary outcome measure
All children:
Grade 2/3/4 clinical and/or grade 3 (confirmed) or 4 (any grade) laboratory adverse events.

For PK substudies:
Plasma pharmacokinetic parameters (AUC, Cmin, Cmax) of ABC, ZDV and 3TC in FDCs with or without NVP and of EFV from the full PK curves determined per age group at week 6.

Secondary outcome measures
All children:
1. Change in skinfold thicknesses from week 0 to 48 and 96 weeks (converted to age and sex-adjusted z-scores)
2. Change in body circumferences from week 0 to 48 and 96 weeks
3. Clinical and/or laboratory adverse events Grade 3 or 4, possibly or probably related to ABC, ZDV or d4T
4. Anaemia, neutropenia, lipodystrophy/lipoatrophy, mitochondrial disease, peripheral neuropathy and hypersensitivity reactions of any grade
5. Any AE leading to dose reduction or permanent/temporary interruption/substitution of ART
6. Changes in endothelial injury (functional and cellular) and inflammatory markers (D-Dimer, CRP, interleukin 6) from week 0 to 48 and 96 weeks. Vascular function parameters (Intima Media Thickness (IMT) of the carotid artery) and pulse wave velocity), CECs and EMPs will be measured using portable equipment, by a single investigator in each site.
7. Adherence as measured by electronic recording devices (MEMScaps) clinic-based pill counts, carer and child questionnaire including visual analogue scale from randomisation
8. Acceptability of once versus twice daily dosing by carer questionnaire
9. Change in HIV RNA viral load and proportion of children with HIV RNA less than 50 and less than 400 copies/ml from week 0 to 48 and 96 weeks (assayed retrospectively)
10. Cost and cost effectiveness

11. Change in CD4 and CD4 percent from week 0 to 48 and 96 weeks
12. Change in growth parameters (weight-for-age, height-for-age, weight-for-height) from week 0 to 48 and 96 weeks (converted to age and sex-adjusted z-scores)
13. Mortality and disease progression

For PK substudies:
Variability in pharmacokinetic parameters (AUC, Cmin, Cmax) at week 6 according to degree of malnourishment, degree of immune activation, age, weight, demographic characteristics, adherence measures, response to treatment, side effects and genetic polymorphisms.

Overall study start date
01/05/2010

Completion date
01/09/2013

Eligibility

Key inclusion criteria
1. Aged 1 month to 13 years, either sex:
1.1. ART naive children in Uganda being randomised to commence therapy on a d4T based regimen must be 0 - 4 years old in accordance with local guidelines
1.2. ART experienced children being randomised to continue therapy on a d4T based regimen must be 5 years or older with no clinical symptoms of lipodystrophy. If severe clinical symptoms of lipodystrophy develop whilst randomised to d4T then children will switch to another regimen.
2. Weighing greater than 3 kg and less than 25 kg (heavier children should receive adult tablets and not be enrolled in CHAPAS-3)
3. Participants must have a confirmed documented diagnosis of HIV-1 infection
4. Parents or guardians, and children where appropriate according to age and knowledge of HIV status, must be willing and able to give informed consent for randomisation to first-line ART strategy and participation in the PK substudy if eligible
5.1. ART naive (except for exposure to perinatal ART for the prevention of mother-to-child HIV transmission), meeting World Health Organisation (WHO) or national (WHO modified) criteria for initiating therapy and ready to start an initial 2NRTI+NNRTI based regimen according to local guidelines (i.e. according to WHO stage/CD4 and guidelines concerning first-line ART in children who have been exposed to NVP perinatally), or
5.2. Currently taking d4T based regimen for at least 2 years with screening HIV RNA viral load less than 50 copies/ml, no history of receiving other ARV drugs and CD4 count and/or CD4 percent stable over the previous 6 months
6. Able and willing to take each of the possible regimens

Participant type(s)
Patient

Age group
Child

Lower age limit
1 Months

Upper age limit

13 Years

Sex
Both

Target number of participants
420

Total final enrolment
480

Key exclusion criteria
1. Cannot, or unlikely to attend regularly (e.g. usual residence too far from study centre)
2. Likelihood of poor adherence
3. Presence of acute infection
4. In receipt of medication contraindicated by ART or on chemotherapy for malignancy. Children under three years of age receiving anti-tuberculosis therapy should not be enrolled (as they will have to receive nevirapine).
5. Laboratory abnormalities which are a contra-indication for the child to start ART/change to any of the 3 possible regimens
6. Being pregnant or breast-feeding an infant
7. Perinatal exposure to NVP (either through pMTCT or breastfeeding) for children aged 3 - 6 months only

Date of first enrolment
01/05/2010

Date of final enrolment
01/09/2013

Locations

Countries of recruitment
England

Uganda

United Kingdom

Zambia

Study participating centre
MRC Clinical Trials Unit
London
United Kingdom
NW1 2DA

Sponsor information

Organisation
Medical Research Council (UK)

Sponsor details
MRC Regional Centre London
Stephenson House
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Sponsor type
Research council

Website
http://www.mrc.ac.uk/index.htm

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research council

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

Funder Name
Medical Research Council (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Funder Name
Department for International Development (DfID) (UK)

Funder Name
The Ministerio de Sanidad y Consumo (Spain)

Funder Name
Health Research Board (Ireland)

Alternative Name(s)
HRB

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
Ireland

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2016	15/11/2019	Yes	No