Double-blind, randomized, placebo-controlled, phase II dose-finding study comparing different doses of norursodeoxycholic acid capsules with placebo in the treatment of primary sclerosing cholangitis

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Primary:* To evalaute the efficacy of three doses of norUDCA vs. placebo for the treatment of PSC* To identify efficacious norUDCA dose(s) for the treatment of PSC for further evaluation in phase III. Secondary:* To study safety and tolerability (...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Gastrointestinal inflammatory conditions
Study type	Interventional

Summary

ID

NL-OMON39746

Source
ToetsingOnline

Brief title
Norursodeoxycholic acid vs. Placebo in PSC

Condition

- Gastrointestinal inflammatory conditions

Synonym
Primary Sclerosing Cholangitis; bile ducts inflammation with scar formation

Research involving

Human

Sponsors and support

Primary sponsor: Dr. Falk Pharma GmbH
Source(s) of monetary or material Support: Falk Pharma GmbH

Intervention

Keyword: Cholangitis, IBD, norUDCA, PSC

Outcome measures

Primary outcome

Mean relative change (%) of serum alkaline phosphatase (sALP) between baselien visit and EOT visit (last observation carried forward).

Secondary outcome

Proportion of patients with at least 50 % reduction in s-ALP between baseline and EOT (LOCF)

Proportion of patients with normalisation of s-ALP (< upper limit of normal, ULN)

Proportion of patients with partial normalisation of s-ALP (< 1.5 ULN) · s-ALP at each study visit (screening to follow-up)

Absolute and relative changes (%) of s-ALP from baseline to each visit up to EOT, and from EOT to the follow-up visit

*-GT, AST, ALT and serum bilirubin levels at each study visit (screening to follow-up)

Absolute and relative changes (%) of *-GT, AST, ALT and serum bilirubin from baseline to each visit up to EOT, and from EOT to the follow-up visit

Course of pruritus (measured by VAS): absolute change in the pruritus score

from baseline to EOT, and from EOT to the follow-up visit

Course of fatigue (measured by questionnaire): absolute change from baseline to

EOT

Therapeutic success and therapeutic benefit according to physician*s global

assessment (PGA) of efficacy at the EOT visit.

Study description

Background summary

This double-blind, randomised, placeo-controlled, dose-finding study will be the proof of concept study and is the third human exposure study with norUDCA and the first human study to assess efficacy in addition to safety and tolerability. The present dose finding study should provide first information on a safe and effective norUDCA dose administered to humans.
Based on the obtained results in this study, the optimal pharmaceutical dose with regard to clinical outcomes as well as to patient's quality of life will be chosen, to be evaluated in further phase III confirmative trials.

Study objective

Primary:
* To evalaute the efficacy of three doses of norUDCA vs. placebo for the treatment of PSC
* To identify efficacious norUDCA dose(s) for the treatment of PSC for further evaluation in phase III.

Secondary:
* To study safety and tolerability (adverse events, laboratory parameters) of norUDCA
* To assess quality of life.

Study design

Double-blind, randomized, placebo-controlled, parallel, explorative phase II dose-finding study.

Intervention

Double-blind, randomised (1:1:1:1) treatment phase:
Patients will be randmised to be treated during 12 weeks with:
Group A: nor-ursodeocholzuur 500 mg once daily 2x250 mg capsules
Group B: nor-ursodeocholzuur 1000 mg once daily 4x250 mg capsules
Group C: nor-ursodeocholzuur 1500 mg once daily 6x250 mg capsules
Group D: placebo capsules for norUDCA once daily.

Study burden and risks

Physical examination 5x
ECG 2x
Echography of the upper abdomen 2x
Vena puncture 9x
Urine examination 9x
Questionnaires regarding pruritus, general well being and fatigue ake 2x
Completion of a diary (only for patients with concommittant inflammatory bowel disease)
10 visits in total.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Signed informed consent,;2. Male or female patients * 18 and < 80 years,;3. PSC verified by 2 of the following criteria:
* Chronische cholestatic diesease of at least 6 month duration
* Retrograde, operative, percutaneous, or magnestic resonance cholangiography *
* Liver biopsy available for review and compatible with the diagnosis of PSC;
4. Alkaline Phosphatase * 1,5 x ULN at baseline
5. PSC Patients with or without IBD
6. Women of child-bearing potential have to apply during the entire duration of the study a highly effective method of birth control

Exclusion criteria

1. History or presence of other concomitant liver diseases including:;* Positive hepatitis B or C serology (Hbs Ag+, anti-HBc+, anti-HCV;;Note: Patients who present with anti-HBc+ only, may be included if they are HBV-DNA negative);* Primary Biliary Cirrhosis, (AMA-positive);* Wilson*s Disease;* Haemochromatosis;* Autoimmune Hepatitis;* Chronic alcoholic consumption (daily consumption >30g/d);* Biopsy proven NASH;* Cholangiocarcinoma,;2. Treatment with any of the following drugs within the last 3 months prior to baseline: any glucocorticosteroids (including budesonide), azathioprine or other immunosuppressive drugs (e.g. cyclophosphamide, cyclosporine, methotrexate, tacrolimus, 6-mercaptopurine), chlorambucil, pentoxyfylline, penicillamine, pirfenidone, fibrates, biologics (e.g., anti-tumor necrosis factor-alpha therapy), or rifampicin,;5. Child B/C liver cirrhosis,;12. Total bilirubin >3.0 mg/dl (> 51,3µmol/L), at screening or baseline,;13. Both total bilirubin levels > ULN within the last 6 months prior to baseline and a rise of this level by more than 50% within the last 6 months prior to baseline,;14. Albumin < 36 g/L, at screening or baseline,;16. Any relevant systemic disease (e.g., AIDS),;17. Abnormal renal function (Cystatin C >1.15 ULN) at screening and/or at baseline visit,;18. TSH> ULN at screening,;20. Any active malignant disease,;21. Known intolerance/hypersensitivity to study drug, or drugs of similar chemical structure or pharmacological profile

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-04-2013
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	norursodeoxycholic acid

Ethics review

Approved WMO Date:	13-06-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-10-2012
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-11-2012
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-11-2012
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	11-07-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-08-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-11-2013
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-05-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2014
Application type:	Amendment

Review commission: METC Amsterdam UMC

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
Other	EU Clinical Trial Directive
EudraCT	EUCTR2011-002754-31-NL
CCMO	NL40829.018.12