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Rosuvastatin for the prevention of aminoglycoside-induced kidney toxicity in children with cystic fibrosis

Submission date
05/09/2014

Recruitment status
No longer recruiting

Registration date
05/09/2014

Overall study status
Completed

Last Edited
21/06/2019

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Cystic fibrosis is a genetic condition where the lungs and digestive system gets clogged with thick sticky mucus. Many children with cystic fibrosis (CF) have treatment with an antibiotic called tobramycin given straight into the blood stream (called intravenous or IV). This helps treat their lung infections, but it can sometimes cause kidney problems. We think that giving a medicine called rosuvastatin at the same time as tobramycin could help protect the kidneys from damage and make it safer to give tobramycin. To help us find out whether this is true or not, we are doing a research study called a clinical trial in children with CF getting IV tobramycin where half of the children taking part also get rosuvastatin, and the other half do not.

Who can participate?
Children aged 10 to 18 years with cystic fibrosis.

What does the study involve?
At the first visit each child will be randomly allocated to their treatment group for the study. There is an equal chance of being in either group. One group will take a rosuvastatin tablet each day they are having IV tobramycin, and the other group will just have their IV tobramycin as normal. Each child will be in the study for about 6 weeks and will normally have five visits as part of the study. As much as possible we will do the study visits and blood tests at the same time as they would normally have them. However, the study will usually mean having two more blood tests and visits than normal, and we will take a little more blood than usual each time. There will be study visits on the day of starting IV tobramycin, on three further occasions during the course of treatment (usually 14 days), and 4 weeks after completing treatment. In addition, daily urine samples will be collected during the course of tobramycin.

What are the possible benefits and risks of participating?
Like any medicine, rosuvastatin can have side effects. Rarely, it can have serious effects on the liver or muscles. These, and other possible side effects, will be explained to potential participants before agreeing to the study. We will monitor each child very closely for any side effects during the study. If the study shows that rosuvastatin does protect the kidneys, then

there may be a benefit to the children who take part, and the study may help children and young people in the future. However, we will not be able to continue prescribing rosuvastatin at the end of the study, even if they have benefitted from it.

Where is the study run from?
The study is run by the University of Liverpool and University College London, and will be recruiting participants at the following hospitals in the UK: Alder Hey Childrens Hospital, Liverpool, Great Ormond Street Hospital, Nottingham Childrens Hospital, and Bristol Royal Hospital for Children.

When is the study starting and how long is it expected to run for?
October 2014 to September 2016.

Who is funding the study?
The JP Moulton Charitable Foundation (UK).

Who is the main contact?
Dr Stephen McWilliam
stevemcw@liv.ac.uk

Contact information

Type(s)
Scientific

Contact name
Dr Stephen McWilliam

Contact details
Alder Hey Hospital
Eaton Road West Derby
Liverpool
United Kingdom
L12 2AP
-
stevemcw@liv.ac.uk

Additional identifiers

EudraCT/CTIS number
2014-002387-32

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
16993

Study information

Scientific Title
Phase IIa, randomised, controlled, open-label trial of rosuvastatin for the prevention of aminoglycoside-induced kidney toxicity in children with cystic fibrosis

Acronym
PROteKT

Study objectives
Does co-administration of rosuvastatin prevent kidney toxicity caused by aminoglycoside antibiotics in children with cystic fibrosis?

Ethics approval required
Old ethics approval format

Ethics approval(s)
14/NW/1067; First MREC approval date 05/08/2014

Study design
Randomised; Interventional; Design type: Treatment

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
Topic: Children; Subtopic: All Diagnoses; Disease: All Diseases

Interventions
Patients will be randomised equally to either receive rosuvastatin 10 mg once daily or no intervention (control), throughout a course of treatment with IV tobramycin (usually lasting 14 days).

Study visits will be conducted on the day of starting IV tobramycin, on three further occasions during the course of treatment (usually 14 days), and 4 weeks after completing treatment. In addition, daily urine samples will be collected during the course of tobramycin.

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Mean fold-change in urinary KIM-1; Timepoint(s): Urinary KIM-1 measured daily during tobramycin exposure. This will be assessed using the difference in mean fold-change in urinary KIM-1 from baseline to peak concentration during exposure to tobramycin between the rosuvastatin-treated arm and control arm.

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/10/2014

Completion date
01/09/2016

Eligibility

Key inclusion criteria
1. Age 10 to 18 years inclusive
2. Diagnosis of cystic fibrosis (established by sweat test or genotype)
3. Planned, clinically indicated, course of treatment with IV tobramycin
4. Ability to give informed consent
5. Willingness to comply with all study requirements.

Participant type(s)
Patient

Age group
Child

Lower age limit
10 Years

Upper age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Total final enrolment
50

Key exclusion criteria

1. Unable to take tablets
2. Existing treatment with a statin
3. Previous adverse reaction to a statin
4. Coenrolment in other drug trials, or completion of a previous CTIMP within the last 30 days
5. Patients taking any of the following medications: ciclosporin, protease inhibitors, fibrates, ezetimibe, erythromycin (but not other macrolides), eltrombopag, dronedarone, itraconazole, coumarins, oral contraceptives, nicotinic acid, fusidic acid
6. Female participants who are pregnant or lactating or refuse a pregnancy test if of childbearing potential (female participants of childbearing potential must use a barrier method of contraception if sexually active whilst taking rosuvastatin and for 7 days afterwards)
7. Patients of Asian ancestry (Japanese, Chinese, Filipino, Vietnamese, Korean and Indian).
8. Patients with renal disease (eGFR < 60 ml/min/1.73sq. m, using the Schwartz formula, in the 6 months preceding randomisation)
9. Patients with current elevation in transaminases exceeding 3x the upper limit of normal
10. Family history, or personal history, of hereditary muscular disorders
11. Patients with myopathy
12. Patients with a history of, or active alcohol abuse
13. Patients with hypothyroidism
14. Patients with galactose intolerance, the Lapp lactase deficiency, or glucosegalactose malabsorption

Date of first enrolment
01/10/2014

Date of final enrolment
01/09/2016

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Alder Hey Hospital
Liverpool
United Kingdom
L12 2AP

Sponsor information

Organisation
University of Liverpool (UK)

Sponsor details

Department of Clinical Psychology
Thompson Yates Building
Quadrangle Brownlow Hill
Liverpool
England
United Kingdom
L69 3GB

Sponsor type
University/education

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Charity

Funder Name
The JP Moulton Charitable Foundation (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date
31/05/2019

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?
Basic results			21/06/2019	No	No
HRA research summary			26/07/2023	No	No