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Intracellular boosting of human immunodeficiency virus (HIV) protease inhibitors

Submission date	Recruitment status	[_] Prospectively registered
15/09/2008	Stopped	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/11/2008	Stopped	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
21/05/2014	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
http://www.nres.nhs.uk/researchsummaries/?entryid29=177620&q=0~intracellular+boosting~

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2008-002627-90

Protocol serial number
3589

Study information

Scientific Title
Intracellular boosting of human immunodeficiency virus (HIV) protease inhibitors through inhibition of transport: a novel strategy for potentiating HIV therapy

Study objectives
The intracellular accumulation of the HIV protease inhibitor lopinavir may be pharmacologically enhanced in-vivo through inhibition of drug transporters using dipyridamole and furosemide.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Liverpool (Adult) Research Ethics Committee, 07/07/2008, ref: 08/H1005/64

Study design
A single centre, prospective, randomised open-labelled crossover study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
During the study period, patients will continue to take their normal antiretroviral therapy including lopinavir. Following screening subjects will attend at study visit 1 for a 12 hour pharmacokinetic assessment. Subjects will return the next day for study visit 2 and receive a stat dose of either furosemide 40 mg or dipyridamole modified release (Persantin®; Retard) 200 mg followed by a 12 hour pharmacokinetic assessment. After a 7 day washout period, subjects will return for study visit 3 and receive a stat dose of either furosemide 40 mg or dipyridamole MR 200 mg followed by a 12 hour pharmacokinetic assessment. After a 7 day washout period subjects will return for study visit 4 and receive stat doses of both furosemide 40 mg and dipyridamole MR 200 mg followed by a 12 hour pharmacokinetic assessment. Following a 7 day washout period subjects will attend for a clinical assessment (study visit 4).

Updated 21/05/2014: this trial was stopped early on 29/02/2012 due to slow recruitment and safety concerns.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Lopinavir, furosemide, dipyridamole

Primary outcome(s)
A change in cellular accumulation ratio (CAR) of lopinavir following treatment with dipyridamole and/or furosemide. CAR will be calculated as a ratio of intracellular and plasma area under curve (AUC) of lopinavir.

The outcomes will be measured at the study visits 1, 2, 3 and 4 by pharmacokinetic assessment. Serial blood specimens will be obtained at trough, 1, 2, 4, 8, 12 hours post lopinavir dose.

Key secondary outcome(s))
1. Absolute change in plasma AUC
2. Absolute change in intracellular AUC
3. Safety and tolerability of furosemide and dipyridamole
4. Correlation between drug transporter expression on peripheral blood mononuclear cells (PBMCs) at baseline and
4.1. Intracellular drug exposure
4.2. Intracellular boosting effect of furosemide and/or dipyridamole
4.3. Polymorphisms in host genotype of transporter

The outcomes will be measured at the study visits 1, 2, 3 and 4 by pharmacokinetic assessment. Serial blood specimens will be obtained at trough, 1, 2, 4, 8, 12 hours post lopinavir dose.

Completion date
01/10/2010

Reason abandoned (if study stopped)
Participant recruitment issue

Eligibility

Key inclusion criteria
1. The ability to understand and sign a written informed consent form, prior to participation in any screening procedures and must be willing to comply with all study requirements
2. Male or female patients
3. Aged 18 years and above
4. HIV positive

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. History of drug sensitivity or drug allergy to lopinavir, ritonavir, furosemide or dipyridamole
2. Aged less than 18 years
3. Pregnant or lactating women
4. CD4 less than 100 x 10^6 L
5. Viral load greater than 5000 copies
6. Anaemia (haemoglobin [Hb] less than 10.0 g/dl)
7. Severe coronary artery disease
8. Unstable angina
9. Recent myocardial infarction or haemodynamic instability
10. Hypovolaemia or dehydration
11. Renal dysfunction (estimated glomerular filtration rate [eGFR] less than 70 ml/min/1.73 m^2)
12. Severe hypokalaemia (K+ less than 3.0 mmol/l)
13. Severe hyponatraemia (Na+ less than 130 mmol/l)
14. Men with symptomatic urinary outflow obstruction
15. Severe hypotension (systolic less than 100 mmHg or diastolic less than 60 mmHg)
16. Women of childbearing age unless using appropriate contraception
17. Any known bleeding disorders
18. International normalised ratio (INR) less than 1.5
19. Platelets less than 100 x 10^9 L

Date of first enrolment
01/10/2008

Date of final enrolment
01/10/2010

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Liverpool
Liverpool
United Kingdom
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Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospitals Trust (UK)

ROR
https://ror.org/009sa0g06

Funder(s)

Funder type
Government

Funder Name
National Institute of Health Research (NIHR) Biomedical Research Centre at Royal Liverpool and Broadgreen University Hospitals Trust (UK)

Results and Publications

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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes