

# Europe - Africa Research Network for Evaluation of Second-line Therapy (EARNEST) Rifabutin Pharmacokinetics (PK) substudy

<b>Submission date</b> 06/03/2012	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 03/04/2012	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 16/04/2019	<b>Condition category</b> Infections and Infestations	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Some of the drugs used to treat HIV (anti-retrovirals) can affect the blood levels of other drugs used to treat tuberculosis (TB) – called a drug-drug interaction. The main drug used in second-line HIV treatment, Aluvia (lopinavir/ritonavir), is one of the drugs that has this effect. This is why people on second-line anti-retrovirals usually cannot use one of the main TB drugs, rifampicin, and instead will be prescribed a slightly different drug called rifabutin, which is less affected by these drug-drug interactions. Although blood levels of rifabutin are not as badly affected by Aluvia as blood levels of rifampicin, rifabutin blood levels are still increased a lot by taking Aluvia at the same time. This could lead to higher levels of side-effects because there is more of the drug in the body. Doctors have suggested that instead of taking rifabutin every day with Aluvia, it should only be taken three times a week, on Mondays, Wednesdays and Fridays. However, in the last 2 years, new studies have suggested that this three times a week regimen might not be enough and that it may not completely cure TB. So the purpose of this study is to find out whether taking rifabutin every day with Aluvia really does lead to more side-effects, and whether taking rifabutin three times a week with Aluvia really does lead to much lower levels of rifabutin in the blood.

### Who can participate?

Adults/adolescents (aged 12 and older) with HIV and TB who are being treated with Aluvia and rifabutin.

### What does the study involve?

Participants are randomly allocated to one of two groups. One group takes rifabutin three times a week (Monday/Wednesday/Friday). The other group takes rifabutin daily. Both groups also take Aluvia as part of their second-line anti-retroviral treatment.

### What are the possible benefits and risks of participating?

Not provided at time of registration.

Where is the study run from?  
Joint Clinical Research Centre (Uganda).

When is the study starting and how long is it expected to run for?  
March 2012 to January 2014.

Who is funding the study?  
Abbott

Who is the main contact?  
Dr Cissy Kityo Mutuluza  
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**Study website**  
<http://earnest.cineca.org/node/42>

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

**IRAS number**

**ClinicalTrials.gov number**  
NCT01663168

**Secondary identifying numbers**  
N/A

## Study information

**Scientific Title**

Toxicity and pharmacokinetics of different Rifabutin doses in HIV-infected adults and adolescents taking lopinavir / ritonavir as second-line anti-retroviral therapy (ART) (EARNEST Rifabutin PK substudy)

### **Study objectives**

This pilot randomised open-label pharmacokinetic substudy embedded within a larger randomised controlled trial (EARNEST) will compare 150 mg rifabutin daily versus thrice weekly, both in combination with lopinavir/ritonavir taken as part of second-line ART in the EARNEST trial of second-line antiretroviral therapy, in terms of

1. Toxicity
2. Pharmacokinetics of rifabutin, lopinavir/ritonavir, raltegravir (participants enrolled from arm B of main EARNEST trial only) and
3. PK/PD (pharmacokinetic/pharmacodynamic) relationships

EARNEST study registered under ISRCTN37737787

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Joint Clinical Research Centre Institutional Review Board (IRB), Uganda, 14/10/2011

### **Study design**

Parallel two-group open-label multi-centre randomised controlled pilot trial embedded within a larger randomised controlled trial (EARNEST)

### **Primary study design**

Interventional

### **Secondary study design**

Randomised controlled trial

### **Study setting(s)**

Hospital

### **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) / Tuberculosis (TB)

### **Interventions**

Patients will be randomised in a ratio of 1:1 to the following two treatment groups:

Group 1: rifabutin (150 mg) three times a week (Monday/Wednesday/Friday)

Group 2: rifabutin (150 mg) daily

Total duration of intervention: at least 24 weeks

Patients in both groups will also be taking lopinavir/ritonavir as part of their second-line ART

### **Intervention Type**

Drug

### **Phase**

Not Applicable

### **Drug/device/biological/vaccine name(s)**

Lopinavir/ritonavir, rifabutin

### **Primary outcome measure**

Grade 3/4 adverse events over the course of the trial and time to first event

### **Secondary outcome measures**

1. Rifabutin and its 25-o-desacetyl metabolite pharmacokinetic parameters (from a population PK model)
2. Lopinavir/ritonavir pharmacokinetic parameters (from a population PK model)
3. Raltegravir pharmacokinetic parameters (from a population PK model)
4. Response to TB therapy (culture positive at 24 weeks or subsequent relapse/recurrence)
5. Rifamycin resistance

### **Overall study start date**

05/03/2012

### **Completion date**

31/01/2014

## **Eligibility**

### **Key inclusion criteria**

1. HIV-1 infected adults/adolescents (12 years and older) receiving boosted protease inhibitor (almost exclusively lopinavir/ritonavir, Aluvia) containing second-line ART within the EARNEST trial
2. Enrolled with or developing tuberculosis (TB) during EARNEST trial follow-up
3. Currently receiving or planning to initiate rifabutin-containing anti-TB treatment (ie no contraindications to rifabutin)
4. Who provide written informed consent

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Sex**

Both

### **Target number of participants**

**Key exclusion criteria**

1. Patients who have already reached week 132 in the EARNEST trial at time of TB diagnosis will not be enrolled as practical considerations limit follow up to 12 weeks beyond the completion of the week 144 EARNEST visit.
2. Patients who have less than 10 weeks remaining in their course of TB treatment will not be enrolled as they will not contribute to the main PK evaluation at week 12 (window 10-14 weeks)

**Date of first enrolment**

05/03/2012

**Date of final enrolment**

31/01/2014

**Locations****Countries of recruitment**

Uganda

**Study participating centre**

Joint Clinical Research Centre (JCRC)

Kampala

Uganda

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**Sponsor information****Organisation**

MRC Clinical Trials Unit (UK)

**Sponsor details**

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**Sponsor type**

Research council

**Website**

<http://www.ctu.mrc.ac.uk>

ROR

<https://ror.org/001mm6w73>

## Funder(s)

**Funder type**

Industry

**Funder Name**

Abbott

## 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	17/07/2014	16/04/2019	Yes	No