Clinical trial results:
A Randomized, Parallel, Double-Blind, Placebo-Controlled Phase 2b Study to Assess the Safety, Tolerability and Efficacy of AZD8233 Treatment in Participants with Hyperlipidaemia (SOLANO)

Summary

EudraCT number	2020-005845-18
Trial protocol	SK DK CZ NL HU ES PL
Global end of trial date	15 July 2022

Results information

Result version number	v1 (current)
This version publication date	28 July 2023
First version publication date	28 July 2023
Summary attachment (see zip file)	additioanlData (results_solanoERF12July.pdf)

Trial information

Trial identification

Sponsor protocol code	D7990C00004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04964557
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	AstraZeneca, Södertälje, Sweden, 151 85
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 November 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 July 2022
Global end of trial reached?	Yes
Global end of trial date	15 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary safety: To assess the safety and tolerability of AZD8233 as compared with placebo in participants with hyperlipidaemia receiving maximally tolerated statin and/or ezetimibe therapy as defined by the investigator. Primary efficacy: To assess the effect of AZD8233 versus placebo on serum LDL-C at the end of Week 28 compared with baseline, in participants with hyperlipidaemia, receiving maximally tolerated statin and/or ezetimibe therapy as defined by the investigator.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 July 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 87
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Denmark: 52
Country: Number of subjects enrolled	Slovakia: 78
Country: Number of subjects enrolled	Netherlands: 19
Country: Number of subjects enrolled	Czechia: 89
Country: Number of subjects enrolled	Poland: 14
Country: Number of subjects enrolled	Spain: 43
Worldwide total number of subjects	411
EEA total number of subjects	324

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)	231
From 65 to 84 years	180
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted at a total of 66 study centres in 8 countries: Czech Republic (10 centres), Denmark (8 centres), Hungary (4 centres), Netherlands (6 centres), Poland (8 centres), Slovakia (7 centres), Spain (7 centres), and United States (16 centres). First subject enrolled: 07 July 2021 and Last subject last visit: 15 July 2022.

Pre-assignment

Screening details:

A total of 593 subjects were screened in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	AZD8233

Arm description:

AZD8233 for subcutaneous use.

Arm type	Experimental
Investigational medicinal product name	AZD8233 for subcutaneous use.
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

60mg SC Q4W

Arm title	Placebo

Arm description:

Matching placebo solution for subcutaneous injection.

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

Dosage and administration details:

60mg matching place SC Q4W.

Number of subjects in period 1	AZD8233	Placebo
Started	206	205
Completed	196	201
Not completed	10	4
Adverse event, serious fatal	3	-
Consent withdrawn by subject	3	2
Physician decision	2	-
Lost to follow-up	1	2
Reported as completed but didn't fulfil study def.	1	-

Baseline characteristics

Reporting groups	
Reporting group title	AZD8233
Reporting group description: AZD8233 for subcutaneous use.	
Reporting group title	Placebo
Reporting group description: Matching placebo solution for subcutaneous injection.	

Reporting group values	AZD8233	Placebo	Total
Number of subjects	206	205	411
Age categorical Units: Subjects			
Adults (18-64 years)	110	121	231
From 65-84 years	96	84	180
Age Continuous Units: Years			
arithmetic mean	62.4	62.2	
standard deviation	± 8.1	± 7.7	-
Sex: Female, Male Units: Participants			
Female	101	94	195
Male	105	111	216
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	2	2	4
Black or African American	9	3	12
Native Hawaiian or other Pacific Islander	0	1	1
White	194	199	393
Region of Enrollment Units: Subjects			
USA	48	39	87
Czech Republic	45	44	89
Denmark	31	21	52
Hungary	15	14	29
Netherlands	12	7	19
Poland	4	10	14
Slovakia	35	43	78
Spain	16	27	43
LDL-C			
Baseline LDL-C			
Units: mg/dL			
arithmetic mean	103	107.4	
standard deviation	± 31.8	± 31.9	-

Subject analysis sets	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects who were randomly assigned to study intervention. Subjects will be analysed according to their randomised study medication assignment, irrespective of the treatment actually received.

Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis

Subject analysis set description:

The safety analysis set consists of all subjects who have received at least one dose of investigational product. Erroneously treated subjects (e.g., those randomised to treatment A but actually given treatment B) are accounted for in the treatment group of the treatment they actually received. A subject who has on one or several occasions received active IP is classified as active and is accounted for the active IP treatment group.

Reporting group values	Full analysis set	Safety analysis set	
Number of subjects	411	410	
Age categorical Units: Subjects			
Adults (18-64 years)	231		
From 65-84 years	180		
Age Continuous Units: Years			
arithmetic mean	62.3		
standard deviation	± 7.9	±	
Sex: Female, Male Units: Participants			
Female	195		
Male	216		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1		
Asian	4		
Black or African American	12		
Native Hawaiian or other Pacific Islander	1		
White	393		
Region of Enrollment Units: Subjects			
USA	87		
Czech Republic	89		
Denmark	52		
Hungary	29		
Netherlands	19		
Poland	14		
Slovakia	78		
Spain	43		
LDL-C			
Baseline LDL-C			
Units: mg/dL			
arithmetic mean	105.2		
standard deviation	± 31.9	±	

End points

End points reporting groups

Reporting group title	AZD8233
Reporting group description:	
AZD8233 for subcutaneous use.	
Reporting group title	Placebo
Reporting group description:	
Matching placebo solution for subcutaneous injection.	
Subject analysis set title	Full analysis set
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects who were randomly assigned to study intervention. Subjects will be analysed according to their randomised study medication assignment, irrespective of the treatment actually received.	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	
The safety analysis set consists of all subjects who have received at least one dose of investigational product. Erroneously treated subjects (e.g., those randomised to treatment A but actually given treatment B) are accounted for in the treatment group of the treatment they actually received. A subject who has on one or several occasions received active IP is classified as active and is accounted for the active IP treatment group.	

Primary: Percentage change from baseline on serum LDL-C

End point title	Percentage change from baseline on serum LDL-C
End point description:	
Percentage change in Low-density Lipoprotein Cholesterol (LDL-C) from baseline to Day 197.	
End point type	Primary
End point timeframe:	
From baseline to Day 197	

End point values	AZD8233	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	205		
Units: Relative change from baseline in LDL-C %				
least squares mean (confidence interval 95%)	-56.7 (-60.8 to -52.7)	5.6 (1.5 to 9.6)		

Statistical analyses

Statistical analysis title	Relative change in LDL-C
Statistical analysis description:	
Relative change in serum LDL-C from baseline to end of W28	
Comparison groups	Placebo v AZD8233

Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [1]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-62.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-68
upper limit	-56.6

Notes:

[1] - P-Value is <0.001

Secondary: Percentage change from baseline on serum PCSK9

End point title	Percentage change from baseline on serum PCSK9

End point description:

Percentage change in Proprotein convertase subtilisin/kexin type-9 (PCSK9) from baseline to Day 197.

End point type	Secondary

End point timeframe:

From baseline to Day 197

End point values	AZD8233	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	205		
Units: Relative change from baseline in PCSK9 %				
least squares mean (confidence interval 95%)	-77.5 (-81.1 to -74)	-0.8 (-4.3 to 2.6)		

Statistical analyses

Statistical analysis title	Relative change concentrations of PCSK9

Statistical analysis description:

Relative change concentrations of PCSK9 from baseline to end of week 28.

Comparison groups	AZD8233 v Placebo
Number of subjects included in analysis	411
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001 [2]
Method	ANCOVA
Parameter estimate	Mean difference (final values)
Point estimate	-76.7

Confidence interval	
level	95 %
sides	2-sided
lower limit	-81.7
upper limit	-71.7

Notes:

[2] - P-Value is <0.001

Secondary: Plasma concentration of AZD8233

End point title	Plasma concentration of AZD8233[3]

End point description:

AZD8233 full length ASO concentrations in plasma (pre-dose) will be summarised by descriptive statistics by sampling time point and listed on individual level based on the PK analysis set.

End point type	Secondary

End point timeframe:

Day 29, Day 85, Day 141, Day 183, Day 197

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: Only the AZD8233 treatment group has valid PK measurements.

End point values	AZD8233			
Subject group type	Reporting group			
Number of subjects analysed	200			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 29	0.2648 (± 82.8352)			
Day 85	0.3927 (± 84.9378)			
Day 141	0.5749 (± 161.9301)			
Day 183	1.0441 (± 178.5196)			
Day 197	0.6975 (± 208.2431)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On-study: includes adverse events with an onset date on or after the date of first dose of IP.

Adverse event reporting additional description:

The safety analysis set consists of all subjects who have received at least one dose of investigational product. Erroneously treated subjects (e.g., those randomised to treatment A but actually given treatment B) are accounted for in the treatment group of the treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Matching Placebo for subcutaneous use.

Reporting group title	AZD8233

Reporting group description:

AZD8233 for subcutaneous use.

Serious adverse events	Placebo	AZD8233	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 203 (5.91%)	18 / 207 (8.70%)	
number of deaths (all causes)	0	3	
number of deaths resulting from adverse events	0	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung adenocarcinoma			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma urethra			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery stenosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	2 / 203 (0.99%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Haemothorax			

subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar i disorder			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental disorder			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Coagulation time prolonged			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			

subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	1 / 203 (0.49%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	1 / 203 (0.49%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute vestibular syndrome			

subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Amaurosis fugax			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal hernia			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19 pneumonia			

subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Urosepsis			
subjects affected / exposed	0 / 203 (0.00%)	1 / 207 (0.48%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	1 / 203 (0.49%)	0 / 207 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	AZD8233	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	62 / 203 (30.54%)	69 / 207 (33.33%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	13 / 203 (6.40%)	11 / 207 (5.31%)	
occurrences (all)	16	11	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	5 / 203 (2.46%)	22 / 207 (10.63%)	
occurrences (all)	7	56	
Infections and infestations			
Covid-19			
subjects affected / exposed	36 / 203 (17.73%)	33 / 207 (15.94%)	
occurrences (all)	37	33	
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	14 / 203 (6.90%)	18 / 207 (8.70%)	
occurrences (all)	14	19	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

ADA and safety endpoints were evaluated using the safety analysis set and could not be reported in the end points section, thus tables are reported in a separate PDF attachment.

Notes: