Clinical trial results:
A Phase 2b, Multicentre, Randomised, Double-blind, Placebo-controlled, and Open-label Comparator Study of Cotadutide in Participants Who Have Chronic Kidney Disease with Type 2 Diabetes.

Summary

EudraCT number	2020-000255-12
Trial protocol	GB DE
Global end of trial date	08 March 2022

Results information

Result version number	v1 (current)
This version publication date	20 March 2023
First version publication date	20 March 2023

Trial information

Trial identification

Sponsor protocol code	D5676C00001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04515849
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Granta Park, Cambridge, United Kingdom, CB21 6GH
Public contact	Global Clinical Lead, AstraZeneca, +1 18772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 18772409479, 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	21 June 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 March 2022
Global end of trial reached?	Yes
Global end of trial date	08 March 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This Phase 2b study is designed to evaluate the efficacy, safety, tolerability, and pharmacokinetic (PK) profile of cotadutide at different dose levels in participants who have CKD with T2DM.

Protection of trial subjects:

In the study, fasting was minimised and continuous glucose monitoring (CGM) was used instead of more invasive glucose measures to reduce participant discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2020
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	Japan: 26
Country: Number of subjects enrolled	Spain: 61
Country: Number of subjects enrolled	Germany: 34
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Canada: 59
Country: Number of subjects enrolled	New Zealand: 31
Country: Number of subjects enrolled	Australia: 18
Worldwide total number of subjects	248
EEA total number of subjects	111

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)	77
From 65 to 84 years	171
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 79 participating sites in Canada, Australia, New Zealand, Japan, Germany, Poland, Spain and United Kingdom. First subject enrolled 31st August 2020. Last subject last visit: 28th June 2021.

Pre-assignment

Screening details:

This is a parallel treatment, double-blind study with 5 arms.The study had a 14-day run-in period during which participants will be given advice on diet and exercise and asked to wear a CGM sensor, followed by a 26-week treatment period and 28-day follow-up period.

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	Investigator, Monitor, Carer, Data analyst, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Cotadutide 100 ug

Arm description:

Participants randomised to Cotadutide 100 ug daily

Arm type	Experimental
Investigational medicinal product name	Cotadutide 100 ug
Investigational medicinal product code	MEDI0382
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

100 ug, subcutaneous

Arm title	Cotadutide 300 ug

Arm description:

Participants randomised to Cotadutide 300 ug daily

Arm type	Experimental
Investigational medicinal product name	Cotadutide 300 ug
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use

Dosage and administration details:

300 ug, Subcutaneous

Arm title	Cotadutide 600 ug

Arm description:

Participants randomised to Cotadutide 600 ug daily

Arm type	Experimental

Investigational medicinal product name	Cotadutide 600 ug
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details: 600 ug, subcutaneous	
Arm title	Placebo
Arm description: Participants randomised to placebo daily	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled pen
Routes of administration	Subcutaneous use
Dosage and administration details: subcutaneous	
Arm title	Semaglutide 1 mg
Arm description: Participants radomised to active comparator daily	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug
Started	52	49	51
Completed	49	45	50
Not completed	3	4	1
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	1	2	1
Other:randomised by error	-	1	-
Adverse event, non-fatal	-	-	-
Other:family emergency	-	-	-
Protocol deviation	-	1	-

Number of subjects in period 1	Placebo	Semaglutide 1 mg
Started	51	45
Completed	48	43
Not completed	3	2
Adverse event, serious fatal	-	1
Consent withdrawn by subject	-	-
Other:randomised by error	-	-
Adverse event, non-fatal	1	-

Other:family emergency	1	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Cotadutide 100 ug
Reporting group description:	
Participants randomised to Cotadutide 100 ug daily	
Reporting group title	Cotadutide 300 ug
Reporting group description:	
Participants randomised to Cotadutide 300 ug daily	
Reporting group title	Cotadutide 600 ug
Reporting group description:	
Participants randomised to Cotadutide 600 ug daily	
Reporting group title	Placebo
Reporting group description:	
Participants randomised to placebo daily	
Reporting group title	Semaglutide 1 mg
Reporting group description:	
Participants radomised to active comparator daily	

