

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

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

Protocol serial number

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

Study type(s)

Prevention

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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Not Specified

Sex

All

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)

ROR

<https://ror.org/02grkyz14>

Funder(s)

Funder type

University/education

Funder Name

University of Western Ontario (Canada) - the Liver Unit

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration