

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

Submission date
13/07/2009

Recruitment status
No longer recruiting

☐ Prospectively registered

☐ Protocol

Registration date
22/09/2009

Overall study status
Completed

☐ Statistical analysis plan

☒ Results

Last Edited
02/02/2023

Condition category
Infections and Infestations

☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

Dr Nick Paton

Contact details

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

Additional identifiers

ClinicalTrials.gov (NCT)
NCT00988039

Protocol serial number

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

Study type(s)

Treatment

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(s)

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

Key secondary outcome(s)

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

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/mm³ 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

Healthy volunteers allowed

No

Age group

Mixed

Sex

All

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

United Kingdom

England

Kenya

Malawi

Uganda

Zambia

Zimbabwe

Study participating centre

MRC Clinical Trials Unit

London

United Kingdom

WC2B 6NH

Sponsor information

Organisation

Medical Research Council (MRC) (UK)

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 Ensaio Clínicos, The European & Developing Countries Clinical Trials Partnership (EDCTP), 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

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
Study website	Study website	11/11/2025	11/11/2025	No	Yes