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

Summary

EudraCT number	2013-003207-19
Trial protocol	NL ES
Global end of trial date	16 February 2016

Results information

Result version number	v1 (current)
This version publication date	11 May 2021
First version publication date	11 May 2021
Summary attachment (see zip file)	Journal article UDCA for PLD JHEP 2016 (Article D'Agnolo - UDCA for PLD - JHEP 2016.pdf)

Trial information

Trial identification

Sponsor protocol code	PLD11-01

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02021110
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Radboudumc
Sponsor organisation address	Geert Grooteplein Zuid, Nijmegen, Netherlands, 6525GA
Public contact	Dep.of Gastroenterology&Hepatology, Radboud University Nijmegen Medical Center, 0031 0243619190, joostphdrenth@cs.com
Scientific contact	Dep.of Gastroenterology&Hepatology, Radboud University Nijmegen Medical Center, 0031 0243619190, joostphdrenth@cs.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 February 2016
Global end of trial reached?	Yes
Global end of trial date	16 February 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

First, to demonstrate whether UDCA-therapy is effective in reducing total liver volume in PLD patients.

Protection of trial subjects:

data safety monitoring board was involved

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 30
Country: Number of subjects enrolled	Spain: 4
Worldwide total number of subjects	34
EEA total number of subjects	34

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	28
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Inclusion period: May 2015 untill February 2015

Pre-assignment

Screening details:

38 patients were screened for eligibility and 34 patients were randomized. All patients completed the total follow-up of 36 weeks by November 2015.

Period 1

Period 1 title	Baseline period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

not blinded study

Arms

Are arms mutually exclusive?	Yes
Arm title	UDCA

Arm description:

Eligible patients were randomly assigned in blocks of four in a 1:1 ratio to receive UDCA (Ursochol, Zambon, the Netherlands), orally twice a day, in a dose of 15–20 mg/kg/day for 24 weeks.

Arm type	Experimental
Investigational medicinal product name	ursodeoxycholic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

15–20 mg/kg/day

Arm title	Control group

Arm description:

Underwent follow-up without any clinical trial treatment.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	UDCA	Control group
Started	17	17
Completed	17	17

Baseline characteristics

Reporting groups	
Reporting group title	UDCA
Reporting group description:	
Eligible patients were randomly assigned in blocks of four in a 1:1 ratio to receive UDCA (Ursochol, Zambon, the Netherlands), orally twice a day, in a dose of 15–20 mg/kg/day for 24 weeks.	
Reporting group title	Control group
Reporting group description:	
Underwent follow-up without any clinical trial treatment.	

Reporting group values	UDCA	Control group	Total
Number of subjects	17	17	34
Age categorical			
Control group (n = 17): Age (yr) 48 [43;53] UDCA group (n = 15): Age (yr) 53 [42;58]			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	15	16	31
From 65-84 years	2	1	3
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	16	12	28
Male	1	5	6

End points

End points reporting groups

Reporting group title	UDCA
Reporting group description:	
Eligible patients were randomly assigned in blocks of four in a 1:1 ratio to receive UDCA (Ursochol, Zambon, the Netherlands), orally twice a day, in a dose of 15–20 mg/kg/day for 24 weeks.	
Reporting group title	Control group
Reporting group description:	
Underwent follow-up without any clinical trial treatment.	

Primary: Proportional change in liver volume

End point title	Proportional change in liver volume
End point description:	
The main outcome measure will be the proportional change of total liver volume from baseline to 6 months as determined by CT.	
End point type	Primary
End point timeframe:	
Assessment of end point: February 2015	

End point values	UDCA	Control group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: percentage	7	3		

Statistical analyses

Statistical analysis title	Statistical analysis
Statistical analysis description:	
Continuous variables were expressed as mean (95% confidence interval (CI)) if normally distributed, otherwise as median (interquartile range (IQR)). Primary outcome and secondary outcomes on TLV, TKV, HRQL and symptoms, were tested with independent t-tests between groups and paired sampled t tests comparing baseline and end of study within groups.	
Comparison groups	UDCA v Control group
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	< 0.05 [2]
Method	proportional change TLV
Parameter estimate	proportional change TLV

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	8.8
Variability estimate	Standard deviation

Notes:

[1] - Primary outcome of this trial was proportional change in TLV from baseline to week 24 between UDCA group and control group.
[2] - p

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From May 2014 (first baseline) untill Oktober 2015 (last follow-up visit T3)

Adverse event reporting additional description:

Every visit patients were asked about adverse events which were documented in a table. Supplementary Table 4 in the paper contains all information about adverse events.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Adverse events UDCA

Reporting group description:

A total of 15 (94%) participants in the UDCA group and 12 (71%) in the control group had at least one adverse event (p = 0.085) (Supplementary Table 3).
Most common adverse events in the UDCA group compared to the control group were frequent stools or diarrhea (38% vs. 12%, p = 0.017) probably related to the study drug.

Reporting group title	Adverse events control group

Reporting group description:

A total of 15 (94%) participants in the UDCA group and 12 (71%) in the control group had at least one adverse event (p = 0.085) (Supplementary Table 3).

Serious adverse events	Adverse events UDCA	Adverse events control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 16 (0.00%)	3 / 17 (17.65%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer	Additional description: breast cancer in control group		
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Crushed shoulder	Additional description: crushed shoulder in control group		
subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Brain contusion	Additional description: Brain contusion in control group		

subjects affected / exposed	0 / 16 (0.00%)	1 / 17 (5.88%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Adverse events UDCA	Adverse events control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 16 (6.25%)	1 / 17 (5.88%)	
Gastrointestinal disorders			
Diarrhoea	Additional description: adverse event diarrhea in URSODEOXYCHOLZUUR group		
subjects affected / exposed	1 / 16 (6.25%)	1 / 17 (5.88%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

see JHEP article

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27212247