Reporting group values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug
Number of subjects	52	49	51
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	17	13	23
From 65-84 years	35	36	28
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	67.2	65.7	66.1
standard deviation	± 7.3	± 8.8	± 7.4
Sex: Female, Male Units: Participants			
Female	9	3	10
Male	43	46	41
Race (NIH/OMB) Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
ASIAN	10	10	13
BLACK OR AFRICAN AMERICAN	2	0	0
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	2	0	1

OTHER	0	3	1
WHITE	38	36	36

Reporting group values	Placebo	Semaglutide 1 mg	Total
Number of subjects	51	45	248
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	10	14	77
From 65-84 years	41	31	171
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	69.5	67.0	
standard deviation	± 7.3	± 7.8	-
Sex: Female, Male Units: Participants			
Female	13	12	47
Male	38	33	201
Race (NIH/OMB) Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
ASIAN	10	2	45
BLACK OR AFRICAN AMERICAN	1	2	5
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	1	0	4
OTHER	0	0	4
WHITE	39	41	190

Subject analysis sets	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: Intent to treat	

Reporting group values	ITT		
Number of subjects	248		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	171		
From 65-84 years	77		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean	67.1		
standard deviation	± 7.8		
Sex: Female, Male			
Units: Participants			
Female			
Male			
Race (NIH/OMB)			
Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE			
ASIAN			
BLACK OR AFRICAN AMERICAN			
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER			
OTHER			
WHITE			

End points

End points reporting groups

Reporting group title	Cotadutide 100 ug
Reporting group description:	
Participants randomised to Cotadutide 100 ug daily	
Reporting group title	Cotadutide 300 ug
Reporting group description:	
Participants randomised to Cotadutide 300 ug daily	
Reporting group title	Cotadutide 600 ug
Reporting group description:	
Participants randomised to Cotadutide 600 ug daily	
Reporting group title	Placebo
Reporting group description:	
Participants randomised to placebo daily	
Reporting group title	Semaglutide 1 mg
Reporting group description:	
Participants radomised to active comparator daily	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Intent to treat	

Primary: Percentage change in UACR of cotadutide at different dose levels compared to placebo after 14 weeks

End point title	Percentage change in UACR of cotadutide at different dose levels compared to placebo after 14 weeks[1][2]
End point description:	
Percentage change in UACR of cotadutide at different dose levels compared to placebo after 14 weeks. Efficacy endpoints for cotadutide vs. semaglutide are exploratory and are therefore excluded.	
End point type	Primary
End point timeframe:	
Baseline to the end of 14 weeks of dosing	

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: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	43	37	43
Units: UACR ratio				
least squares mean (confidence interval 95%)	-10.96 (-29.60 to 12.61)	-40.47 (-53.00 to -24.60)	-44.60 (-56.21 to -29.91)	4.60 (-18.02 to 33.46)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in UACR of cotadutide at different dose levels compared to placebo after 26 weeks

End point title	Percentage change in UACR of cotadutide at different dose levels compared to placebo after 26 weeks[3]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	46	48	49
Units: UACR ratio				
least squares mean (confidence interval 95%)	-17.85 (-45.47 to 23.78)	-38.68 (-59.61 to -6.88)	-57.87 (-73.33 to -33.34)	11.79 (-27.85 to 73.22)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in body weight of cotatudide at different dose levels versus placebo from baseline to end of 14 weeks of dosing

End point title	Percent change in body weight of cotatudide at different dose levels versus placebo from baseline to end of 14 weeks of dosing[4]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	32	27	35
Units: Absolute value				
least squares mean (standard error)	-2.84 (± 0.65)	-4.15 (± 0.68)	-5.40 (± 0.73)	-1.61 (± 0.66)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change in body weight of cotatudide at different dose levels versus placebo from baseline to end of 26 weeks of dosing

End point title	Percentage change in body weight of cotatudide at different dose levels versus placebo from baseline to end of 26 weeks of dosing[5]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	37	33	27	35
Units: Absolute value				
least squares mean (standard error)	-2.60 (± 0.89)	-5.45 (± 0.92)	-7.35 (± 0.99)	-2.23 (± 0.90)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 14 of dosing

End point title	Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 14 of dosing[6]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	45	48	39
Units: Percent change				
least squares mean (standard error)	-0.76 (± 0.12)	-0.82 (± 0.12)	-0.65 (± 0.12)	-0.08 (± 0.12)

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 26 of dosing

End point title	Percent change in HbA1c of cotadutide at different dose levels versus placebo from baseline to the end of 26 of dosing[7]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	46	48	39
Units: Percent change				
least squares mean (standard error)	-0.92 (± 0.11)	-0.92 (± 0.11)	-0.89 (± 0.11)	-0.25 (± 0.11)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 26 weeks of dosing

End point title	Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 26 weeks of dosing[8]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	43	39	45
Units: mmol/L				
least squares mean (standard error)	-1.78 (± 0.36)	-1.76 (± 0.37)	-1.57 (± 0.39)	-0.72 (± 0.37)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 14 weeks of dosing

End point title	Change in fasting glucose of cotadutide at different dose levels from baseline versus placebo after 14 weeks of dosing[9]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	45	48	49
Units: mmol/L				
least squares mean (standard error)	-1.35 (± 0.37)	-1.57 (± 0.35)	-1.69 (± 0.40)	-0.54 (± 0.37)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing

End point title	Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing[10]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 26 weeks of dosing

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	18	22	30
Units: Percent change				
least squares mean (standard error)	-1.735 (± 0.307)	-1.446 (± 0.334)	-1.118 (± 0.321)	-0.273 (± 0.290)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing

End point title	Change in 10-day average glucose levels of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing[11]

End point description:

End point type	Secondary

End point timeframe:

Baseline to end of 14 weeks of dosing

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	25	26	30
Units: Percent change				
least squares mean (standard error)	-1.556 (± 0.320)	-1.478 (± 0.337)	-1.269 (± 0.334)	-0.440 (± 0.311)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 14 weeks of dosing

End point title	Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 14 weeks of dosing[12]

End point description:

End point type	Secondary

End point timeframe:

Baseline to 14 weeks of dosing

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	25	26	30
Units: Percent Change				
least squares mean (standard error)	-13.87 (± 3.35)	-15.79 (± 3.55)	-13.90 (± 3.52)	-4.09 (± 3.27)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 26 weeks of dosing

End point title	Change in percentage time spent in hyperglycaemia over 10 days of cotadutide at different dose levels compared to placebo after 26 weeks of dosing[13]

End point description:

End point type	Secondary

End point timeframe:

Baseline to 26 weeks of dosing

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: In this study, the efficacy efficacy endpoints vs. semaglutide are exploratory and were therefore excluded

End point values	Cotadutide 100 ug	Cotadutide 300 ug	Cotadutide 600 ug	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	25	18	22	27
Units: Percent change				
least squares mean (standard error)	-18.06 (± 3.33)	-15.38 (± 3.76)	-11.91 (± 3.51)	-3.00 (± 3.17)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From first dose of study drug until last study visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups	
Reporting group title	Cotadutide 300 ug
Reporting group description: -	
Reporting group title	Cotadutide 100 ug
Reporting group description: -	
Reporting group title	Semaglutide 1 mg
Reporting group description: -	
Reporting group title	Cotadutide 600 ug
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Cotadutide 300 ug	Cotadutide 100 ug	Semaglutide 1 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 48 (10.42%)	5 / 55 (9.09%)	4 / 45 (8.89%)
number of deaths (all causes)	0	2	0
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (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
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (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			
Hypoxia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Adjustment disorder with anxiety			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (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
Suspected suicide			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			

subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (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
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (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
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Groin pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
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			
Diverticulitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (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
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular neuronitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Ketosis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (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

Serious adverse events	Cotadutide 600 ug	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 48 (10.42%)	5 / 51 (9.80%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			

subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder with anxiety			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suspected suicide			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Coronary artery disease			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Groin pain			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Ketosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cotadutide 300 ug	Cotadutide 100 ug	Semaglutide 1 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 48 (79.17%)	43 / 55 (78.18%)	39 / 45 (86.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Adrenal neoplasm			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Haemangioma of liver			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
B-cell lymphoma stage III			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	5 / 45 (11.11%)
occurrences (all)	1	0	5
Haematoma			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Hot flush			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Aortic stenosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Surgical and medical procedures			
Meniscus removal			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Skin neoplasm excision			

subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Tooth extraction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	2 / 45 (4.44%)
occurrences (all)	2	0	2
Chest pain			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Early satiety			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Injection site bruising			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Injection site erythema			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Injection site induration			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Fatigue			
subjects affected / exposed	0 / 48 (0.00%)	3 / 55 (5.45%)	1 / 45 (2.22%)
occurrences (all)	0	3	1
Injection site pruritus			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Injection site reaction			

subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Malaise			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Oedema			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Puncture site haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 48 (2.08%)	2 / 55 (3.64%)	1 / 45 (2.22%)
occurrences (all)	1	2	1
Vaccination site pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Atelectasis			

subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Bronchiectasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Cough			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Dyspnoea exertional			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pulmonary congestion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Nasal congestion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Pulmonary mass			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0

Rhinorrhoea			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Sneezing			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 48 (2.08%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	1	2	0
Cardiovascular somatic symptom disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood bicarbonate increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Blood bicarbonate decreased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Blood creatinine increased			

subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Blood calcium increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Cardiac murmur			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Ejection fraction decreased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram change			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Blood sodium increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Blood pressure increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Blood pressure decreased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	2 / 45 (4.44%)
occurrences (all)	1	0	2
Blood glucose increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Blood potassium increased			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	1 / 45 (2.22%)
occurrences (all)	1	1	1
Lipase increased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Occult blood positive			

subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Ventricular internal diameter			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Urine output increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Pulse absent			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pedal pulse decreased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Heat stroke			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Costal cartilage fracture			

subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Epicondylitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Heat illness			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	6	0	0
Contusion			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Ligament rupture			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Skin laceration			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Rib fracture			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Muscle strain			

subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Skin pressure mark			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Skin wound			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Tibia fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Wrist fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Vaccination complication			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Angina unstable			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Conduction disorder			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Cardiac septal hypertrophy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Mitral valve incompetence			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1

Atrioventricular block first degree			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	4	0	0
Atrial flutter			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block second degree			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Palpitations			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Ventricular tachycardia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Akinesia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	4 / 48 (8.33%)	1 / 55 (1.82%)	1 / 45 (2.22%)
occurrences (all)	4	1	1
Cognitive disorder			

subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Dizziness postural			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	2 / 45 (4.44%)
occurrences (all)	1	1	2
Neuralgia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Myelopathy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Ischaemic stroke			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Polyneuropathy			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Sciatica			

subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Anaemia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Retinal haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Glaucoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Diabetic retinopathy			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Eye haemorrhage			

subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Vitreous detachment			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Abdominal distension			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	7 / 48 (14.58%)	5 / 55 (9.09%)	7 / 45 (15.56%)
occurrences (all)	10	5	9
Constipation			
subjects affected / exposed	2 / 48 (4.17%)	7 / 55 (12.73%)	3 / 45 (6.67%)
occurrences (all)	3	7	4
Chronic gastritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	4 / 48 (8.33%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	5	1	0

Eructation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Faeces hard			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Flatulence			
subjects affected / exposed	2 / 48 (4.17%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	2	1	0
Nausea			
subjects affected / exposed	7 / 48 (14.58%)	6 / 55 (10.91%)	12 / 45 (26.67%)
occurrences (all)	9	7	23
Large intestine polyp			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Haemorrhoids			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 48 (4.17%)	1 / 55 (1.82%)	3 / 45 (6.67%)
occurrences (all)	2	1	4
Gastrointestinal disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Oral lichen planus			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	3 / 48 (6.25%)	2 / 55 (3.64%)	7 / 45 (15.56%)
occurrences (all)	4	2	9
Hepatobiliary disorders			
Hepatic cirrhosis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Hepatomegaly			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Dermatitis contact			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Dermatitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Blister			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Actinic keratosis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Lichenification			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0

Macule			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	1	1	0
Scab			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Skin exfoliation			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	3	0	0
Renal and urinary disorders			
Urinary hesitation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Renal mass			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Polyuria			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			

subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Nocturia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Urinary incontinence			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	2
Joint swelling			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Back pain			
subjects affected / exposed	2 / 48 (4.17%)	2 / 55 (3.64%)	2 / 45 (4.44%)
occurrences (all)	2	2	2
Flank pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Joint contracture			
subjects affected / exposed	2 / 48 (4.17%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Arthritis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	1 / 45 (2.22%)
occurrences (all)	1	1	1
Musculoskeletal chest pain			

subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Musculoskeletal discomfort			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	2 / 45 (4.44%)
occurrences (all)	1	0	4
Pain in jaw			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Tenosynovitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Conjunctivitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
Cystitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Eye infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0

Cellulitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	1	0	1
Giardiasis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Localised infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Periodontitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	3 / 45 (6.67%)
occurrences (all)	0	2	3
Rhinitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1

Tinea infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Vestibular neuronitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	3 / 48 (6.25%)	0 / 55 (0.00%)	2 / 45 (4.44%)
occurrences (all)	3	0	2
Tonsillitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	1 / 45 (2.22%)
occurrences (all)	0	1	1
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	1 / 48 (2.08%)	2 / 55 (3.64%)	2 / 45 (4.44%)
occurrences (all)	1	2	2
Asymptomatic COVID-19			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 48 (6.25%)	0 / 55 (0.00%)	8 / 45 (17.78%)
occurrences (all)	3	0	8
Electrolyte imbalance			

subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
Hypercalcaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Hypervolaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	3 / 45 (6.67%)
occurrences (all)	1	1	3
Hypernatraemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	1 / 45 (2.22%)
occurrences (all)	0	2	1
Hypoglycaemia			
subjects affected / exposed	16 / 48 (33.33%)	13 / 55 (23.64%)	4 / 45 (8.89%)
occurrences (all)	106	88	28
Hypophagia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
Iron deficiency			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1

Non-serious adverse events	Cotadutide 600 ug	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 48 (79.17%)	38 / 51 (74.51%)	

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Seborrhoeic keratosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Adrenal neoplasm			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Haemangioma of liver			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
B-cell lymphoma stage III			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	3 / 48 (6.25%)	0 / 51 (0.00%)	
occurrences (all)	4	0	
Haematoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Hot flush			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Aortic stenosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Surgical and medical procedures			
Meniscus removal			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin neoplasm excision			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	

Tooth extraction			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Early satiety			
subjects affected / exposed	2 / 48 (4.17%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Injection site pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			
subjects affected / exposed	0 / 48 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Injection site erythema			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Injection site induration			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Injection site pruritus			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Injection site reaction			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Malaise			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Oedema			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	0 / 48 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Pain			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Puncture site haemorrhage			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Vaccination site pain			
subjects affected / exposed	2 / 48 (4.17%)	1 / 51 (1.96%)	
occurrences (all)	2	1	
Reproductive system and breast disorders			
Breast tenderness			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Allergic cough			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Atelectasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Bronchiectasis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	2 / 48 (4.17%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Dyspnoea			
subjects affected / exposed	0 / 48 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Dyspnoea exertional			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Pulmonary congestion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 48 (0.00%)	2 / 51 (3.92%)	
occurrences (all)	0	2	
Nasal congestion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Pulmonary mass			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Rales			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	

Sinus congestion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Sneezing			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Cardiovascular somatic symptom disorder			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Depression			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Irritability			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood bicarbonate increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Blood bicarbonate decreased			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Amylase increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Blood calcium increased			

subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Ejection fraction decreased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Electrocardiogram change			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Blood sodium increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Blood pressure increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Blood pressure decreased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Blood glucose increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Blood potassium increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Lipase increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Occult blood positive			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Weight decreased			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Ventricular internal diameter			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Urine output increased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Pulse absent			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Pulmonary arterial pressure increased			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Pedal pulse decreased			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Injury, poisoning and procedural complications			
Animal bite			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Heat stroke			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Costal cartilage fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Epicondylitis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Fall			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Heat illness			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Ligament rupture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Ligament sprain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin laceration			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Rib fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Muscle strain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin pressure mark			

subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Skin wound			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Tibia fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Wrist fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Vaccination complication			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	2 / 48 (4.17%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Angina unstable			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Conduction disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Cardiac septal hypertrophy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Mitral valve incompetence			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	

Atrial flutter			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Atrial fibrillation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Atrioventricular block second degree			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Ventricular tachycardia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Tachycardia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Pericardial effusion			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Akinesia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	2 / 48 (4.17%)	1 / 51 (1.96%)	
occurrences (all)	2	1	
Cognitive disorder			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Dizziness postural			

subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	3 / 48 (6.25%)	1 / 51 (1.96%)	
occurrences (all)	5	2	
Neuralgia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Migraine			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Myelopathy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Ischaemic stroke			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Polyneuropathy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Restless legs syndrome			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Blood loss anaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Anaemia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Cataract			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Retinal haemorrhage			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Macular oedema			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Glaucoma			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Conjunctival haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Diabetic retinopathy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Eye haemorrhage			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Eye pain			

subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Vitreous detachment			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Vitreous floaters			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 48 (4.17%)	1 / 51 (1.96%)	
occurrences (all)	2	1	
Abdominal distension			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Abdominal discomfort			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	2 / 48 (4.17%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Diarrhoea			
subjects affected / exposed	6 / 48 (12.50%)	4 / 51 (7.84%)	
occurrences (all)	9	8	
Constipation			
subjects affected / exposed	5 / 48 (10.42%)	2 / 51 (3.92%)	
occurrences (all)	7	3	
Chronic gastritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Eructation			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	

Faeces hard			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Flatulence			
subjects affected / exposed	2 / 48 (4.17%)	1 / 51 (1.96%)	
occurrences (all)	2	1	
Nausea			
subjects affected / exposed	14 / 48 (29.17%)	5 / 51 (9.80%)	
occurrences (all)	18	5	
Large intestine polyp			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 48 (6.25%)	0 / 51 (0.00%)	
occurrences (all)	3	0	
Gastrointestinal disorder			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Oral lichen planus			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	2 / 48 (4.17%)	0 / 51 (0.00%)	
occurrences (all)	2	0	
Vomiting			
subjects affected / exposed	7 / 48 (14.58%)	2 / 51 (3.92%)	
occurrences (all)	12	2	
Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Hepatomegaly			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Diabetic foot			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	3	1	
Dermal cyst			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Blister			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Actinic keratosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Eczema			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Lichenification			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Macule			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	

Night sweats			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Scab			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin exfoliation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Skin ulcer			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urinary hesitation			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Renal mass			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Polyuria			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Nocturia			

subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Thyroid mass			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 48 (4.17%)	3 / 51 (5.88%)	
occurrences (all)	2	3	
Joint swelling			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	3 / 48 (6.25%)	4 / 51 (7.84%)	
occurrences (all)	3	4	
Flank pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Joint contracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Arthritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal discomfort			

subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Pain in jaw			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Tenosynovitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Pain in extremity			
subjects affected / exposed	0 / 48 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Fungal skin infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Cystitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Eye infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	

Gastroenteritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Giardiasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Localised infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Onychomycosis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Paronychia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Periodontitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Nasopharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	3 / 51 (5.88%)	
occurrences (all)	0	3	
Rhinitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Tinea infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	

Vestibular neuronitis			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Tooth abscess			
subjects affected / exposed	1 / 48 (2.08%)	1 / 51 (1.96%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	2 / 48 (4.17%)	1 / 51 (1.96%)	
occurrences (all)	2	2	
Tonsillitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	1 / 48 (2.08%)	2 / 51 (3.92%)	
occurrences (all)	1	2	
Asymptomatic COVID-19			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 48 (10.42%)	1 / 51 (1.96%)	
occurrences (all)	5	1	
Electrolyte imbalance			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Gout			

subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Hypercalcaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Hypervolaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	2	
Hyperkalaemia			
subjects affected / exposed	1 / 48 (2.08%)	2 / 51 (3.92%)	
occurrences (all)	1	2	
Hypernatraemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	13 / 48 (27.08%)	13 / 51 (25.49%)	
occurrences (all)	83	148	
Hypophagia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)	
occurrences (all)	0	0	
Iron deficiency			
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2020	This global amendment contains revisions to the original global protocol dated (01Apr2020) to remove Cohort 2, which is no longer needed due to completion of Study D5671C00003 earlier than originally planned. Other minor revisions such as clarifications and correction of typos were made. This amendment is considered to be non-substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union because it neither significantly impacts the safety or physical/mental integrity of participants nor the scientific value of the study.
04 January 2021	This global amendment contains revisions to Amendment 1 of the global protocol dated (29Jun2020) to add time windows for specific visits to make the study more accessible to participants during the current coronavirus disease (COVID-19) pandemic. Other minor revisions such as clarifications and correction of typos were made. This amendment is considered to be non-substantial based on the criteria set forth in Article 10(a) of Directive 2001/20/EC of the European Parliament and the Council of the European Union because it neither significantly impacts the safety or physical/mental integrity of participants nor the scientific value of the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported