

The formation of carbamazepine metabolites and carbamazepine-protein conjugates in epilepsy patients

Submission date 18/02/2015	Recruitment status No longer recruiting	☐ Prospectively registered
		☐ Protocol
Registration date 19/02/2015	Overall study status Completed	☐ Statistical analysis plan
		☒ Results
Last Edited 21/09/2021	Condition category Nervous System Diseases	☐ Individual participant data

Plain English summary of protocol

Background and study aims

Carbamazepine is an effective drug that is used in the treatment of epilepsy, neuralgia and psychiatric disorders. Although generally well tolerated, it can cause hypersensitivity reactions such as a skin rash in up to 10% of patients. These reactions can result in hospital admission, long-term complications such as blindness, and can cause death in up to 30% of patients. These reactions are caused by the immune system. Recent research has identified that patients with specific genes are at a higher risk of developing this hypersensitivity. Carbamazepine is converted by the liver to other chemical products called metabolites. It is believed that one or more of these metabolites activate the immune system. However, it is not known how this happens. This aim of this study is to assess the stable and toxic products formed in the blood and urine of patients receiving carbamazepine.

Who can participate?

Adults aged at least 18 who have either just been prescribed carbamazepine or have received the treatment at the same dose for at least 4 weeks

What does the study involve?

Participants provide blood and urine samples in order to identify the chemicals responsible for triggering the immune system in susceptible people. Genetic variations are also analysed to determine their effects on carbamazepine.

What are the possible benefits and risks of participating?

These results may help to explain the variation in carbamazepine hypersensitivity between patients. Lessons learned from this research will provide valuable information for other drugs that cause similar hypersensitivity reactions (e.g. penicillins). Improved understanding of the mechanism of carbamazepine hypersensitivity will enable safer drug design in future and the development of predictive tests that can diagnose and identify patients susceptible to adverse reactions.

Where is the study run from?
University of Liverpool (UK)

When is the study starting and how long is it expected to run for?
November 2013 to April 2015

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Dr Vincent Yip

Contact information

Type(s)
Scientific

Contact name
Dr Vincent Yip

Contact details
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Liverpool
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Additional identifiers

Clinical Trials Information System (CTIS)
2013-002743-28

Protocol serial number
15543

Study information

Scientific Title
A pharmacokinetic investigation into the formation of carbamazepine metabolites and carbamazepine-protein conjugates in epilepsy patients

Acronym
PICME II

Study objectives

This study aims to improve our mechanistic understanding of carbamazepine hypersensitivity by using high sensitivity mass spectrometry to characterise and quantify the stable and toxic products formed in the blood and urine of patients receiving carbamazepine therapy.

Ethics approval required

Old ethics approval format

Ethics approval(s)

13/NW/0503

Primary study design

Interventional

Study design

Non-randomised; Both; Treatment

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Topic: Neurological; Subtopic: Neurological (all Subtopics); Disease: Epilepsy

Interventions

Patients in the auto-induction group will be newly prescribed carbamazepine. All other subjects in the study will have been prescribed carbamazepine by their neurologist as part of clinical care for patient for at least 4 weeks.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Carbamazepine

Primary outcome(s)

Pharmacokinetic analyses; Timepoint(s): Time points dependent on time of presentation to clinic

Key secondary outcome(s)

N/A

Completion date

30/04/2015

Eligibility**Key inclusion criteria**

Autoinduction group:

1. Subject is willing and able to give written informed consent
2. Subject is aged 18 or over
3. Subject is newly prescribed carbamazepine by their attending physician

Maintenance group:

1. Subject is willing and able to give written informed consent
2. Subject is aged 18 or over
3. Subject has received CBZ therapy at the same dosage for at least 4 weeks

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 Years

Sex

All

Key exclusion criteria**Autoinduction group:**

1. Subject is not willing to take part or unable to give written informed consent
2. Subject has in the past 4 weeks received other medication that is a CYP3A4 inducer or inhibitor (see medications below)
3. Subject has taken part on another research study within 90 days of commencement
4. Subject has any condition which in the opinion of the investigator will interfere with the study

Excluded medications:

Rifampicin, Amiodarone, Fluvoxamine, Saquinavir, Rifampin, Amprenavir, Indinavir, SVerapamil, Isoniazid, Atazanavir, Lopinavir, Verapamil, Phenytoin, Azithromycin, Mifepristone, Phenobarbital, Grapefruit juice, Nelfinavir, Omeprazole, Clarithromycin, Norverapamil, Clotrimazole, Cyclosporine A, Ritonavir, HMGCoA reductase inhibitors, Delavirdine, Ndesmethylethromycin, Cyclophosphamide, Erythromycin, Roxithromycin, Spironolactone, Fluoxetine, RVerapamil

Maintenance group:

1. Subject is not willing to take part or unable to give written informed consent
2. Subject has any condition which in the opinion of the investigator will interfere with the study

Date of first enrolment

05/11/2013

Date of final enrolment

30/04/2015

Locations

Countries of recruitment

United Kingdom

England

Study participating centre

University of Liverpool

Wolfson Centre for Personalised Medicine

Department of Pharmacology

Block A: Waterhouse Buildings

1–5 Brownlow Street

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Sponsor information

Organisation

University of Liverpool

ROR

<https://ror.org/04xs57h96>

Funder(s)

Funder type

Government

Funder Name

Medical Research Council

Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

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?
Results article		01/06/2021	21/09/2021	Yes	No
HRA research summary			28/06/2023	No	No