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A randomised pilot trial of a steroid-free immunosuppressant regimen in paediatric liver transplantation

Submission date 23/04/2010	**Recruitment status** Stopped	[ ] Prospectively registered [ ] Protocol
Registration date 23/04/2010	**Overall study status** Stopped	[ ] Statistical analysis plan [ ] Results
Last Edited 22/10/2013	**Condition category** Surgery	[ ] Individual participant data [ ] Record updated in last year

Plain English summary of protocol

Background and study aims

Who can participate?
This study aims to recruit 30 children and young people under the age of 18 who have a liver transplant at Birmingham Childrens Hospital.

What does the study involve?
Partcipants will be randomly allocated to one of two groups. Half of the patients will receive the immunosuppressive treatment with steroids and the other half will receive the immunosuppressive treatment without steroids. During the year of this study participants will be seen at the normal planned intervals in the outpatient clinic. These planned visits will be at 1, 2, 3, 6, 9 and 12 months after transplant. At each visit the participants will have routine blood tests. These will be the normal blood tests that we do to see how well the liver is working and to check the levels of the immunosuppressive drugs. At one year after the transplant, all of the patients in the study will have a liver biopsy. Liver biopsies are usually carried out if we think the new liver is not working and the biopsy will tell us why. To see whether the liver is working well, all patients should have a routine liver biopsy at one and every five years after transplant.

What are the possible benefits and risks of participating?
With the steroid-free treatment there may be a reduction in the side effects seen compared to the steroid-containing treatment. Patients may also develop tolerance which may allow them to stop taking immunosuppressants. There are no anticipated risks of participating in this study as all extra blood samples will be done at the time when blood is taken for routine blood tests.

Where is the study run from?
The study is being run from the Liver Unit, Birmingham Childrens Hospital, Birmingham, UK.

When is the study starting and how long is it expected to last for?
The study started in May 2008. The trial will run for two years and individual participants will take part in the study for a maximum of one year after liver transplant.

Who is funding the study?
Funding has been provided by Roche Pharmaceuticals.

Who is the main contact?
Dr Patrick McKiernan, pat.mckiernan@bch.nhs.uk
Mrs Carla Lloyd, carla.lloyd@bch.nhs.uk

Contact information

Type(s)
Scientific

Contact name
Dr Patrick McKiernan

Contact details
Birmingham Children's Hospital Liver Unit
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Additional identifiers

EudraCT/CTIS number
2007-004822-26

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
5311

Study information

Scientific Title
Pilot study of a steroid-free nephro-protective immune suppressant regimen in paediatric liver transplantation: a randomised interventional treatment trial

Study objectives
Current hypothesis as of 22/10/2013:
After liver transplant, the immune system will try to reject the new liver. The immune system is very important as it fights off infections caused by foreign bodies such as bacteria and viruses but it will think the new liver is a foreign body and will try to reject it. This is why immunosuppressive medications are given to stop the immune system from rejecting the new liver.

There are many types of immunosuppressive drugs but the ones that we use in the long term are tacrolimus (also known as FK506 or Prograf), mycophenolate mofetil (MMF), and steroids. Daclizumab is also given on the day of transplant, and day 4 and day 18 after the transplant.

In this study we plan to have two regimens, one with steroids and one without. This is to help us compare the two regimens and see whether the new regimen, the steroid-free regimen, works as effectively at stopping the immune system from rejecting the new liver.

Steroids have been used as immunosuppressive drugs since liver transplantation started. We know they are useful in preventing rejection and if rejection does happen are also used in treating the rejection.

However, steroids can cause many side effects and these are listed below:
1. High blood pressure. Patients who develop high blood pressure will also need to take extra drugs
2. Weight gain. Patients who are on steroids put on weight as their appetite increases
3. Height (growth) problems
4. Extra fat in the blood
5. Weak bones

If steroids are taken for a long time the immune system becomes resistant to them so patients may need more steroids to have the same effect.

Steroids may also prevent tolerance developing.

It is hypothesised that a steroid-free regimen is safe and as effective at preventing rejection post transplantation.

Recent evidence suggests that it might be possible to have an immunosuppressive regimen that did not use steroids at all. Steroids would only be used if a patient developed rejection. If this steroid-free immunosuppressive regimen is possible then there would be a number of benefits. There would no side effects from steroids and it would mean that if steroids were only needed to treat rejection they would work better as the body had not had a chance to become used to them. Another benefit might be to help tolerance.

Steroids can stop this happening so those who do not take steroids may become tolerant to their new transplanted organ and eventually may not need to take immunosuppressive drugs at all.

At the moment we don't know whether these benefits of avoiding steroids completely are preferable to a possibly increased risk of rejection. To decide which of these is the best treatment we need to a randomised study.

Previous hypothesis:
The overall objectives are to investigate whether a steroid-free immunosuppressive regimen is as safe and effective as a steroid-containing regimen following paediatric liver transplantation and whether it promotes tolerance.

On 22/10/2013, the following changes were made to the trial record:
1. The public title was changed from " Pilot study of a steroid-free nephro-protective immune suppressant regimen " to "A randomised pilot trial of a steroid-free immunosuppressant regimen in paediatric liver transplantation".

2. The study design was changed from "Randomised interventional treatment trial" to "Two-year open randomised parallel group, single site trial".
3. The anticipated start date was changed from 23/06/2008 to 01/05/2008
4. The anticipated end date was changed from 22/06/2011 to 01/05/2010
Other changes are indicated in the corresponding fields.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Birmingham MREC approved on the 21/02/2008 (ref: 07/H1207/262)

Study design
Two-year open randomised parallel group, single site trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Patient information material available on request from carla.lloyd@bch.nhs.uk

Health condition(s) or problem(s) studied
Topic: Oral and Gastrointestinal; Subtopic: Oral and Gastrointestinal (all Subtopics); Disease: Hepatology

Interventions
Arm 1: Patients randomised to steroid containing immunousppresion regimen post isolated liver transplant
Arm 2: Patients randomised to steroid free immunosuppression regiment post isolated liver transplant

Follow-up length: 12 months
Study entry: single randomisation only

Added 22/10/2013:

Blood tests
Participants will have a little extra blood taken at the same time as routine blood tests. This extra blood will be tested to see how well the participants immune system is working to help prevent infections and also see how it is reacting to the new liver.

Measuring tolerance
Participants will have a planned liver biopsy one year after transplant. This biopsy will be tested to see if we can see any evidence of special cells that help tolerance to develop. Should participants require any extra unplanned biopsies for suspected rejection, these will also be tested for evidence of tolerance.

The trial was prematurely discontinued as Roche withdrew daclizumab from the market, so it was decided to close the study rather than apply for a new authorisation from the MHRA to continue the study with an alternative monoclonal antibody. Recruitment closed September 2009.

Intervention Type
Procedure/Surgery

Phase
Not Specified

Primary outcome measure
Current primary outcome measures as of 22/10/2013:
The development of histologically proven acute rejection within 12 months.

Previous primary outcome measures:
Development of acute rejection; this can occur at any time post-transplant

Secondary outcome measures
Current secondary outcome measures as of 22/10/2013:
1. The development of steroid-resistant acute rejection within 12 months
2. The expression of tissue and circulating markers of immune tolerance in the first year post transplant
3. The incidence of infection in the first year post transplant

Previous secondary outcome measures:
1. Development of steroid-resistant rejection
2. Expression of tissue and circulating markers, analysed in batches. We intend to wait until all the study is closed and all the tests can be run at a single time. This may occur 24 months after the start of the study

Overall study start date
01/05/2008

Completion date
01/05/2010

Reason abandoned (if study stopped)
Objectives no longer viable

Eligibility

Key inclusion criteria

1. Children undergoing primary isolated hepatic transplantation
2. Aged less than or equal to 18 years, either sex
3. Ability to provide informed consent

Participant type(s)
Patient

Age group
Child

Upper age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 30

Key exclusion criteria
1. Children undergoing retransplantation
2. Transplantation for Intestinal failure associated liver disease
3. Multi-organ transplantation
4. Transplantation for autoimmune liver disease
5. Transplantation for extra-hepatic malignancy
6. Pre-existing need for oral steroids, or high-dose inhaled steroids sufficient to require a steroid warning card

Date of first enrolment
01/05/2008

Date of final enrolment
01/05/2010

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Birmingham Children's Hospital Liver Unit
Birmingham
United Kingdom
B4 6NH

Sponsor information

Organisation
Birmingham Children's Hospital (UK)

Sponsor details
Diana Princess Of Wales Childrens Hospital
Steelhouse Lane
Birmingham
England
United Kingdom
B4 6NH

Sponsor type
Hospital/treatment centre

Website
http://www.bch.org.uk/

ROR
https://ror.org/017k80q27

Funder(s)

Funder type
Industry

Funder Name
Current sources of funding as of 22/10/2013:

Funder Name
Roche Ltd (UK) and Local Research Networks

Funder Name
Previous sources of funding:

Funder Name
Roche Ltd (UK)

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