

Interaction between human immunodeficiency virus (HIV) drugs (non-nucleoside reverse transcriptase inhibitors [NNRTIs]) and anti-platelet agents

Submission date 28/10/2009	Recruitment status No longer recruiting	☐ Prospectively registered
Registration date 17/12/2009	Overall study status Completed	☐ Protocol
Last Edited 19/05/2022	Condition category Infections and Infestations	☐ Statistical analysis plan
		☒ Results
		☐ Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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Contact details

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Additional identifiers

Clinical Trials Information System (CTIS)

2008-006371-67

Protocol serial number

RLBUHT 3729

Study information

Scientific Title

Effect of thienopyridine derivative (clopidogrel) on the disposition of efavirenz and nevirapine in human immunodeficiency virus (HIV) positive patients: a randomised single-phase multi-dose proof-of-concept study

Study objectives

The plasma concentration of non-nucleoside reverse transcriptase inhibitors (NNRTIs) (nevirapine and efavirenz) may be pharmacologically enhanced in-vivo through inhibition of CYP2B6 with clopidogrel.

Ethics approval required

Old ethics approval format

Ethics approval(s)

National Research Ethics Service (Northwest Research Ethics Committee) (UK) approved on the 28th August 2009 (ref: 09/H1010/6)

Study design

Open-label sequential randomised single phase multi-dose proof-of-concept study

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Human immunodeficiency virus (HIV)

Interventions

Study patients on nevirapine should be receiving 200 mg 12-hourly. Study patients on efavirenz who are taking 600 mg at night would be converted to 600 mg in the morning as follows: 400 mg mane, 200 mg nocte for 1 day, then 600 mg for 1 day followed by the study day.

Study Day 1:

Patients are fasted from midnight and attend at 08:00 hours without taking their pills. After breakfast and blood sampling for pharmacokinetic profiles patients would then be administered initial dose of clopidogrel (Plavix®, 75 mg once daily; Sanofi Synthelabo, Guildford, United Kingdom) and would self-administer the remaining dose at home for the remaining 6 days.

Joint sponsor details:

The University of Liverpool (UK)

Pembroke Place

Liverpool L69 3GF

United Kingdom

<http://www.liv.ac.uk/>

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Efavirenz, nevirapine, clopidogrel

Primary outcome(s)

Absolute change (demonstrated by significant difference) in plasma AUC of efavirenz alone or nevirapine alone if the respective 90% classical confidence interval for geometric mean ratio lies within 0.80 - 1.25 of the reference AUC 0 - 24 hours.

All measures determined at the end of the study duration and data analysis (entire study duration is 8 days and data analysis approximately 3 weeks to a month).

Key secondary outcome(s)

1. Change in C_{max}, C_{min}, and weight-corrected apparent oral clearance (CL/F)/kg of efavirenz/nevirapine
2. Safety and tolerability of co-administration of clopidogrel and efavirenz/nevirapine

All measures determined at the end of the study duration and data analysis (entire study duration is 8 days and data analysis approximately 3 weeks to a month).

Completion date

15/12/2009

Eligibility

Key inclusion criteria

1. Aged greater than 18 years, either sex
2. On efavirenz (EFV) or nevirapine (NVP) containing regimen for greater than or equal to 6 months
3. Viral load less than or equal to 40 copies/ml and any CD4 count
4. No laboratory evidence of NNRTI toxicity:
 - 4.1. Alanine aminotransferase (ALT) less than or equal to upper limit of normal (ULN)
 - 4.2. Bilirubin less than or equal to ULN
 - 4.3. Albumin greater than or equal to 30 g
 - 4.4. Creatinine less than or equal to ULN
5. Not pregnant (for contraception, patients would be advised to use non-oestrogen based contraceptive devices)
6. No inter-current acute illness
7. No past medical history of coronary heart disease
8. No history of bleeding diathesis
9. No history of allergy to thienopyridines

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Key exclusion criteria

1. Unable to provide informed consent
2. Known or suspected poor adherence to anti-retroviral therapy (ART)
3. Continuing intravenous (IV) drug user
4. On a HIV protease inhibitor or any known P450 inhibitors or inducers
5. Platelets less than or equal to $100 \times 10^9/l$
6. Neutrophils less than or equal to $1.0 \times 10^9/ml$

Date of first enrolment

15/11/2009

Date of final enrolment

15/12/2009

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

Professor and Hon Consultant Infectious Diseases

Liverpool

United Kingdom

L69 3GF

Sponsor information

Organisation

Royal Liverpool University Hospital and the University of Liverpools Biomedical Research Centre (UK)

ROR

Funder(s)

Funder type

Government

Funder Name

National Institute for Health Research (NIHR) (UK) - through the Royal Liverpool University Hospital and the University of Liverpool's Biomedical Research Centre (ref: UoL000399. R&D 3729)

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?
Basic results		08/09/2021	19/05/2022	No	No
HRA research summary			28/06/2023	No	No