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Europe - Africa Research Network for Evaluation of Second-line Therapy

Submission date	Recruitment status	[_] Prospectively registered
13/07/2009	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
22/09/2009	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
02/02/2023	Infections and Infestations	

Plain English summary of protocol
Not provided at time of registration

Study website
http://www.earnest.eu/

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT00988039

Secondary identifying numbers

Version 3.0, 6th September 2010

Study information

Scientific Title
A randomised controlled trial to evaluate options for second-line therapy in patients failing a first-line 2 nucleoside reverse transcriptase inhibitors (2NRTI) and non-nucleoside reverse transcriptase inhibitor (NNRTI) regimen in Africa

Acronym
EARNEST

Study objectives
The trial aims to determine whether, in patients failing a first-line nucleoside reverse transcriptase inhibitor (NRTI) and non-nucleoside reverse transcriptase inhibitor (NNRTI)-containing regimen:
1. The use of boosted protease inhibitor (bPI) plus raltegravir (an integrase inhibitor) is superior to standard of care (bPI plus two new NRTIs) in achieving good human immunodeficiency virus (HIV) disease control at 96 weeks after randomisation
2. The use of bPI monotherapy is non-inferior to standard of care in achieving good HIV disease control at 96 weeks after randomisation

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. University College London (UCL) Research Ethics Committee, 13/05/2009
2. Joint Clinical Research Centre Institutional Review Board (IRB), Uganda, 10/06/2009
3. Medical Research Council of Zimbabwe
4. University of Malawi COMREC
5. Moi Teaching Referral Hospital IREC
6. University Teaching Hospital, Lusaka, ERES CONVERGE

Study design
Three-arm parallel-group open-label multicentre randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

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

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

Interventions
Arm A (bPI + NRTIs):
Patients randomised to this arm will receive Aluvia® (lopinavir/ritonavir 400 mg/100 mg) twice daily and 2 NRTIs. The choice of NRTIs will be at the discretion of the managing clinician and based on the local standard of care and drug availability, taking into account patient's previous drug exposure and side effects on first-line therapy. For patients who have been treated with a first-line regimen containing stavudine or zidovudine, clinicians will be encouraged to follow the current World Health Organization (WHO) recommendations for second-line treatment regimens of either:
1. Tenofovir with emtricitabine (Truvada®) or lamivudine
2. Didanosine with abacavir

The NRTIs will be given in the following standard doses:
Tenofovir - 300 mg once daily
Emtricitabine - 200 mg once daily
Lamivudine - 150 mg twice daily or 300 mg once daily
Didanosine - 400 mg once daily (250 mg once daily if weight is less than 60 kg)
Abacavir - 300 mg twice daily or 600 mg once daily
Zidovudine - 300 mg twice daily

Arm B (bPI + raltegravir):
Patients randomised to this arm will receive Aluvia® (lopinavir/ritonavir 400 mg/100 mg) twice daily and raltegravir 400 mg twice daily.

Arm C (bPI monotherapy):
Patients randomised to this arm will receive Aluvia® (lopinavir/ritonavir 400 mg/100 mg) twice daily (and raltegravir 400 mg twice daily for the first 12 weeks only). If patients interrupt treatment for more than 4 weeks (in induction phase or in Aluvia® monotherapy phase), treatment will be resumed with a further induction period of raltegravir for the first 12 weeks.

Patients will be randomised to receive study drugs according to the treatment arms. Treatment will be open-label, and will be distributed at 4 to 16 weekly intervals from a dedicated supply of study drugs that will be stored separately from routine clinic drug supplies in a designated section of the research pharmacy at the study site. Each patient will be treated and followed up for a total of 144 weeks regardless of which arm of the trial they are randomised to. All trial drugs will be in tablet form.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Aluvia®, raltegravir

Primary outcome measure
Good HIV disease control defined as a composite endpoint consisting of all of:
1. No new WHO Stage 4 events between randomisation and week 96, and
2. CD4 count greater than 250 cells/mm3 at week 96, and
3. VL less than 10,000 copies/ml or greater than 10,000 copies/ml with no PI resistance mutations at week 96

Secondary outcome measures
1. Good HIV disease control at week 144
2. Proportion with CD4 cell count greater than 250 cells/mm3 at week 96 and week 144
3. Proportion with new or recurrent WHO Stage 4 event by week 96 and week 144
4. Proportion of patients with plasma VL less than 50 copies at week 48, week 96 and week 144
5. Adverse events (AEs)
6. Quality of life change from randomisation
7. Neurocognitive function change from randomisation
8. Healthcare costs

Overall study start date
15/09/2009

Completion date
15/09/2013

Eligibility

Key inclusion criteria
1. Previously documented HIV infection on at least one standard antibody-based test
2. Aged 12 years and above, either sex
3. Taking 2NRTI + NNRTI-based regimen continuously for at least 12 months
4. Naive to protease inhibitor therapy
5. Good adherence to anti-retroviral therapy (ART) in the 12 weeks prior to screening defined as no more than 10% of doses missed (patients who do not have good adherence should be given adherence
counselling and re-assessed after an appropriate time interval of not less than 4 weeks)
6. Clinically stable and receiving treatment for any known opportunistic infections
7. HIV treatment failure defined by the one or more of the following clinical, immunological and virological criteria (modified from World Health Organization [WHO] 2006 criteria):
7.1. Clinical: A1 and A2 and A3 must be fulfilled:
A1: New or recurrent WHO stage 4 condition occurring after at least 12 months on ART
A2: CD4 cell count less than 200 cells/mm^3 after at least 12 months on ART, and confirmed at screening
A3: Viral load (VL) greater than 400 copies/ml at screening
7.2. Immunological: (B1 or B2 or B3) and B4 must be fulfilled:
B1: Fall of CD4 count to pre-therapy baseline (or below) after at least 12 months on ART and confirmed at screening
B2: Fall of CD4 count from previous value greater than 400 cells on treatment (x 2) to less than 200 cells/mm3 after at least 12 months on ART and confirmed at screening
B3: CD4 count less than 100 cells after at least 12 months on ART and confirmed at screening
B4: VL greater than 400 copies/ml at screening
7.3. Virological: VL greater than 10,000 copies/ml after at least 6 months on ART, and confirmed

at screening after at least 12 months on ART
8. Willing and able to provide written informed consent
9. Able to attend for regular study follow-up visits

Participant type(s)
Patient

Age group
Mixed

Sex
Both

Target number of participants
1200 (Recruitment complete as of 04/08/2011. 1277 participants have been recruited)

Key exclusion criteria
1. Any major clinical contraindications to the use of bPI, the NRTIs that are available to be selected for a second-line regimen, or raltegravir
2. Known Hepatitis B carrier (Hepatitis B surface antigen positive)
3. Requirement for concomitant medication with known major interactions with study drugs for which drug substitutions or dose alterations are not available or acceptable
4. Currently receiving chemotherapy for malignancy
5. Women who are currently pregnant or breastfeeding
6. Current participation in another clinical trial involving a treatment intervention (may be permitted in some circumstances, but must first be discussed with the EARNEST chief investigator)
7. Life expectancy of less than one month in the opinion of the treating physician

Date of first enrolment
15/09/2009

Date of final enrolment
04/08/2011

Locations

Countries of recruitment
England

Kenya

Malawi

Uganda

United Kingdom

Zambia

Zimbabwe

Study participating centre
MRC Clinical Trials Unit
London
United Kingdom
WC2B 6NH

Sponsor information

Organisation
Medical Research Council (MRC) (UK)

Sponsor details
MRC Clinical Trials Unit
Aviation House
125 Kingsway
London
United Kingdom
WC2B 6NH

Sponsor type
Research council

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

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research organisation

Funder Name
European and Developing Countries Clinical Trials Partnership

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, European and Developing Countries Clinical Trials, EDCTP

Funding Body Type
Private sector organisation

Funding Body Subtype
International organizations

Location
Netherlands

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

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	17/07/2014		Yes	No
Results article	observational analysis results	01/08/2017		Yes	No
Results article	follow-up results	01/01/2018		Yes	No
Other publications	Substudy results	23/01/2023	02/02/2023	Yes	No