



## 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
This version publication date	20 March 2023
First version publication date	20 March 2023

#### Trial information

##### Trial identification

Sponsor protocol code	D5676C00001
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##### 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
<b>Arm title</b>	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

<b>Arm title</b>	Cotadutide 300 ug
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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

<b>Arm title</b>	Cotadutide 600 ug
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Arm description:

Participants randomised to Cotadutide 600 ug daily

Arm type	Experimental
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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	
<b>Arm title</b>	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	
<b>Arm title</b>	Semaglutide 1 mg
Arm description: Participants randomised to active comparator daily	
Arm type	No intervention
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 1</b>	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	-

<b>Number of subjects in period 1</b>	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 randomised 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

<b>Reporting group values</b>	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	

<b>Reporting group values</b>	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 randomised 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 <sup>[1][2]</sup>
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 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 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 <sup>[3]</sup>
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End point description:

End point type	Secondary
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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 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 cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing

End point title	Percent change in body weight of cotadutide at different dose levels versus placebo from baseline to end of 14 weeks of dosing <sup>[4]</sup>
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End point description:

End point type	Secondary
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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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing

End point title	Percentage change in body weight of cotadutide at different dose levels versus placebo from baseline to end of 26 weeks of dosing <sup>[5]</sup>
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End point description:

End point type	Secondary
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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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 <sup>[6]</sup>
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End point description:

End point type	Secondary
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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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 <sup>[7]</sup>
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End point description:

End point type	Secondary
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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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 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 <sup>[8]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

Baseline to end of 14 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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 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 <sup>[9]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

Baseline to end of 26 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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 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 <sup>[10]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

Baseline to end of 14 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 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 ( $\pm$ 0.320)	-1.478 ( $\pm$ 0.337)	-1.269 ( $\pm$ 0.334)	-0.440 ( $\pm$ 0.311)

## 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 <sup>[11]</sup>
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End point description:

End point type	Secondary
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End point timeframe:

Baseline to end of 26 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 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 ( $\pm$ 0.307)	-1.446 ( $\pm$ 0.334)	-1.118 ( $\pm$ 0.321)	-0.273 ( $\pm$ 0.290)

## Statistical analyses

No statistical analyses for this end point

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**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**

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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 <sup>[12]</sup>
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End point description:

End point type	Secondary
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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 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)

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**Statistical analyses**

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No statistical analyses for this end point

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**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**

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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 <sup>[13]</sup>
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End point description:

End point type	Secondary
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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 endpoints vs. semaglutide are exploratory and were therefore excluded

<b>End point values</b>	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 ( $\pm$ 3.33)	-15.38 ( $\pm$ 3.76)	-11.91 ( $\pm$ 3.51)	-3.00 ( $\pm$ 3.17)

## Statistical analyses

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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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	24.1
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### Reporting groups

Reporting group title	Cotadutide 300 ug
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Reporting group description: -

Reporting group title	Cotadutide 100 ug
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Reporting group description: -

Reporting group title	Semaglutide 1 mg
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Reporting group description: -

Reporting group title	Cotadutide 600 ug
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

<b>Serious adverse events</b>	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
<b>Respiratory, thoracic and mediastinal disorders</b>			
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
<b>Psychiatric disorders</b>			
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
<b>Injury, poisoning and procedural complications</b>			
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
<b>Cardiac disorders</b>			
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
<b>Nervous system disorders</b>			
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
<b>Gastrointestinal disorders</b>			
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
<b>Hypoglycaemia</b>			
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

<b>Serious adverse events</b>	Cotadutide 600 ug	Placebo	
<b>Total subjects affected by serious adverse events</b>			
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	
<b>Neoplasms benign, malignant and unspecified (incl cysts and polyps)</b>			
<b>Adenocarcinoma</b>			
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	
<b>Vascular disorders</b>			
<b>Hypertension</b>			
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	
<b>General disorders and administration site conditions</b>			
<b>Chest pain</b>			
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	
<b>Respiratory, thoracic and mediastinal disorders</b>			
<b>Hypoxia</b>			
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	
<b>Pulmonary embolism</b>			

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	
<b>Pulmonary mass</b>			
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	
<b>Pulmonary oedema</b>			
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	
<b>Psychiatric disorders</b>			
<b>Adjustment disorder with anxiety</b>			
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	
<b>Suspected suicide</b>			
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	
<b>Injury, poisoning and procedural complications</b>			
<b>Humerus fracture</b>			
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	
<b>Cardiac disorders</b>			
<b>Acute myocardial infarction</b>			
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	
<b>Angina pectoris</b>			
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	
<b>Infections and infestations</b>			
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	
<b>Metabolism and nutrition disorders</b>			
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 %

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

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	2 / 55 (3.64%) 2	0 / 45 (0.00%) 0
Malaise subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Oedema subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Pyrexia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	1 / 45 (2.22%) 1
Pain subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Peripheral swelling subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Puncture site haemorrhage subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	2 / 55 (3.64%) 2	1 / 45 (2.22%) 1
Vaccination site pain subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 2	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Reproductive system and breast disorders Breast tenderness subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Allergic cough subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 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 occurrences (all)	2 / 48 (4.17%) 4	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Atrial flutter subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Atrial fibrillation subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Atrioventricular block second degree subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Palpitations subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Ventricular tachycardia subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Tachycardia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Sinus tachycardia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Nervous system disorders			
Akinesia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	1 / 45 (2.22%) 1
Dizziness subjects affected / exposed occurrences (all)	4 / 48 (8.33%) 4	1 / 55 (1.82%) 1	1 / 45 (2.22%) 1
Cognitive disorder			

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

subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Restless legs syndrome subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
<b>Blood and lymphatic system disorders</b>			
Blood loss anaemia subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Anaemia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	2 / 55 (3.64%) 2	0 / 45 (0.00%) 0
<b>Ear and labyrinth disorders</b>			
Vertigo subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
<b>Eye disorders</b>			
Cataract subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	1 / 45 (2.22%) 1
Retinal haemorrhage subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Macular oedema subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Glaucoma subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Diabetic retinopathy subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	1 / 55 (1.82%) 1	0 / 45 (0.00%) 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 occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Hepatomegaly subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
<b>Skin and subcutaneous tissue disorders</b>			
Diabetic foot subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Dermatitis contact subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Dermatitis subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Dermal cyst subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	1 / 45 (2.22%) 1
Blister subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Actinic keratosis subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Eczema subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	1 / 45 (2.22%) 1
Lichenification subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 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 occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Nocturia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Urinary incontinence subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Endocrine disorders Thyroid mass subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	1 / 45 (2.22%) 1
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 55 (0.00%) 0	1 / 45 (2.22%) 2
Joint swelling subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Back pain subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 2	2 / 55 (3.64%) 2	2 / 45 (4.44%) 2
Flank pain subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 2	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Joint contracture subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 2	0 / 55 (0.00%) 0	0 / 45 (0.00%) 0
Arthritis subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 55 (1.82%) 1	0 / 45 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	1 / 55 (1.82%) 1	1 / 45 (2.22%) 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
<b>Infections and infestations</b>			
<b>Bronchitis</b>			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
<b>Fungal skin infection</b>			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
<b>Conjunctivitis</b>			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	2	0	0
<b>Cystitis</b>			
subjects affected / exposed	1 / 48 (2.08%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	1	0	0
<b>Eye infection</b>			
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
<b>Gout</b>			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	0 / 45 (0.00%)
occurrences (all)	0	2	0
<b>Hypercalcaemia</b>			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
<b>Hypervolaemia</b>			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	0 / 45 (0.00%)
occurrences (all)	0	0	0
<b>Hyperkalaemia</b>			
subjects affected / exposed	1 / 48 (2.08%)	1 / 55 (1.82%)	3 / 45 (6.67%)
occurrences (all)	1	1	3
<b>Hypernatraemia</b>			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
<b>Hyperuricaemia</b>			
subjects affected / exposed	0 / 48 (0.00%)	1 / 55 (1.82%)	0 / 45 (0.00%)
occurrences (all)	0	1	0
<b>Hyperglycaemia</b>			
subjects affected / exposed	0 / 48 (0.00%)	2 / 55 (3.64%)	1 / 45 (2.22%)
occurrences (all)	0	2	1
<b>Hypoglycaemia</b>			
subjects affected / exposed	16 / 48 (33.33%)	13 / 55 (23.64%)	4 / 45 (8.89%)
occurrences (all)	106	88	28
<b>Hypophagia</b>			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1
<b>Iron deficiency</b>			
subjects affected / exposed	0 / 48 (0.00%)	0 / 55 (0.00%)	1 / 45 (2.22%)
occurrences (all)	0	0	1

<b>Non-serious adverse events</b>	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 occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Chest pain subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Early satiety subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 2	0 / 51 (0.00%) 0	
Injection site pain subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 0	
Injection site bruising subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	2 / 51 (3.92%) 2	
Injection site erythema subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Injection site induration subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Fatigue subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	1 / 51 (1.96%) 1	
Injection site pruritus subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Injection site reaction subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Malaise			

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

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 occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Sneezing subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Psychiatric disorders			
Insomnia subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Cardiovascular somatic symptom disorder subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 0	
Depressed mood subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Depression subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Irritability subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 0	
Investigations			
Blood bicarbonate increased subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Blood bicarbonate decreased subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 3	1 / 51 (1.96%) 1	
Amylase increased subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 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 occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Ventricular internal diameter subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Urine output increased subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Pulse absent subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Pulmonary arterial pressure increased subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Pedal pulse decreased subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 3	0 / 51 (0.00%) 0	
Injury, poisoning and procedural complications			
Animal bite subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Arthropod bite subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Heat stroke subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Costal cartilage fracture subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 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 occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 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	
Gastroesophageal 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 occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Skin and subcutaneous tissue disorders</b>			
<b>Diabetic foot</b>			
subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 0	
<b>Dermatitis contact</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Dermatitis</b>			
subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 3	1 / 51 (1.96%) 1	
<b>Dermal cyst</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Blister</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Actinic keratosis</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Dry skin</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Eczema</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Hyperhidrosis</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Lichenification</b>			
subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 0	
<b>Macule</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 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 occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Urinary incontinence subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Endocrine disorders Thyroid mass subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	2 / 48 (4.17%) 2	3 / 51 (5.88%) 3	
Joint swelling subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
Back pain subjects affected / exposed occurrences (all)	3 / 48 (6.25%) 3	4 / 51 (7.84%) 4	
Flank pain subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Joint contracture subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Arthritis subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Muscle spasms subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
Musculoskeletal discomfort			

subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 0	
<b>Myalgia</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Pain in jaw</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Spinal pain</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Tenosynovitis</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Pain in extremity</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	3 / 51 (5.88%) 3	
<b>Infections and infestations</b>			
<b>Bronchitis</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	1 / 51 (1.96%) 1	
<b>Fungal skin infection</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Conjunctivitis</b>			
subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	1 / 51 (1.96%) 1	
<b>Cystitis</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Eye infection</b>			
subjects affected / exposed occurrences (all)	0 / 48 (0.00%) 0	0 / 51 (0.00%) 0	
<b>Cellulitis</b>			
subjects affected / exposed occurrences (all)	1 / 48 (2.08%) 1	0 / 51 (0.00%) 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
<b>Hypercalcaemia</b>		
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	1
<b>Hypervolaemia</b>		
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	2
<b>Hyperkalaemia</b>		
subjects affected / exposed	1 / 48 (2.08%)	2 / 51 (3.92%)
occurrences (all)	1	2
<b>Hypernatraemia</b>		
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)
occurrences (all)	1	0
<b>Hyperuricaemia</b>		
subjects affected / exposed	0 / 48 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	1
<b>Hyperglycaemia</b>		
subjects affected / exposed	1 / 48 (2.08%)	0 / 51 (0.00%)
occurrences (all)	1	0
<b>Hypoglycaemia</b>		
subjects affected / exposed	13 / 48 (27.08%)	13 / 51 (25.49%)
occurrences (all)	83	148
<b>Hypophagia</b>		
subjects affected / exposed	0 / 48 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0
<b>Iron deficiency</b>		
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:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported