Clinical trial results:
Double-blind, randomised, placebo-controlled, phase II dose-finding study comparing different doses of RhuDex granules with placebo in the treatment of primary biliary cholangitis

Summary

EudraCT number	2020-001961-34
Trial protocol	DE GB HU SK NL BE PL IT
Global end of trial date	03 May 2023

Results information

Result version number	v1 (current)
This version publication date	06 March 2024
First version publication date	06 March 2024

Trial information

Trial identification

Sponsor protocol code	RDG-1/PBC

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 im Breisgau, Germany, 79108
Public contact	Headquarters, Dr. Falk Pharma GmbH, +49 76115140, zentrale@drfalkpharma.de
Scientific contact	Headquarters, 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	17 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 May 2023
Global end of trial reached?	Yes
Global end of trial date	03 May 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of 3 doses of RhuDex versus (vs) placebo for the treatment of primary biliary cholangitis (PBC) in patients with an inadequate response to ursodeoxycholic acid (UDCA)

Protection of trial subjects:

Close supervision of subjects by implementing interim visits every 14 days for the first 4 weeks and every 4 weeks up to week 12 and one follow up visit at week 16 to guarantee their safety and wellbeing. 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.

Background therapy:

All patients were to continue their pre-trial dose of UDCA throughout trial participation without changing the dosing regimen

Evidence for comparator:

As all patients will continue standard of care treatment with UDCA, a placebo arm will be included as control due to regulatory recommendations to evaluate dose-related benefits and adverse effects in randomised, double-blind, placebo controlled studies.

Actual start date of recruitment	03 March 2021
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	Netherlands: 3
Country: Number of subjects enrolled	Poland: 2
Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United Kingdom: 7

Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Czechia: 20
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Italy: 5
Worldwide total number of subjects	82
EEA total number of subjects	75

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)	68
From 65 to 84 years	14
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In total 82 patients were included in Belgium, Czech republic, Germany, Hungary, Italy, The Netehrlands, Poland, Slovakia, Spain and United Kingdom from March 2021 to May 2023.

Pre-assignment

Screening details:

A total of 120 patients were screened for the trial, 38 of whom were screening failures. A total of 82 patients were randomized. 79 patients were treated and included in the full analysis set.

Period 1

Period 1 title	Treatment Phase (overall trial) (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:

Blinding was achieved by the application of the same amount of granules for each verum dose and placebo to each patient. Placebo granules matched verum granules in size, taste, and appearance; the granules of both verum and placebo were filled in identical sachets.

Arms

Are arms mutually exclusive?	Yes
Arm title	RhuDex 25 mg twice daily

Arm description:

RhuDex 25 mg twice daily

Arm type	Experimental
Investigational medicinal product name	25 mg RhuDex orally twice daily
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use

Dosage and administration details:

RhuDex 25 mg twice daily
To be taken orally unchewed twice daily in the morning and evening about 30 to 60 minutes before a meal with plenty of water.

Arm title	RhuDex 50 mg twice daily

Arm description:

RhuDex 50 mg twice daily

Arm type	Experimental
Investigational medicinal product name	50 mg RhuDex orally twice daily
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use

Dosage and administration details:

50 mg RhuDex orally twice daily
To be taken orally unchewed twice daily in the morning and evening about 30 to 60 minutes before a meal with plenty of water.

Arm title	RhuDex 100 mg orally twice daily

Arm description:	
RhuDex 100 mg orally twice daily	
Arm type	Experimental
Investigational medicinal product name	100 mg RhuDex orally twice daily
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use
Dosage and administration details:	
RhuDex 100 mg twice daily To be taken orally unchewed twice daily in the morning and evening about 30 to 60 minutes before a meal with plenty of water.	
Arm title	Placebo
Arm description:	
Placebo	
Arm type	Placebo
Investigational medicinal product name	Placebo for RhuDex orally twice daily
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules in sachet
Routes of administration	Oral use
Dosage and administration details:	
Placebo for RhuDex twice daily To be taken orally unchewed twice daily in the morning and evening about 30 to 60 minutes before a meal with plenty of water.	

Number of subjects in period 1[1]	RhuDex 25 mg twice daily	RhuDex 50 mg twice daily	RhuDex 100 mg orally twice daily
Started	20	21	19
Completed	15	14	11
Not completed	5	7	8
Consent withdrawn by subject	-	2	1
Adverse event, non-fatal	3	1	5
violation of inclusion/exclusion criteria	-	-	2
study terminated by sponsor	2	3	-
other reason	-	1	-

Number of subjects in period 1[1]	Placebo
Started	19
Completed	18
Not completed	1
Consent withdrawn by subject	-
Adverse event, non-fatal	-
violation of inclusion/exclusion criteria	-

study terminated by sponsor	1
other reason	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 82 patients were randomized. 3 patients have been randomized but not treated. Baseline characteristics are only reported for the 79 patients having received treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Phase (overall trial)
Reporting group description:	
82 patients were randomized. 3 patients have been randomized but not treated. Baseline characteristics are only reported for the 79 patients having received treatment.	

Reporting group values	Treatment Phase (overall trial)	Total	
Number of subjects	79	79	
Age categorical Units: Subjects			
Adults (18-64 years)	66	66	
From 65-84 years	13	13	
Age continuous Units: years			
median	56		
full range (min-max)	37 to 70	-	
Gender categorical Units: Subjects			
Female	74	74	
Male	5	5	

End points

End points reporting groups

Reporting group title	RhuDex 25 mg twice daily
Reporting group description: RhuDex 25 mg twice daily	
Reporting group title	RhuDex 50 mg twice daily
Reporting group description: RhuDex 50 mg twice daily	
Reporting group title	RhuDex 100 mg orally twice daily
Reporting group description: RhuDex 100 mg orally twice daily	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Relative change (%) in alkaline phosphatase from Baseline to end of treatment

End point title	Relative change (%) in alkaline phosphatase from Baseline to end of treatment
End point description:	
End point type	Primary
End point timeframe: 12 weeks treatment: from Baseline to end of treatment , LOCF (last observation carried forward)	

End point values	RhuDex 25 mg twice daily	RhuDex 50 mg twice daily	RhuDex 100 mg orally twice daily	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	21	19	19
Units: %				
arithmetic mean (confidence interval 95%)	3.50 (-1.71 to 8.70)	1.75 (-8.35 to 11.85)	9.86 (-1.69 to 21.42)	-1.53 (-8.03 to 4.97)

Statistical analyses

Statistical analysis title	Rhudex 25mg twice daily vs Placebo
Comparison groups	Placebo v RhuDex 25 mg twice daily

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7884 [1]
Method	pairwise Wilcoxon rank sum test

Notes:

[1] - P-value from pairwise Wilcoxon rank sum test, one sided

Statistical analysis title	Rhudex 50mg twice daily vs Placebo
Comparison groups	Placebo v RhuDex 50 mg twice daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6068 [2]
Method	pairwise Wilcoxon rank sum test

Notes:

[2] - P-value from pairwise Wilcoxon rank sum test, one sided

Statistical analysis title	Rhudex 100mg twice daily vs Placebo
Comparison groups	Placebo v RhuDex 50 mg twice daily
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9575 [3]
Method	pairwise Wilcoxon rank sum test

Notes:

[3] - P-value from pairwise Wilcoxon rank sum test, one sided

Secondary: Partial normalization of serum alkaline phsophatase (ALP)	
End point title	Partial normalization of serum alkaline phsophatase (ALP)

End point description:

Partial normalization ALP serum level <1.5 × upper limit of normal at 1 or more scheduled postbaseline visits up to EOT

End point type	Secondary

End point timeframe:

12 weeks treatment: from Baseline to end of treatment , LOCF (last observation carried forward)

End point values	RhuDex 25 mg twice daily	RhuDex 50 mg twice daily	RhuDex 100 mg orally twice daily	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	21	19	19
Units: Patients	0	2	2	5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse Events were assessed at V1 (Baseline visit), V2, V3, V4, V5 (End of Treatment visit) and V6 (Follow-Up Visit) .	
Adverse event reporting additional description:	
Treatment emergent adverse events	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups	
Reporting group title	RhuDex 25 mg twice daily
Reporting group description: -	
Reporting group title	RhuDex 50 mg twice daily
Reporting group description: -	
Reporting group title	RhuDex 100 mg twice daily
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	RhuDex 25 mg twice daily	RhuDex 50 mg twice daily	RhuDex 100 mg twice daily
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	1 / 19 (5.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo		
Total subjects affected by serious adverse events			

subjects affected / exposed	0 / 19 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	RhuDex 25 mg twice daily	RhuDex 50 mg twice daily	RhuDex 100 mg twice daily
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 20 (60.00%)	12 / 21 (57.14%)	16 / 19 (84.21%)
Vascular disorders			
Hot flush			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Axillary pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Chest pain			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0

Discomfort			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 20 (5.00%)	3 / 21 (14.29%)	3 / 19 (15.79%)
occurrences (all)	1	3	3
Influenza like illness			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood cholesterol increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Glutamate dehydrogenase increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Weight decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	4 / 20 (20.00%)	3 / 21 (14.29%)	5 / 19 (26.32%)
occurrences (all)	4	3	7
Lethargy			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Tremor			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			

Leukopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Photopsia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	3 / 19 (15.79%)
occurrences (all)	0	3	3
Abdominal pain upper			
subjects affected / exposed	2 / 20 (10.00%)	1 / 21 (4.76%)	2 / 19 (10.53%)
occurrences (all)	2	1	2
Diarrhoea			
subjects affected / exposed	1 / 20 (5.00%)	2 / 21 (9.52%)	5 / 19 (26.32%)
occurrences (all)	1	2	5
Dyspepsia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	3 / 20 (15.00%)	2 / 21 (9.52%)	3 / 19 (15.79%)
occurrences (all)	3	2	3
Toothache			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Vomiting			

subjects affected / exposed	1 / 20 (5.00%)	1 / 21 (4.76%)	2 / 19 (10.53%)
occurrences (all)	1	2	2
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 20 (10.00%)	2 / 21 (9.52%)	2 / 19 (10.53%)
occurrences (all)	2	2	2
Renal and urinary disorders			
Urinary incontinence			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 21 (9.52%)	1 / 19 (5.26%)
occurrences (all)	0	2	1
Back pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Plantar fasciitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Cystitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Fungal infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pharyngitis streptococcal			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Pneumonia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Respiratory tract infection bacterial			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Tonsillitis bacterial			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 20 (0.00%)	1 / 21 (4.76%)	2 / 19 (10.53%)
occurrences (all)	0	1	2
Hyperglycaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Impaired fasting glucose			
subjects affected / exposed	0 / 20 (0.00%)	0 / 21 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus			

subjects affected / exposed	1 / 20 (5.00%)	0 / 21 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 19 (52.63%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Axillary pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Chest pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Discomfort			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Influenza like illness			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		

Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Restlessness			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Blood cholesterol increased			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Glutamate dehydrogenase increased			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			

subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0 0 / 19 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Lethargy subjects affected / exposed occurrences (all) Restless legs syndrome subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 2 2 / 19 (10.53%) 2 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0		
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0		
Ear and labyrinth disorders Meniere's disease subjects affected / exposed occurrences (all)	 1 / 19 (5.26%) 1		
Eye disorders Photopsia subjects affected / exposed occurrences (all)	 0 / 19 (0.00%) 0		
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0		
Dyspepsia subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0		
Flatulence subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0		
Nausea subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 2		
Toothache subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 3		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Pruritus subjects affected / exposed occurrences (all)	2 / 19 (10.53%) 6		
Renal and urinary disorders Urinary incontinence subjects affected / exposed occurrences (all)	1 / 19 (5.26%) 1		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Plantar fasciitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Muscular weakness			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Cystitis			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Fungal infection			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Herpes zoster			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	4 / 19 (21.05%)		
occurrences (all)	4		
Pharyngitis streptococcal			
subjects affected / exposed	0 / 19 (0.00%)		
occurrences (all)	0		
Pneumonia			

subjects affected / exposed occurrences (all) Respiratory tract infection bacterial subjects affected / exposed occurrences (all) Tonsillitis bacterial subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Impaired fasting glucose subjects affected / exposed occurrences (all) Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0 0 / 19 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2021	One global amendment was issued to Clinical Trial Protocol Version 1.0, dated 06-Jul-2020. The new protocol version 2.0, dated 27-Jan-2021, has been made to consolidate and implement all comments of the Competent Authorities and the Ethics Committees.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported