An international, multicenter, randomized controlled clinical trial assessing the efficacy of Ursodeoxycholic acid as a volume reducing treatment for symptomatic polycystic livers

Published: 07-08-2013
Last updated: 24-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and biliary neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON38971

Source
ToetsingOnline

Brief title
CURSOR

Condition

- Hepatic and biliary neoplasms benign

Synonym
polycystic liver disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: farmaceutische industie,Zambon

Intervention

Keyword: autosomal dominant kidney disease, liver volume, polycystic liver disease, ursodeoxycholic acid

Outcome measures

Primary outcome

Proportional change of total liver volume in UDCA treated patients versus non

treated patients, as assessed by CT at baseline and 6 months.

Secondary outcome

Main secondary outcome variables:

• To demonstrate whether UDCA-therapy changes absolute total liver volume

• To demonstrate whether UDCA-therapy changes gastro-intestinal symptoms

measured by a GI-questionnaire

• To demonstrate whether UDCA-therapy changes quality of life as measured by

SF-36

• To demonstrate which proportion of patients has any reduction in total liver

volume after 24 weeks

• To demonstrate whether UDCA is well tolerated

• To demonstrate whether UDCA-therapy changes absolute total kidney volume

(TKV).

Study description

Background summary

Polycystic liver disease (PLD) is a rare disorder characterized by >20 fluid-filled hepatic cysts. (1) Polycystic livers are present in the combination with renal cysts as a manifestation of autosomal dominant polycystic kidney disease (ADPKD), or isolated in the absence of renal cysts as autosomal dominant polycystic liver disease (ADPLD or PCLD). PLD patients are confronted with symptoms caused by the mass effect of their polycystic liver every day for the rest of their life. There is no standard therapeutic option for symptomatic PLD patients. Current options are fairly invasive or their efficacy is only moderate.
Preliminary data in our research lab have shown that ursodeoxycholic acid (UDCA) inhibited the proliferation of polycystic human cholangiocytes in vitro through the normalization of the intracellular calcium levels in cystic cholangiocytes. We also found that daily oral administration of UDCA for 5 months to PCK rats, an animal model of ARPKD that spontaneously develops hepato-renal cystogenesis, resulted in inhibition of hepatic cystogenesis.
We hypothesize that UDCA is an effective therapeutic tool in reducing liver volume in PLD.

Study objective

First, to demonstrate whether UDCA-therapy is effective in reducing total liver volume in PLD patients. Second, we want to assess if UDCA modifies quality of life. Finally, we want to assess safety and tolerability.

Study design

International, multicenter, randomized, controlled trial

Intervention

Intervention: The patients will be randomized (1:1) into two groups. One group of patients will receive 15-20mg/kg/day UDCA for 24 weeks. The other group will receive standard care.

Study burden and risks

When compared to routine clinical care the burden and risk associated with participation
are:
• In general PLD patients suffering from isolated liver cysts visit an out-patient department about 1-2 times a year. PLD patients suffering ADPKD with more advanced renal disease (eGFR <= 60 ml/min/1.73 m2) visit an out-patient department once every 3 months routinely. Therefore this study imposes at least 6 extra visits to an outpatient department (screening,

baseline, week 4, 12, 24 and 36)
• For patients that are treated outside the participating UMC hospitals, study visits to the UMCs may lead to extra travel time.
• At screening, baseline and week 24, three blood samples will be drawn. During visit week 4, 12 and 36, two blood samples will be drawn.
• Two times a CT-scan of liver and kidneys
• Two times two questionnaires need to be completed
• Half of the patients will be exposed to the UDCA-therapy

The potential benefit for participating subjects is that UDCA-therapy may reduce total liver volume and thereby potentially leading to less complaints that are related to cyst size and abdominal distension (e.g. abdominal pain, early satiety and dyspnea).

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-Zuid 8
Nijmegen 6525GA
NL
Scientific
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-Zuid 8
Nijmegen 6525GA
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• 18 <= age <= 80 years
• Polycystic liver disease with underlying diagnosis of (PCLD or ADPKD), defined as >= 20 liver cysts
• Total liver volume >= 2500 mL ;• Symptomatic defined as ECOG-PS >= 1 (2), and having at least three out of ten PCLD symptoms:
- Abdominal pain
- Abdominal distension
- Abdominal fullness
- Dyspnea
- Early satiety
- Back pain
- Nausea/vomiting
- Anorexia
- Weight loss
- Jaundice
• Informed consent, patients are willing and able to comply with the study drug regimen and all other study requirements.

Exclusion criteria

• Use of oral anticonceptives or estrogen supplementation
• Use of UDCA in 3 months before baseline
• Females who are pregnant or breast-feeding or patients of reproductive potential not employing an effective method of birth control.
• Intervention (aspiration or surgical intervention) within six months before baseline
• Treatment with somatostatin analogues within months before baseline
• Renal dysfunction (MDRD-GFR < 30 ml/min/1.73m2)
• Patients with a kidney transplant
• Hypersensitivity reaction to UDCA or patients with galactose-intolerance, lactase deficiency or glucose-galactose malabsorption
• Acute cholecystitis or frequent biliary colic attacks
• Acute stomach or duodenal ulcers
• Inflammation of small intestine or colon
• Use of drugs that can interact with UDCA, such as colestyramine or aluminium hydroxide
• Enrolment in another clinical trial of an investigational agent while participating in this study
• History or other evidence of severe illness or any other conditions which would make the patient, in the opinion of the investigator, unsuitable for the study
• Mental illness that interferes with the patient ability to comply with the protocol

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-05-2014
Enrollment:	22
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ursodiol
Generic name:	ursodeoxycholic acid
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	07-08-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	29-11-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	24-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-11-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2013-003207-19-NL
CCMO	NL45792.091.13