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Children with human immunodeficiency virus (HIV) in Africa - Pharmacokinetics and Adherence of Simple Antiretroviral Regimens

Submission date	Recruitment status	[_] Prospectively registered
16/01/2006	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
23/02/2006	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
07/07/2014	Infections and Infestations	

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
N/A

Study information

Scientific Title

Acronym
CHAPAS 1

Study objectives
The overall aim of the CHAPAS 1 trial is to study the appropriate dosing of, and adherence to, a fixed-dose combination of stavudine (d4T), lamivudine (3TC) and nevirapine (NVP) in a new formulation specifically developed for children (Pedimune). The specific objectives are:
1. To describe toxicity (e.g. rash, hepatic toxicity) probably or possibly related to NVP when NVP is initiated at full dose versus half-dose, in order to determine the necessity for dose escalation in African HIV-infected children using fixed dose combinations (FDCs)
2. To determine the pharmacokinetics (PK) of NVP, d4T and 3TC in two daily paediatric doses co-formulated fixed-dose crushable/dispersible tablet combinations (Pedimune) in African HIV-infected children, with and without malnutrition and in different age groups, from a subset of children enrolled in the CHAPAS 1 trial
3. To determine possible PK interactions between NVP and common concomitant medications, such as rifampicin and fluconazole in children and adolescents enrolled in the CHAPAS 1 trial
4. To evaluate a visual analogue scale for assessing 28-day adherence to antiretroviral therapy (ART), by comparing with 3-day recall, pill and bottle counts (including unannounced checks at home and measures from Medication Event Monitoring System caps [MEMs caps], which records when the pill bottle has been opened). Unannounced pill counts and MEMs caps will be performed on a subset of children enrolled in the CHAPAS 1 trial.
5. To describe mortality, disease progression, hospital admission rates and laboratory markers (CD4 percent, haemoglobin, viral load as measured by plasma HIV RNA) after starting effective ART
6. To estimate the budget impact and cost-effectiveness of effective ART in human immunodeficiency virus (HIV) infected children in Zambia

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval has been sought and gained from boards in Zambia and UK. Zambia: approved 06 /09/05, reference number 003-07-05. UK: approved 28/11/05, reference number 0567/001.

Study design
Open randomised controlled phase I/II trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Human immunodeficiency virus (HIV)

Interventions
Children will be randomised in a 1:1 ratio to start with Pedimune either at full dose in a twice daily schedule or in a dose escalation schedule of once-daily administration for 14 days, which is then increased to full dose. This latter schedule thus has 50% of the normal daily dose of NVP for the first 14 days; an additional 3TC/d4T tablet (Lamivir-S) will be provided during this period to allow full dosing of 3TC and D4T.

Intervention Type
Drug

Phase
Phase I/II

Drug/device/biological/vaccine name(s)
Stavudine (d4T), lamivudine (3TC) and nevirapine (NVP)

Primary outcome measure
For Dose Escalation Trial (all children): Adverse events (AEs) of grade 3 or 4, possibly or probably related to NVP

For PK Substudy (64 children): Pharmacokinetic parameters (area under curve [AUC], Cmin, Cmax) of 3TC, d4T and NVP from the full PK curves determined per age group

Secondary outcome measures
For Dose Escalation Trial (all children):
1. All AEs (Grade 2, 3 or 4) possibly or probably related to NVP
2. Viral load change between weeks 0 and 4 and between weeks 0 and 24
3. Adherence and acceptability measurements (from questionnaires, visual analogue scale, pill counts and MEMs caps)
4. Mortality, disease progression, growth parameters (weight for age, height for age, weight for height), change in CD4 count and percent from baseline
5. Population pharmacokinetic parameters of 3TC, d4T and NVP, determined per age group (and according to concomitant medication)

For PK Sub-study (64 children): Variability in pharmacokinetic parameters (AUC, Cmin, Cmax) according to degree of malnourishment

For Adherence Sub-study (96 children): Validity of visual analogue scale as a simple measure of adherence compared to scheduled and unannounced pill counts

Overall study start date
21/12/2005

Completion date
22/12/2008

Eligibility

Key inclusion criteria
1. Aged 3 months to 14 years inclusive
2. Less than 30 kg in weight (heavier children should receive Triomune 30 and not be enrolled in the CHAPAS 1 trial)
3. Carers and children where appropriate, willing and able to give informed consent
4. HIV-infected, as determined by:
a. Two separate HIV-antibody enzyme-linked immunosorbent assay (ELISA) or rapid tests on the same sample in children >18 months
b. Two positive proviral DNA tests taken on separate samples in children <18 months
5. Previously untreated with antiretrovirals, including any ART given to prevent mother to child transmission
6. Fulfilling one of the World Health Organisation (WHO) criteria for initiating treatment:
a. WHO paediatric stage 4 or severe stage 3 disease regardless of CD4 %
b. CD4 percent <15% if >18 months of age, or <20% if <18 months of age
c. WHO paediatric stage 2 disease with consideration of CD4 percentage (<15% for children >18 months; <20% for children <18 months)
(Note current WHO guidelines are under review and the above criteria may be changed, particularly by raising the CD4 percentage cut-off to 25% in children <18 months; inclusion criteria would be changed accordingly for children to start ART in CHAPAS 1 trial.)

Participant type(s)
Patient

Age group
Child

Lower age limit
3 Months

Upper age limit
14 Years

Sex
Both

Target number of participants
200

Key exclusion criteria
1. Cannot or unwilling to regularly attend the CHAPAS clinic
2. Severe laboratory abnormalities (contra-indicating NVP based regimen) i.e. serum creatinine >5 times upper limit of normal (ULN) or aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >10 times ULN
3. Active opportunistic infection and/or serious bacterial infection at the time of study entry including tuberculosis (TB) (children may be enrolled after the acute phase)

4. Current treatment with any medication known to be contra-indicated with any of the drugs prescribed for the patient's ART-therapy in this trial, including rifampicin

Date of first enrolment
21/12/2005

Date of final enrolment
22/12/2008

Locations

Countries of recruitment
Zambia

Study participating centre
University Teaching Hospital
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Sponsor information

Organisation
Medical Research Council (UK)

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Sponsor type
Charity

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Charity

Funder Name
Funding secured from the European and Developing Countries Clinical Trials Partnership (EDCTP). Reference number: 2004.01.H.d2 CHAPAS Trials.

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	24/08/2013		Yes	No