



Clinical trial results:

Double-blind, randomised, placebo-controlled, phase IIb trial on the efficacy and safety of norursodeoxycholic acid tablets in patients with non-alcoholic steatohepatitis (NASH)

Summary

EudraCT number	2018-003443-31
Trial protocol	CZ GB AT HU PL ES DE LV BE GR NL FR DK PT IT
Global end of trial date	11 March 2025

Results information

Result version number	v1 (current)
This version publication date	06 May 2026
First version publication date	06 May 2026

Trial information

Trial identification

Sponsor protocol code	NUT-3/NAS
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Dr. Falk Pharma GmbH
Sponsor organisation address	Leinenweberstr. 5, Freiburg, Germany, 79108
Public contact	Department of Clinical Research, Dr. Falk Pharma GmbH, +49 76115140, zentrale@drfalkpharma.de
Scientific contact	Department of Clinical Research, Dr. Falk Pharma GmbH, +49 76115140, zentrale@drfalkpharma.de

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	30 June 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	11 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of norursodeoxycholic acid (norUDCA) 1500 mg vs. norUDCA 1000 mg vs. placebo for the treatment of NASH

Protection of trial subjects:

Prior to recruitment of patients, all relevant documents of the clinical study were submitted and approved by the Independent Ethics Committees (IECs) responsible for the participating investigators. Written consent documents embodied the elements of informed consent as described in the Declaration of Helsinki, the ICH Guidelines for Good Clinical Practice (GCP) and were in accordance with all applicable laws and regulations. The informed consent form and patient information sheet described the planned and permitted uses, transfers and disclosures of the patient's personal data and personal health information for purposes of conducting the study. The informed consent form and the patient information sheet further explained the nature of the study, its objectives and potential risks and benefits as well as the date informed consent was given. Before being enrolled in the clinical trial, every patient was informed that participation in this trial was voluntary and that he/she could withdraw from the study at any time without giving a reason and without having to fear any loss in his/her medical care. The patient's consent was obtained in writing before the start of the study. By signing the informed consent, the patient declared that he/she was participating voluntarily and intended to follow the study protocol instructions and the instructions of the investigator and to answer the questions asked during the course of the trial.

The chosen dose range, schedule, and treatment duration was proved to be clinically safe and justifiable. Furthermore, an independent Data and Safety Monitoring Board (DSMB) has been established to closely monitor the patients' safety parameters during the trial

Background therapy:

The treatment of accompanying illnesses not subject to the exclusion criteria in the protocol was permissible if this was not expected to have any effect on the outcome measures used in the trial, the safety of the patient, or to interfere with the trial medication.

Based on the protocol existing, permitted concomitant medication are not to be changed during the treatment phase of the trial.

A Modification of the intake regimen (dosage change, switch between drugs etc.) following ongoing drugs from 6 months prior to screening until EOT/withdrawal visit:

- Antidiabetic drugs (any; including insulin)
- Statins (any)

Evidence for comparator:

As no effective therapy is authorised for the treatment of NASH, a placebo arm was included as control for the assessment of efficacy and safety of the trial drug

Actual start date of recruitment	01 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Austria: 17
Country: Number of subjects enrolled	Czechia: 15
Country: Number of subjects enrolled	Poland: 45
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	Türkiye: 9
Country: Number of subjects enrolled	Ireland: 6
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	Georgia: 3
Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Switzerland: 2
Country: Number of subjects enrolled	France: 2
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Denmark: 1
Worldwide total number of subjects	216
EEA total number of subjects	163

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)	168
From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total 216 patients were enrolled in the study in Austria, Belgium, Czech Republic, Denmark, France, Georgia, Germany, Greece, Hungary, Ireland, Israel, Italy, Latvia, Netherlands, Poland, Portugal, Spain, Switzerland, Turkey and United Kingdom.

Pre-assignment

Screening details:

In total 912 patients were screened for enrolment of the trial, 692 patients with screening failures, 220 were randomized into the trial groups. 216 patients were treated and included in the full analysis set.

Period 1

Period 1 title	Treatment Phase (overall trial) (overall (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The trial was conducted with 3 treatment groups in the form of a parallel group comparison. Participants were assigned to one of the 3 treatment groups via a central randomisation procedure using a 1:1:1 balance.

To guarantee the double-blinding, the trial was conducted using placebo tablets identical in appearance, shape and taste to active substance.

An independent DSMB was established to closely monitor the patients safety parameters.

Arms

Are arms mutually exclusive?	Yes
Arm title	1500 mg norUDCA

Arm description:

Treatment with 1500mg norUDCA once daily (OD) - 3 norUDCA tablets a 500mg

Arm type	Experimental
Investigational medicinal product name	1500 mg norUDCA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

3 norUDCA tablets a 500mg

Arm title	1000 mg norUDCA
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Arm description:

Treatment with 1000 mg norUDCA, once daily (OD), 2 norUDCA tablets a 500 mg, 1 placebo tablet

Arm type	Experimental
Investigational medicinal product name	1000 mg norUDCA
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 norUDCA tablets a 500 mg and 1 placebo tablet once daily (OD)

Arm title	Placebo
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Arm description:

3 placebo tablets once daily (OD)

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

Dosage and administration details:

3 placebo tablets once daily

Number of subjects in period 1	1500 mg norUDCA	1000 mg norUDCA	Placebo
Started	83	70	63
Completed	77	66	54
Not completed	6	4	9
other reasons	-	-	2
Adverse event, non-fatal	5	2	1
changes diabetes treatment	1	-	-
Lack of patients cooperaiton	-	1	1
Patients wish	-	1	5

Baseline characteristics

Reporting groups

Reporting group title	1500 mg norUDCA
Reporting group description:	
Treatment with 1500mg norUDCA once daily (OD) - 3 norUDCA tablets a 500mg	
Reporting group title	1000 mg norUDCA
Reporting group description:	
Treatment with 1000 mg norUDCA, once daily (OD), 2 norUDCA tablets a 500 mg, 1 placebo tablet	
Reporting group title	Placebo
Reporting group description:	
3 placebo tablets once daily (OD)	

Reporting group values	1500 mg norUDCA	1000 mg norUDCA	Placebo
Number of subjects	83	70	63
Age categorical			
Age Group 1 ≤ 65 years			
Units: Subjects			
Adults (18-64 years)	62	59	47
From 65-84 years	21	11	16
Gender categorical			
subgroup analysis for gender (Male/ Female)			
Units: Subjects			
Female	45	37	31
Male	38	33	32

Reporting group values	Total		
Number of subjects	216		
Age categorical			
Age Group 1 ≤ 65 years			
Units: Subjects			
Adults (18-64 years)	168		
From 65-84 years	48		
Gender categorical			
subgroup analysis for gender (Male/ Female)			
Units: Subjects			
Female	113		
Male	103		

End points

End points reporting groups

Reporting group title	1500 mg norUDCA
Reporting group description:	
Treatment with 1500mg norUDCA once daily (OD) - 3 norUDCA tablets a 500mg	
Reporting group title	1000 mg norUDCA
Reporting group description:	
Treatment with 1000 mg norUDCA, once daily (OD), 2 norUDCA tablets a 500 mg, 1 placebo tablet	
Reporting group title	Placebo
Reporting group description:	
3 placebo tablets once daily (OD)	

Primary: Resolution of NASH and/or improvement of fibrosis

End point title	Resolution of NASH and/or improvement of fibrosis
End point description:	
Resolution of NASH, assessed by centrally scored liver histology with NAS component ballooning = 0 and improvement of NAS component inflammation to 0 or 1, and no worsening of fibrosis, defined as no increase in NASH CRN fibrosis stage, from baseline to EOT/withdrawal visit	
AND/OR	
Improvement of fibrosis, defined as decrease in NASH CRN fibrosis stage by at least 1 stage, and no worsening of NASH, defined as neither worsening in NAS component ballooning nor worsening in NAS component inflammation, from baseline to EOT/withdrawal visit	
[binary: yes, no]	
End point type	Primary
End point timeframe:	
Baseline to V9/EOT	

End point values	1500 mg norUDCA	1000 mg norUDCA	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	70	63	
Units: binary				
Yes	28	14	19	
No	55	56	44	

Statistical analyses

Statistical analysis title	Primary efficacy variable 1500 FAS
Statistical analysis description:	
The Primary efficacy variable (PEV) was the resolution of NASH, assessed by centrally scored liver histology with NAS component ballooning = 0 and improvement of NAS component inflammation to 0 or 1, and no worsening of fibrosis, defined as no increase in NASH CRN fibrosis stage, from baseline to EOT/withdrawal visit	
Comparison groups	1500 mg norUDCA v Placebo

Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.2969 ^[2]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.213
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.597
upper limit	2.464

Notes:

[1] - The variable was tested according to the following a priori hierarchical ordering.

1. norUDCA 1500 vs. placebo

2. norUDCA 1000 vs. placebo

[2] - Significance testing was performed in the above defined order. If the first test did not reach statistical significance (alpha = 0.025 one-sided), the second test was only performed in an exploratory manner

Statistical analysis title	Primary efficacy variable 1000 FAS
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Statistical analysis description:

The Primary efficacy variable (PEV) was the resolution of NASH, assessed by centrally scored liver histology with NAS component ballooning = 0 and improvement of NAS component inflammation to 0 or 1, and no worsening of fibrosis, defined as no increase in NASH CRN fibrosis stage, from baseline to EOT/withdrawal visit

Comparison groups	1000 mg norUDCA v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.9165 ^[4]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.256
upper limit	1.266

Notes:

[3] - The variable was tested according to the following a priori hierarchical ordering.

1. norUDCA 1500 vs. placebo

2. norUDCA 1000 vs. placebo

[4] - Significance testing was performed in the above defined order. If the first test did not reach statistical significance (alpha = 0.025 one-sided), the second test was only performed in an exploratory manner

Secondary: Change in NAS

End point title	Change in NAS
End point description:	
NAS Score at V9/EOT minus NAS Score at V0	
End point type	Secondary
End point timeframe:	
From Baseline to EOT/ Withdrawal visit	

End point values	1500 mg norUDCA	1000 mg norUDCA	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	83	70	63	
Units: points				
arithmetic mean (standard deviation)	-1.7 (± 1.58)	-1.1 (± 1.45)	-0.9 (± 1.71)	

Statistical analyses

Statistical analysis title	ANCOVA NAS Score 1500 (FAS)
Statistical analysis description: analysis of covariance (ANCOVA) models with baseline value as covariate and the class variables treatment, country and T2DM	
Comparison groups	1500 mg norUDCA v Placebo
Number of subjects included in analysis	146
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0046
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.229
upper limit	-0.224

Statistical analysis title	ANCOVA NAS Score 1000 (FAS)
Statistical analysis description: analysis of covariance (ANCOVA) models with baseline value as covariate and the class variables treatment, country and T2DM	
Comparison groups	1000 mg norUDCA v Placebo
Number of subjects included in analysis	133
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4051
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.742
upper limit	0.3

Secondary: Normalization of ALT

End point title	Normalization of ALT
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End point description:

ALT \leq 0.8 ULN at EOT/withdrawal visit

End point type	Secondary
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End point timeframe:

at EOT / withdrawal visit

End point values	1500 mg norUDCA	1000 mg norUDCA	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	69	62	57	
Units: binary	20	8	6	

Statistical analyses

Statistical analysis title	Secondary Efficacy Variables, 1500 (FAS)
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Statistical analysis description:

Normalization of ALT

Comparison groups	1500 mg norUDCA v Placebo
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Number of subjects included in analysis	126
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Analysis specification	Pre-specified
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Analysis type	superiority
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P-value	= 0.0134
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Method	ANCOVA
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Parameter estimate	Odds ratio (OR)
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Point estimate	3.512
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	1.298
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upper limit	9.506
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Statistical analysis title	Secondary Efficacy Variables, 1000 (FAS)
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Statistical analysis description:

Normalization of ALT

Comparison groups	1000 mg norUDCA v Placebo
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Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6926
Method	ANCOVA
Parameter estimate	Odds ratio (OR)
Point estimate	1.255
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.407
upper limit	3.87

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period of observation for AEs comprised the time the patient gave informed consent until 4 weeks after EOT/withdrawal visit last.

Adverse event reporting additional description:

treatment-emergent adverse events

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	norUDCA 1500
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Reporting group description:

norUDCA 1500 group Treatment emergent Adverse Events - occurring in at least 5% of the participants

Reporting group title	norUDCA 1000
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Reporting group description:

Treatment emergent adverse events group norUDCA1000

Reporting group title	Placebo Group
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Reporting group description:

Placebo group with number of participants with at least one AE/TEAE

Serious adverse events	norUDCA 1500	norUDCA 1000	Placebo Group
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 83 (15.66%)	11 / 70 (15.71%)	6 / 63 (9.52%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 83 (1.20%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular carcinoma			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroendocrine tumour of the lung			

subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Breast tumour excision			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm surgery			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shoulder operation			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal operation			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia repair			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteral stent removal			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Chest pain			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Product issues			
Unevaluable device issue			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Occult blood			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			

subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Deafness neurosensory			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			

subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric stenosis			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 83 (1.20%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal instability			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 83 (0.00%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
COVID-19 pneumonia			
subjects affected / exposed	1 / 83 (1.20%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst congenital			
subjects affected / exposed	0 / 83 (0.00%)	1 / 70 (1.43%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 83 (2.41%)	0 / 70 (0.00%)	0 / 63 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	norUDCA 1500	norUDCA 1000	Placebo Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 83 (89.16%)	64 / 70 (91.43%)	55 / 63 (87.30%)
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 83 (6.02%)	3 / 70 (4.29%)	5 / 63 (7.94%)
occurrences (all)	6	4	5
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 83 (9.64%)	5 / 70 (7.14%)	6 / 63 (9.52%)
occurrences (all)	10	5	6

Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	1 / 83 (1.20%)	4 / 70 (5.71%)	0 / 63 (0.00%)
occurrences (all)	1	4	0
Abdominal pain upper			
subjects affected / exposed	5 / 83 (6.02%)	4 / 70 (5.71%)	6 / 63 (9.52%)
occurrences (all)	5	4	6
Constipation			
subjects affected / exposed	5 / 83 (6.02%)	5 / 70 (7.14%)	1 / 63 (1.59%)
occurrences (all)	6	7	1
Diarrhoea			
subjects affected / exposed	6 / 83 (7.23%)	4 / 70 (5.71%)	6 / 63 (9.52%)
occurrences (all)	8	4	8
Dry mouth			
subjects affected / exposed	5 / 83 (6.02%)	2 / 70 (2.86%)	0 / 63 (0.00%)
occurrences (all)	5	2	0
Dyspepsia			
subjects affected / exposed	5 / 83 (6.02%)	2 / 70 (2.86%)	3 / 63 (4.76%)
occurrences (all)	5	2	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 83 (7.23%)	3 / 70 (4.29%)	1 / 63 (1.59%)
occurrences (all)	7	3	1
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	5 / 83 (6.02%)	1 / 70 (1.43%)	4 / 63 (6.35%)
occurrences (all)	5	1	4
Rash			
subjects affected / exposed	5 / 83 (6.02%)	1 / 70 (1.43%)	1 / 63 (1.59%)
occurrences (all)	6	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 83 (9.64%)	3 / 70 (4.29%)	4 / 63 (6.35%)
occurrences (all)	8	3	4
Back pain			

subjects affected / exposed occurrences (all)	3 / 83 (3.61%) 3	2 / 70 (2.86%) 2	6 / 63 (9.52%) 6
Infections and infestations			
COVID-19			
subjects affected / exposed	11 / 83 (13.25%)	9 / 70 (12.86%)	8 / 63 (12.70%)
occurrences (all)	11	10	10
Influenza			
subjects affected / exposed	2 / 83 (2.41%)	0 / 70 (0.00%)	4 / 63 (6.35%)
occurrences (all)	2	0	4
Nasopharyngitis			
subjects affected / exposed	6 / 83 (7.23%)	6 / 70 (8.57%)	4 / 63 (6.35%)
occurrences (all)	6	7	5
Upper respiratory tract infection			
subjects affected / exposed	5 / 83 (6.02%)	4 / 70 (5.71%)	1 / 63 (1.59%)
occurrences (all)	5	7	1
Urinary tract infection			
subjects affected / exposed	8 / 83 (9.64%)	6 / 70 (8.57%)	4 / 63 (6.35%)
occurrences (all)	12	8	7
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	5 / 83 (6.02%)	4 / 70 (5.71%)	5 / 63 (7.94%)
occurrences (all)	5	4	5
Dyslipidaemia			
subjects affected / exposed	5 / 83 (6.02%)	0 / 70 (0.00%)	1 / 63 (1.59%)
occurrences (all)	5	0	1
Vitamin D deficiency			
subjects affected / exposed	2 / 83 (2.41%)	4 / 70 (5.71%)	0 / 63 (0.00%)
occurrences (all)	2	4	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2020	Global version 2.0; Inclusion of local amendments in the global protocol
22 April 2020	Global Version 3.0: - Enabling of phone visits instead of site visits due to COVID-19 pandemic - Local laboratories are allowed for visits V2 to V8 in case of restrictions due to COVID-19 pandemic
25 January 2021	Global version 4.0; Change in the time window for screening liver biopsy from 90 to 180 days * Deletion of inclusion criterion 3 ("ALT > 0.8 ULN") * Additional questions regarding compliance added in the eCRF at V5, V7, and EoT * Estimated number of centres increased from 90 to 120 * Extension of the trial to Asia

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported