



Clinical trial results:

A Phase II Randomized, Double-blind, Placebo-controlled, Proof-of-Concept Study to Evaluate the Safety and Efficacy of Cotadutide in Participants with Non-cirrhotic Non-alcoholic Steatohepatitis with Fibrosis

Summary

EudraCT number	2021-005484-53
Trial protocol	DE GR AT ES IT FR HU
Global end of trial date	19 April 2024

Results information

Result version number	v1 (current)
This version publication date	03 May 2025
First version publication date	03 May 2025

Trial information

Trial identification

Sponsor protocol code	D5671C00006
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05364931
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Karlebyhusentrén, B674, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.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	11 June 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 April 2024
Global end of trial reached?	Yes
Global end of trial date	19 April 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the safety and tolerability of cotadutide as compared with placebo in participants with non-cirrhotic NASH with fibrosis
- To assess the immunogenicity of cotadutide

Protection of trial subjects:

The study was conducted in accordance with ethical principles that had their origin in the Declaration of Helsinki and were consistent with International Committee on Harmonization of Good Clinical Practice (ICH GCP), the AstraZeneca policy on Bioethics and Human Biological Samples, and all applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 July 2022
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	United States: 22
Country: Number of subjects enrolled	Japan: 8
Country: Number of subjects enrolled	Malaysia: 3
Country: Number of subjects enrolled	Korea, Republic of: 2
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Austria: 3
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Greece: 1
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	New Zealand: 1
Country: Number of subjects enrolled	South Africa: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 2
Worldwide total number of subjects	54
EEA total number of subjects	11

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)	41
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The screening period was up to 56 days, during which time eligibility criteria were assessed and the participant received a liver biopsy if they did not have a historical biopsy that could be used to determine eligibility for the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cotadutide 300 ug

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 ug daily

Arm title	Cotadutide 600 ug
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

600 ug daily

Arm title	Placebo 300 ug
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Arm description: -

Arm type	Placebo
Investigational medicinal product name	Placebo for cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

300 ug daily

Arm title	Placebo 600 ug
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Arm description: -	
Arm type	Placebo
Investigational medicinal product name	Placebo for cotadutide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
600 ug daily	

Number of subjects in period 1	Cotadutide 300 ug	Cotadutide 600 ug	Placebo 300 ug
Started	17	18	10
Completed	14	14	8
Not completed	3	4	2
Consent withdrawn by subject	1	1	2
Adverse event, non-fatal	-	2	-
Discontinued	1	-	-
study terminated by sponsor	-	1	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Placebo 600 ug
Started	9
Completed	5
Not completed	4
Consent withdrawn by subject	3
Adverse event, non-fatal	1
Discontinued	-
study terminated by sponsor	-
Lost to follow-up	-

Baseline characteristics

Reporting groups

Reporting group title	Cotadutide 300 ug
Reporting group description: -	
Reporting group title	Cotadutide 600 ug
Reporting group description: -	
Reporting group title	Placebo 300 ug
Reporting group description: -	
Reporting group title	Placebo 600 ug
Reporting group description: -	

Reporting group values	Cotadutide 300 ug	Cotadutide 600 ug	Placebo 300 ug
Number of subjects	17	18	10
Age Categorical Units: Participants			
>= 65	4	4	3
>=50 - <65	7	7	4
< 50	6	7	3
Age Continuous Units: Years			
arithmetic mean	54.4	53.0	56.9
standard deviation	± 12.4	± 12.6	± 11.6
Sex: Female, Male Units: Participants			
Female	11	10	4
Male	6	8	6
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	5	9	2
Black or African American	0	1	0
Multiple	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Not Reported	1	0	0
Other	0	0	0
White	11	8	7

Reporting group values	Placebo 600 ug	Total	
Number of subjects	9	54	
Age Categorical Units: Participants			
>= 65	2	13	
>=50 - <65	5	23	
< 50	2	18	
Age Continuous Units: Years			
arithmetic mean	56.4		

standard deviation	± 9.4	-	
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Sex: Female, Male			
Units: Participants			
Female	6	31	
Male	3	23	
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	1	2	
Asian	2	18	
Black or African American	0	1	
Multiple	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Not Reported	0	1	
Other	0	0	
White	6	32	

End points

End points reporting groups

Reporting group title	Cotadutide 300 ug
Reporting group description: -	
Reporting group title	Cotadutide 600 ug
Reporting group description: -	
Reporting group title	Placebo 300 ug
Reporting group description: -	
Reporting group title	Placebo 600 ug
Reporting group description: -	

Primary: Safety and tolerability will be evaluated in terms of AEs, vital signs, clinical and laboratory assessments, and ECG.

End point title	Safety and tolerability will be evaluated in terms of AEs, vital signs, clinical and laboratory assessments, and ECG. ^[1]
End point description:	
End point type	Primary
End point timeframe:	
From first dose of IP through the end of study.	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The CSP was amended to stop enrollment into the trial early and in the same amendment all primary and secondary efficacy endpoints were reclassified as exploratory endpoints and the primary objective for the trial was changed to one related to safety. Analyses of safety were descriptive only and thus there were not statistical analyses of a primary endpoint.

