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

Submission date
06/03/2012

Recruitment status
No longer recruiting

Registration date
03/04/2012

Overall study status
Completed

Last Edited
16/04/2019

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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?
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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

140

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
Aviation House
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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?
Results article	results	17/07/2014	16/04/2019	Yes	No