

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

<b>Submission date</b> 31/03/2010	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 15/04/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 15/11/2019	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

Not provided at time of registration

## Contact information

### Type(s)

Scientific

### Contact name

Prof Diana Gibb

### Contact details

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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, C<sub>min</sub>, C<sub>max</sub>) 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  
158-160 North Gower Street  
London  
United Kingdom  
NW1 2ND

## 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?
<a href="#">Results article</a>	results	01/02/2016	15/11/2019	Yes	No