End point values	Cotadutide 300 ug	Cotadutide 600 ug	Placebo 300 ug	Placebo 600 ug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	18	10	9
Units: Number of participants				
Number of participants with an adverse event	16	17	8	5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of IP through the end of study.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	26.1
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Reporting groups

Reporting group title	Cotadutide 300 ug
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Reporting group description:

Description (Arm-group)

Reporting group title	Placebo 600 ug
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Reporting group description:

Description (Arm-group)

Reporting group title	Placebo 300 ug
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Reporting group description:

Description (Arm-group)

Reporting group title	Cotadutide 600 ug
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Reporting group description:

Description (Arm-group)

Serious adverse events	Cotadutide 300 ug	Placebo 600 ug	Placebo 300 ug
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Cardiac disorders			
Atrioventricular block complete			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (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
Atrioventricular block second degree			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (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
General disorders and administration site conditions			
Pacemaker generated arrhythmia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (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

Serious adverse events	Cotadutide 600 ug		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 18 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Cardiac disorders			
Atrioventricular block complete			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrioventricular block second degree			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pacemaker generated arrhythmia			
subjects affected / exposed	0 / 18 (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: 1 %

Non-serious adverse events	Cotadutide 300 ug	Placebo 600 ug	Placebo 300 ug
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	5 / 9 (55.56%)	8 / 10 (80.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			

Face oedema subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Exercise tolerance decreased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Early satiety subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Injection site bruising subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Injection site pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Injection site pruritus subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	2 / 9 (22.22%) 2	0 / 10 (0.00%) 0
Injection site reaction subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 9 (0.00%) 0	2 / 10 (20.00%) 3
Pyrexia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Injection site haemorrhage subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Reproductive system and breast disorders Testicular pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Respiratory, thoracic and mediastinal disorders			

Obstructive sleep apnoea syndrome subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Productive cough subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Sinus congestion subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Cough subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Amylase increased subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Blood pressure increased subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Lipase increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood cholesterol increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Epicondylitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Head injury			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Tendon rupture			

subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 9 (11.11%) 2	0 / 10 (0.00%) 0
Ligament sprain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Joint injury subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Immunisation reaction subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	0 / 9 (0.00%) 0	2 / 10 (20.00%) 2
Lethargy subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Somnolence subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Ear and labyrinth disorders			

Excessive cerumen production subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Vertigo subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal disorders			
Food poisoning subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Abdominal discomfort subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 9 (11.11%) 1	1 / 10 (10.00%) 1
Diarrhoea subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Dry mouth subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Flatulence subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Gastrointestinal pain			

subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	5 / 17 (29.41%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	7	0	1
Toothache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Umbilical hernia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	5 / 17 (29.41%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	7	0	0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Onychoclasia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 17 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Vitiligo			
subjects affected / exposed	0 / 17 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Nephrolithiasis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Musculoskeletal and connective tissue disorders			
Flank pain subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Intervertebral disc degeneration subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Intervertebral disc protrusion subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Osteopenia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Rotator cuff syndrome subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Tendon disorder subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 9 (11.11%) 1	0 / 10 (0.00%) 0
Infections and infestations			
Pneumonia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Folliculitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Gingivitis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Helicobacter gastritis subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Influenza			

subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 17 (11.76%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Covid-19			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Iron deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyperamylasaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Folate deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Decreased appetite subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Increased appetite subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 9 (0.00%) 0	1 / 10 (10.00%) 1
Vitamin d deficiency subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0
Vitamin b12 deficiency subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 9 (0.00%) 0	0 / 10 (0.00%) 0

Non-serious adverse events	Cotadutide 600 ug		
Total subjects affected by non-serious adverse events subjects affected / exposed	17 / 18 (94.44%)		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
General disorders and administration site conditions Face oedema subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Exercise tolerance decreased subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Early satiety subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Injection site bruising subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Injection site pain			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injection site pruritus			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injection site reaction			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Pyrexia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Injection site haemorrhage			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Testicular pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Obstructive sleep apnoea syndrome			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Productive cough			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Sinus congestion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Cough			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Amylase increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood pressure increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Glycosylated haemoglobin increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Blood cholesterol increased			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Injury, poisoning and procedural complications			
Fibula fracture			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Fall			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Epicondylitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Contusion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Tendon rupture			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Ligament sprain			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Immunisation reaction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Cardiac disorders			

Palpitations subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Headache subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Lethargy subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Somnolence subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Ear and labyrinth disorders Excessive cerumen production subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Vertigo subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Gastrointestinal disorders Food poisoning subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Abdominal discomfort subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		

Abdominal distension			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	7		
Dry mouth			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gastrointestinal pain			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	9 / 18 (50.00%)		
occurrences (all)	14		
Toothache			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Umbilical hernia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	8		

Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Onychoclasia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pruritus			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Vitiligo			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Intervertebral disc degeneration			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Osteopenia			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Rotator cuff syndrome			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Tendon disorder			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		
Gingivitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Helicobacter gastritis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Influenza			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Nasopharyngitis			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	4		
Otitis media			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pharyngitis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		

Urinary tract infection subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Covid-19 subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 5		
Metabolism and nutrition disorders			
Iron deficiency subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Hypoglycaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 3		
Hyperamylasaemia subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Folate deficiency subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Decreased appetite subjects affected / exposed occurrences (all)	4 / 18 (22.22%) 4		
Type 2 diabetes mellitus subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Increased appetite subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Vitamin d deficiency subjects affected / exposed occurrences (all)	0 / 18 (0.00%) 0		
Vitamin b12 deficiency			

subjects affected / exposed	0 / 18 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2022	Version No 2.0
15 May 2023	Version No 3.0

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported