Clinical trial results:
A Randomized, Parallel, Double-blind, Placebo-controlled, Dose-ranging, Phase 2b Study to Evaluate the Efficacy, Safety and Tolerability of AZD8233 Treatment in Participants With Dyslipidemia

Summary

EudraCT number	2020-000767-23
Trial protocol	SK DK
Global end of trial date	20 July 2021

Results information

Result version number	v1
This version publication date	03 August 2022
First version publication date	03 August 2022

Trial information

Trial identification

Sponsor protocol code	D7990C00003

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Astraalléen, Södertälje, Sweden,
Public contact	Information Center, AstraZeneca, 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	26 August 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 July 2021
Global end of trial reached?	Yes
Global end of trial date	20 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the effect of AZD8233 on level of dyslipidemia related biomarker (LDL-C) across different dose levels (absolute change from baseline in log transformed LDL-C in plasma).

Protection of trial subjects:

This study was performed in compliance with International Council for Harmonisation (ICH) Good Clinical Practice, including the archiving of essential documents.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 October 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Denmark: 25
Country: Number of subjects enrolled	Slovakia: 44
Country: Number of subjects enrolled	United States: 50
Worldwide total number of subjects	119
EEA total number of subjects	69

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)	72
From 65 to 84 years	47
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at 19 clinical research center in Denmark, Slovakia and the USA. First subject enrolled (First subject first visit/first consent signed date): 28 October 2020. Last subject last visit: 20 July 2021.

Pre-assignment

Screening details:

Following a screening period of up to 42 days, eligible participants received an SC injection of study intervention on Days 1, 8, 29, and 57.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AZD8233 low dose

Arm description:

AZD8233 low dose for subcutaneous injection.

Arm type	Experimental
Investigational medicinal product name	AZD8233 low dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection on Days 1, 8, 29, and 57

Arm title	AZD8233 medium dose

Arm description:

AZD8233 medium dose

Arm type	Experimental
Investigational medicinal product name	AZD8233 medium dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection on Days 1, 8, 29, and 57.

Arm title	AZD8233 high dose

Arm description:

AZD8233 high dose

Arm type	Experimental

Investigational medicinal product name	AZD8233 high dose
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection on Days 1, 8, 29, and 57.

Arm title	Placebo

Arm description:

Placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Subcutaneous injection on Days 1, 8, 29, and 57

Number of subjects in period 1	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose
Started	30	30	29
Completed	28	29	27
Not completed	2	1	2
Consent withdrawn by subject	1	-	-
Reason not given	1	-	-
Adverse event, non-fatal	-	-	2
Lost to follow-up	-	1	-

Number of subjects in period 1	Placebo
Started	30
Completed	30
Not completed	0
Consent withdrawn by subject	-
Reason not given	-
Adverse event, non-fatal	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	AZD8233 low dose
Reporting group description:	
AZD8233 low dose for subcutaneous injection.	
Reporting group title	AZD8233 medium dose
Reporting group description:	
AZD8233 medium dose	
Reporting group title	AZD8233 high dose
Reporting group description:	
AZD8233 high dose	
Reporting group title	Placebo
Reporting group description:	
Placebo	

Reporting group values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose
Number of subjects	30	30	29
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)	18	20	18
From 65-84 years	12	10	11
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	61.8	60.6	60.4
standard deviation	± 7.1	± 7.4	± 8.4
Sex: Female, Male Units: Participants			
Female	16	12	11
Male	14	18	18
Race (NIH/OMB) Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	0
ASIAN	1	0	0
BLACK OR AFRICAN AMERICAN	2	2	1
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	0	0
WHITE	27	28	28

Reporting group values	Placebo	Total	

Number of subjects	30	119	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	72	
From 65-84 years	14	47	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	63.9		
standard deviation	± 7.3	-	
Sex: Female, Male Units: Participants			
Female	18	57	
Male	12	62	
Race (NIH/OMB) Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	0	0	
ASIAN	0	1	
BLACK OR AFRICAN AMERICAN	3	8	
NATIVE HAWAIIAN OR OTHER PACIFIC ISLANDER	0	0	
WHITE	27	110	

End points

End points reporting groups

Reporting group title	AZD8233 low dose
Reporting group description: AZD8233 low dose for subcutaneous injection.	
Reporting group title	AZD8233 medium dose
Reporting group description: AZD8233 medium dose	
Reporting group title	AZD8233 high dose
Reporting group description: AZD8233 high dose	
Reporting group title	Placebo
Reporting group description: Placebo	

Primary: Change in LDL-C at week 12.

End point title	Change in LDL-C at week 12.[1]
End point description:	
End point type	Primary
End point timeframe: Baseline to week 12	

Notes:

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

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	29	30
Units: Ratio				
geometric mean (confidence interval 95%)	0.606 (0.517 to 0.710)	0.270 (0.230 to 0.317)	0.206 (0.174 to 0.242)	0.978 (0.834 to 1.147)

Statistical analyses

No statistical analyses for this end point

Secondary: Relative change from baseline in PCSK9 concentration in plasma at week 12.

End point title	Relative change from baseline in PCSK9 concentration in plasma at week 12.
End point description:	
End point type	Secondary

End point timeframe:

Baseline to week 12

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	29	30
Units: Ratio				
geometric mean (confidence interval 95%)	0.420 (0.340 to 0.520)	0.110 (0.090 to 0.140)	0.060 (0.050 to 0.080)	0.950 (0.770 to 1.180)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in concentration of TC, HDL-C, Non-HDL-C, VLDL-C, ApoA1, ApoB, Lp(a), Triglycerides, Remnants cholesterol

End point title	Percentage change from baseline in concentration of TC, HDL-C, Non-HDL-C, VLDL-C, ApoA1, ApoB, Lp(a), Triglycerides, Remnants cholesterol

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 12

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	29	30
Units: Percent				
least squares mean (confidence interval 95%)				
Triglycerides	-7.70 (-18.44 to 3.05)	-12.95 (-23.77 to -2.12)	-12.70 (-23.88 to -1.52)	2.69 (-8.19 to 13.56)
Total cholesterol	-21.13 (-26.56 to -15.70)	-43.90 (-49.43 to -38.37)	-47.58 (-53.37 to -41.78)	-1.11 (-6.56 to 4.35)
HDL-C	3.37 (-1.12 to 7.86)	6.50 (1.96 to 11.04)	5.57 (0.90 to 10.25)	1.34 (-3.28 to 5.97)
Non-HDL-C	-29.57 (-36.58 to -22.56)	-61.25 (-68.38 to -54.11)	-67.92 (-75.38 to -60.45)	-0.65 (-7.81 to 6.51)
VLDL-C	-7.54 (-18.36 to 3.27)	-12.09 (-23.04 to -1.15)	-11.13 (-22.59 to 0.33)	3.22 (-7.90 to 14.35)
ApoB	-29.50 (-35.64 to -23.35)	-60.13 (-66.33 to -53.93)	-67.07 (-73.46 to -60.68)	-1.65 (-7.83 to 4.53)
Remnants cholesterol	-13.50 (-39.57 to 12.56)	-16.54 (-42.97 to 9.88)	-26.84 (-54.23 to 0.54)	6.38 (-20.28 to 33.05)

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentration of AZD8233

End point title	Plasma concentration of AZD8233[2]

End point description:

End point type	Secondary

End point timeframe:

Measurement at week 1, week 4, week 6, week 8, week 10, week 12, week 16, week 20, week 24 after first dose administration.

Notes:

[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: No plasma concentrations were measured in placebo arm.

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	30	29	
Units: ug/L				
arithmetic mean (standard deviation)				
Week 1	0.346 (± 0.59)	0.681 (± 0.24)	1.201 (± 0.49)	
Week 4	0.238 (± 0.21)	0.699 (± 0.33)	1.366 (± 0.71)	
Week 6	0.288 (± 0.21)	0.870 (± 0.34)	1.917 (± 1.09)	
Week 8	0.152 (± 0.10)	0.628 (± 0.57)	1.000 (± 0.68)	
Week 10	0.241 (± 0.15)	0.751 (± 0.29)	1.562 (± 0.84)	
Week 12	0.134 (± 0.07)	0.476 (± 0.23)	0.976 (± 0.75)	
Week 16	0.087 (± 0.09)	0.297 (± 0.53)	0.507 (± 0.70)	
Week 20	0.053 (± 0.004)	0.153 (± 0.26)	0.376 (± 0.68)	
Week 24	0.111 (± 0.31)	0.111 (± 0.15)	0.350 (± 0.62)	

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-drug antibodies (ADAs) during the treatment period and follow-up period

End point title	Anti-drug antibodies (ADAs) during the treatment period and follow-up period

End point description:

ADA titre results for subjects with positive ADA.

End point type	Secondary

End point timeframe:

Measurement at week 0, week 1, week 4, week 8, week 12, week 16, week 20, week 24

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	29	30
Units: ADA titre				
median (full range (min-max))				
Baseline	100 (100 to 100)	200 (200 to 200)	0 (0 to 0)	100 (100 to 100)
Week 1	100 (50 to 800)	200 (200 to 200)	0 (0 to 0)	100 (100 to 100)
Week 4	150 (100 to 1600)	200 (100 to 400)	75 (50 to 100)	100 (100 to 100)
Week 8	400 (200 to 3200)	200 (100 to 400)	75 (50 to 100)	100 (100 to 100)
Week 12	200 (200 to 1600)	200 (100 to 400)	200 (200 to 200)	50 (50 to 50)
Week 16	400 (100 to 1600)	200 (50 to 400)	300 (200 to 400)	100 (100 to 100)
Week 20	400 (200 to 1600)	200 (100 to 400)	500 (200 to 800)	100 (100 to 100)
Week 24	400 (200 to 800)	300 (100 to 400)	200 (50 to 800)	100 (100 to 100)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline in levels of LDL-C in plasma

End point title	Percentage change from baseline in levels of LDL-C in plasma

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 12

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	29	30
Units: Percent				
least squares mean (confidence interval 95%)	-32.22 (-39.79 to -24.66)	-69.26 (-76.89 to -61.63)	-76.50 (-84.37 to -68.63)	-1.53 (-9.14 to 6.09)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage change from baseline to week 12 in Lp(a)

End point title	Percentage change from baseline to week 12 in Lp(a)

End point description:

End point type	Secondary

End point timeframe:

Baseline to week 12

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	28	26	24
Units: Percent				
median (full range (min-max))	-6.94 (-68.0 to 15.2)	-38.89 (-88.2 to 0.0)	-44.66 (-84.1 to 0.0)	0.0 (-43.3 to 50.7)

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of subjects with an ECG determined to be abnormal and clinically significant

End point title	Number of subjects with an ECG determined to be abnormal and clinically significant

End point description:

End point type	Other pre-specified

End point timeframe:

Baseline to end of treatment

End point values	AZD8233 low dose	AZD8233 medium dose	AZD8233 high dose	Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	30	30	29	30
Units: Number of subjects				
Baseline	0	0	0	0
End of treatment	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	24

Reporting groups	
Reporting group title	AZD8233 (90 mg)
Reporting group description: -	
Reporting group title	AZD8233 (50 mg)
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Reporting group title	AZD8233 (15 mg)
Reporting group description: -	

Serious adverse events	AZD8233 (90 mg)	AZD8233 (50 mg)	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)	2 / 30 (6.67%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (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
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure acute			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
Infections and infestations			
Staphylococcal infection			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	AZD8233 (15 mg)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure acute			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Staphylococcal infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AZD8233 (90 mg)	AZD8233 (50 mg)	Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 29 (68.97%)	17 / 30 (56.67%)	12 / 30 (40.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic keratosis			

subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	3 / 29 (10.34%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	4	1	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Feeling cold			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Injection site haematoma			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	2	0
Injection site pain			
subjects affected / exposed	2 / 29 (6.90%)	2 / 30 (6.67%)	0 / 30 (0.00%)
occurrences (all)	2	2	0
Injection site reaction			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	4	0
Oedema peripheral			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Ovarian mass			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Pelvic pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Restlessness			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			

subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Hepatic enzyme increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Lipids increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Protein urine present			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Fall			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Post-traumatic neck syndrome			

subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	0	1	1
Radius fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Skin laceration			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Tooth fracture			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Wrist fracture			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Sinus bradycardia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	2
Hypoaesthesia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Paraesthesia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Radiculopathy			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Spinal cord compression			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Leukopenia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Spontaneous haematoma			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Ear disorder			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	3 / 29 (10.34%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	3	0	0
Abdominal pain upper			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Diarrhoea			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	2 / 30 (6.67%)
occurrences (all)	1	0	3
Nausea			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Haemorrhoids			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 29 (0.00%)	2 / 30 (6.67%)	1 / 30 (3.33%)
occurrences (all)	0	2	1
Back pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	1 / 30 (3.33%)
occurrences (all)	0	1	1

Cervical spinal stenosis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 29 (3.45%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Sacroiliitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Spinal pain			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Wrist deformity			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis viral			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Nasal vestibulitis			

subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	0 / 29 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	0	0	0
Osteomyelitis			
subjects affected / exposed	0 / 29 (0.00%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Upper respiratory tract infection			
subjects affected / exposed	2 / 29 (6.90%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	2	0	0
Tooth infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Asymptomatic COVID-19			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0
COVID-19			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	1 / 30 (3.33%)
occurrences (all)	1	0	1
Hypokalaemia			
subjects affected / exposed	1 / 29 (3.45%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	AZD8233 (15 mg)		
Total subjects affected by non-serious adverse events			

subjects affected / exposed	14 / 30 (46.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of thyroid gland			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Seborrhoeic keratosis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hypertension			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Feeling cold			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Injection site haematoma			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Injection site pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Injection site reaction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oedema peripheral			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Ovarian mass			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Pelvic pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Dyspnoea			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Oropharyngeal pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Restlessness			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
C-reactive protein increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hepatic enzyme increased			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Lipids increased			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Liver function test increased			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Protein urine present			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Transaminases increased			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Urine albumin/creatinine ratio increased			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Facial bones fracture			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Head injury			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Joint injury			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Post-traumatic neck syndrome			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Radius fracture			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Skin abrasion			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Skin laceration			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Tooth fracture			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Wrist fracture			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Sinus bradycardia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Hypoaesthesia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Migraine			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Radiculopathy			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Spinal cord compression			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Leukopenia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Spontaneous haematoma			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Ear disorder			

subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

Back pain subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Cervical spinal stenosis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Neck pain subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Pain in extremity subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Sacroiliitis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Spinal pain subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Wrist deformity subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Infections and infestations Gastroenteritis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Herpes zoster			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nasal vestibulitis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Osteomyelitis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Tooth infection			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Asymptomatic COVID-19			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2020	•Clarifications made to study visit/assessment timings and procedures in relation to screening, pre-dose assessments, home visits, and coagulation parameters • Minor clarifications made in inclusion criterion #7(b) and exclusion criteria #12 and #29 • Clarification that participants must not make changes to or take new concomitant medications without Investigator consultation • Discontinuation of study intervention criteria in relation to ALT/AST parameters expanded

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported