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Randomised controlled trial of total immunosuppression withdrawal in liver transplant recipients: role of ursodeoxycholic acid

Submission date	Recruitment status	[ ] Prospectively registered
14/03/2007	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
28/03/2007	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
02/09/2008	Injury, Occupational Diseases, Poisoning	[ ] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title

Study objectives
In this study we investigate whether oral administration of ursodeoxycholic acid reduces the risk of rejection and recurrence of underlying disease in liver transplant recipients undergoing total immunosuppression withdrawal (TIW).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics approval received from the University of Western Ontario, London, Ontario, Canada on 01 /01/1995. Patients were informed about possible consequences of immunosuppression withdrawal (rejection, recurrence of disease, renal function).

Study design
Randomised, placebo-controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet

Health condition(s) or problem(s) studied
Liver transplantation, rejection, withdrawal of immunosuppressions

Interventions
26 liver recipients who had been free of rejection while on immunosuppressive agents for a minimum of two years will be randomised to receive either 15 mg/kg of ursodeoxycholic acid (UDCA) (N = 14) or identical placebo (N = 12) followed by sequential withdrawal of their immunosuppressive regimen over several months.

Prior to TIW a baseline liver biopsy was obtained and reviewed with a pathologist to exclude sub-clinical rejection and co-existent disease in the graft. Within one week of initiating TIW, patients underwent the following evaluations:

1. Alanine aminotransferase (ALT)
2. Aspartate aminotransferase (AST)
3. Alkaline phosphatase
4. Total bilirubin
5. Creatinine
6. Complete blood count (CBC)
7. Cyclosporin (CyA) levels by means of monoclonal antibody radioimmunoassay on whole blood (Cyclotrac, INCSTAR)

These same parameters were repeated every two weeks for the initial six months post-TIW and then monthly for a year thereafter. Liver biopsies were repeated in those who developed elevated liver enzymes (greater than 2 x normal) and in those who had completed six months of follow up with no immunosuppression other than the study medication. Secondary aims or endpoints such as development of renal failure, hypertension, extent of liver enzymes abnormalities as well as safety and compliance were assessed accordingly.

Intervention Type
Other

Phase
Not Specified

Primary outcome measure
1. Biochemical and histological evidence of rejection
2. Graft dysfunction without rejection
3. Recurrence of pre-transplant disease
4. Six months without immunosuppression and no rejection or dysfunction on repeat liver biopsy

Secondary outcome measures
1. Development of renal failure
2. Hypertension
3. Extent of liver enzymes abnormalities
4. Safety and compliance

Overall study start date
01/01/1995

Completion date
01/12/1996

Eligibility

Key inclusion criteria
Recipients of liver transplantation at the University of Western Ontario, Canada who had stable graft function (no clinical or biochemical evidence of liver disease) for a minimum of two years were offered TIW if they met the following criteria:
1. No documented rejection episodes for at least 24 months prior to the study
2. A minimum post-transplant follow up period of at least 2 years
3. A history of compliance with medications, blood testing for laboratory analyses and in the case of patients transplanted for alcohol-induced liver disease, abstinence from all alcohol beverages during the study period

Participant type(s)
Patient

Age group
Not Specified

Sex
Both

Target number of participants
46

Key exclusion criteria
1. Patients requiring triple anti-rejection therapy for frequent or severe episodes of rejection in the past
2. More than one liver transplant
3. Requiring anti rejection therapy for non-liver disorders (psoriasis, rheumatoid arthritis [RA] etc)

Date of first enrolment
01/01/1995

Date of final enrolment
01/12/1996

Locations

Countries of recruitment
Canada

Study participating centre
Section of hepatology
Ontario
Canada
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Sponsor information

Organisation
University of Western Ontario (Canada)

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Sponsor type
University/education

ROR
https://ror.org/02grkyz14

Funder(s)

Funder type
University/education

Funder Name
University of Western Ontario (Canada) - the Liver Unit

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