



Clinical trial results:

A Randomised, Double-blind, Placebo-controlled, Multi-centre Phase2b Study to Evaluate the Efficacy, Safety and Tolerability of AZD2693 in Participants with Non-cirrhotic Non-alcoholic Steatohepatitis(NASH) with Fibrosis Who Are Carriers of the PNPLA3rs738409148M Risk Allele

Summary

EudraCT number	2022-001629-65
Trial protocol	IT
Global end of trial date	04 November 2025

Results information

Result version number	v1 (current)
This version publication date	03 October 2026
First version publication date	03 October 2026

Trial information

Trial identification

Sponsor protocol code	D7830C00004
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05809934
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	151 85, Södertälje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 8772409479, 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	04 November 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2025
Global end of trial reached?	Yes
Global end of trial date	04 November 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the effect of AZD2693 versus placebo on histological resolution of NASH in participants with non-cirrhotic NASH with fibrosis and PNPLA3 risk allele carriers after 52 weeks

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	15 March 2023
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	Argentina: 5
Country: Number of subjects enrolled	Brazil: 14
Country: Number of subjects enrolled	Chile: 7
Country: Number of subjects enrolled	China: 10
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Hong Kong: 5
Country: Number of subjects enrolled	Italy: 14
Country: Number of subjects enrolled	Japan: 30
Country: Number of subjects enrolled	Malaysia: 4
Country: Number of subjects enrolled	Mexico: 32
Country: Number of subjects enrolled	Peru: 3
Country: Number of subjects enrolled	Philippines: 5
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Singapore: 3
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Taiwan: 1
Country: Number of subjects enrolled	Thailand: 3
Country: Number of subjects enrolled	Türkiye: 5
Country: Number of subjects enrolled	United States: 66
Country: Number of subjects enrolled	Viet Nam: 1

Worldwide total number of subjects	216
EEA total number of subjects	20

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)	172
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening is performed up to 10 weeks before randomization.

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
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Arm title	AZD2693 25 mg
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Arm description:

Participants in this arm will receive AZD2693 25 mg

Arm type	Experimental
Investigational medicinal product name	AZD2693
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg daily

Arm title	AZD2693 50 mg
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Arm description:

Participants in this arm will receive AZD2693 50 mg

Arm type	Experimental
Investigational medicinal product name	AZD2693
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg daily

Arm title	Placebo
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Arm description:

Participants in this arm will receive placebo

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablet once daily

Number of subjects in period 1	AZD2693 25 mg	AZD2693 50 mg	Placebo
Started	73	69	74
Completed	67	61	69
Not completed	6	8	5
Consent withdrawn by subject	5	6	5
SAE	-	1	-
Lost to follow-up	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	AZD2693 25 mg
Reporting group description:	
Participants in this arm will receive AZD2693 25 mg	
Reporting group title	AZD2693 50 mg
Reporting group description:	
Participants in this arm will receive AZD2693 50 mg	
Reporting group title	Placebo
Reporting group description:	
Participants in this arm will receive placebo	

Reporting group values	AZD2693 25 mg	AZD2693 50 mg	Placebo
Number of subjects	73	69	74
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)	60	56	56
From 65-84 years	13	13	18
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	53.7	51.8	53.7
standard deviation	± 13.0	± 13.3	± 13.6
Sex: Female, Male			
Units: Participants			
Female	39	41	37
Male	34	28	37
Race (NIH/OMB)			
Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	5	0	2
ASIAN	19	19	27
BLACK OR AFRICAN AMERICAN	0	0	3
MULTIPLE	1	0	0
NOT REPORTED	2	4	2
OTHER	0	5	9
WHITE	46	41	31
Region of Enrollment			
ARG=Argentina, BRA=Brazil, CHL=Chile, CHN=China, COL=Colombia, DEU=Germany, ESP=Spain, HKG=Hong Kong, ITA=Italy, JPN=Japan, MAL=Malaysia, MEX=Mexico, MYS=Malaysia, PER=Peru, KOR=Republic of Korea, SGP=Singapore, TWN=Taiwan, THA=Thailand, TUR=Turkey, USA=United States of America, VNM=Vietnam			

Units: Subjects			
ARG	1	3	1
BRA	3	3	8
CHL	1	6	0
CHN	2	4	4
COL	1	0	0
DEU	2	0	0
ESP	2	1	1
HKG	2	3	0
ITA	6	4	4
JPN	8	8	14
KOR	1	0	0
MEX	8	11	13
MYS	3	1	0
PER	2	0	1
PHL	1	1	3
SGP	1	1	1
THA	1	1	1
TUR	4	1	0
TWN	0	0	1
USA	24	21	21
VNM	0	0	1

Reporting group values	Total		
Number of subjects	216		
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)	172		
From 65-84 years	44		
85 years and over	0		
Age Continuous			
Units: Years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: Participants			
Female	117		
Male	99		
Race (NIH/OMB)			
Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	7		
ASIAN	65		
BLACK OR AFRICAN AMERICAN	3		

MULTIPLE	1		
NOT REPORTED	8		
OTHER	14		
WHITE	118		
Region of Enrollment			
ARG=Argentina, BRA=Brazil, CHL=Chile, CHN=China, COL=Colombia, DEU=Germany, ESP=Spain, HKG=Hong Kong, ITA=Italy, JPN=Japan, MAL=Malaysia, MEX=Mexico, MYS=Malaysia, PER=Peru, KOR=Republic of Korea, SGP=Singapore, TWN=Taiwan, THA=Thailand, TUR=Turkey, USA=United States of America, VNM=Vietnam			
Units: Subjects			
ARG	5		
BRA	14		
CHL	7		
CHN	10		
COL	1		
DEU	2		
ESP	4		
HKG	5		
ITA	14		
JPN	30		
KOR	1		
MEX	32		
MYS	4		
PER	3		
PHL	5		
SGP	3		
THA	3		
TUR	5		
TWN	1		
USA	66		
VNM	1		

End points

End points reporting groups

Reporting group title	AZD2693 25 mg
Reporting group description:	
Participants in this arm will receive AZD2693 25 mg	
Reporting group title	AZD2693 50 mg
Reporting group description:	
Participants in this arm will receive AZD2693 50 mg	
Reporting group title	Placebo
Reporting group description:	
Participants in this arm will receive placebo	

Primary: Proportion of participants achieving NASH resolution without worsening of fibrosis based on histology after 52 weeks treatment

End point title	Proportion of participants achieving NASH resolution without worsening of fibrosis based on histology after 52 weeks treatment
End point description:	
To assess the effect of AZD2693 versus placebo on histological resolution of NASH in participants with non-cirrhotic NASH with fibrosis and PNPLA3 risk allele carriers after 52 weeks	
End point type	Primary
End point timeframe:	
From baseline to week 54	

End point values	AZD2693 25 mg	AZD2693 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	69	74	
Units: Participants				
Participants with response	4	1	5	

Statistical analyses

Statistical analysis title	Comparing groups: AZD2693 50 mg vs Placebo
Comparison groups	AZD2693 50 mg v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.116
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	1.78

Statistical analysis title	Comparing groups: AZD2693 25 mg vs Placebo
Comparison groups	AZD2693 25 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.783
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	3.23

Secondary: Proportion of participants with at least one stage of liver fibrosis improvement with no worsening of NASH based on biopsy after 52 weeks treatment

End point title	Proportion of participants with at least one stage of liver fibrosis improvement with no worsening of NASH based on biopsy after 52 weeks treatment
End point description:	
To assess the effects of AZD2693 versus placebo on histological fibrosis improvement	
End point type	Secondary
End point timeframe:	
From baseline to week 54	

End point values	AZD2693 25 mg	AZD2693 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	69	74	
Units: Participants				
Participants with response	12	6	8	

Statistical analyses

Statistical analysis title	Comparing groups: AZD2693 50 mg vs Placebo
Comparison groups	AZD2693 50 mg v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.693
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	2.44

Statistical analysis title	Comparing groups: AZD2693 25 mg vs Placebo
Comparison groups	AZD2693 25 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	4.37

Secondary: Proportion of participants with $\geq$ 2-point improvement from baseline in NAS based on biopsy after 52 weeks treatment

End point title	Proportion of participants with $\geq$ 2-point improvement from baseline in NAS based on biopsy after 52 weeks treatment
End point description: To assess the effect of AZD2693 versus placebo on $\geq$ 2-point improvement in NAS	
End point type	Secondary
End point timeframe: From baseline to week 54	

End point values	AZD2693 25 mg	AZD2693 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	69	74	
Units: Participants				
Participants with response	22	12	23	

Statistical analyses

Statistical analysis title	Comparing groups: AZD2693 50 mg vs Placebo
Comparison groups	AZD2693 50 mg v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.053
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.01

Statistical analysis title	Comparing groups: AZD2693 25 mg vs Placebo
Comparison groups	AZD2693 25 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.885
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.92

Secondary: Proportion of participants with improvement in fibrosis by at least one stage based on biopsy after 52 weeks treatment

End point title	Proportion of participants with improvement in fibrosis by at least one stage based on biopsy after 52 weeks treatment
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End point description:

To assess the effect of AZD2693 versus placebo on improvement in fibrosis by at least one stage

End point type	Secondary
End point timeframe:	
From baseline to week 54	

End point values	AZD2693 25 mg	AZD2693 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	69	74	
Units: Participants				
Participants with response	14	7	10	

Statistical analyses

Statistical analysis title	Comparing groups: AZD2693 50 mg vs Placebo
Comparison groups	AZD2693 50 mg v Placebo
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.542
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	0.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.26
upper limit	2.03

Statistical analysis title	Comparing groups: AZD2693 25 mg vs Placebo
Comparison groups	AZD2693 25 mg v Placebo
Number of subjects included in analysis	147
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.375
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	1.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	3.8

Other pre-specified: Number of participants with Adverse Events/Serious Adverse Events (AEs/SAEs) and abnormal laboratory test results

End point title	Number of participants with Adverse Events/Serious Adverse Events (AEs/SAEs) and abnormal laboratory test results
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End point description:

Haematology, urinalysis, clinical chemistry and eGFR.

Number of participants with abnormalities.

A result of $\geq ++$ for urinalysis (dipstick) results means ++ or worse (+++ or ++++).

End point type	Other pre-specified
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End point timeframe:

Baseline to 64 weeks

End point values	AZD2693 25 mg	AZD2693 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	69	74	
Units: Participants				
ALT > 3ULN	18	33	10	
ALP > 3ULN	1	0	0	
AST > 3ULN	11	18	11	
direct Bilirubin > ULN	5	7	4	
Creatinine > ULN	1	2	7	
B-platelet count > ULN	9	5	9	
Blood $\geq ++$	6	14	7	
Glucose $\geq ++$	13	24	29	
Protein $\geq ++$	6	4	4	
eGFR > 25% decrease	1	3	10	

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Number of participants with abnormal laboratory test results

End point title	Number of participants with abnormal laboratory test results
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End point description:

Vital signs and electrocardiogram (ECG) assessments.

Number of participants with abnormalities.

End point type	Other pre-specified
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End point timeframe:

Baseline to 64 weeks

End point values	AZD2693 25 mg	AZD2693 50 mg	Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	73	69	74	
Units: Participants				
Diastolic blood pressure from normal to high	15	26	25	
Systolic blood pressure from normal to high	29	30	28	
Pulse rate from normal to high	2	3	7	
Temperature from normal to high	12	10	18	
QTcF increase from baseline by more than 60 ms	3	1	1	

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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description: -

Reporting group title	AZD2693 25 mg
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Reporting group description: -

Reporting group title	AZD2693 50 mg
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Reporting group description: -

Serious adverse events	Placebo	AZD2693 25 mg	AZD2693 50 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 74 (8.11%)	6 / 73 (8.22%)	3 / 69 (4.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Radius fracture			
subjects affected / exposed	1 / 74 (1.35%)	1 / 73 (1.37%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 69 (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			
Myocardial ischaemia			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			

subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 69 (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
Nervous system disorders			
Cerebral infarction			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 69 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Melaena			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 69 (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
Large intestine polyp			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 69 (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
Abdominal pain lower			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 69 (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
Pancreatitis acute			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 69 (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
Hepatobiliary disorders			
Autoimmune hepatitis			

subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 69 (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
Cholelithiasis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Neck pain			
subjects affected / exposed	1 / 74 (1.35%)	0 / 73 (0.00%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 74 (0.00%)	1 / 73 (1.37%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Neurosyphilis			
subjects affected / exposed	0 / 74 (0.00%)	0 / 73 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	AZD2693 25 mg	AZD2693 50 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 74 (70.27%)	47 / 73 (64.38%)	47 / 69 (68.12%)
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 74 (1.35%)	1 / 73 (1.37%)	4 / 69 (5.80%)
occurrences (all)	1	1	6
Alanine aminotransferase increased			
subjects affected / exposed	1 / 74 (1.35%)	3 / 73 (4.11%)	9 / 69 (13.04%)
occurrences (all)	2	3	10

Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 74 (5.41%)	1 / 73 (1.37%)	2 / 69 (2.90%)
occurrences (all)	4	1	2
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 74 (6.76%)	7 / 73 (9.59%)	8 / 69 (11.59%)
occurrences (all)	6	8	9
Dizziness			
subjects affected / exposed	4 / 74 (5.41%)	4 / 73 (5.48%)	1 / 69 (1.45%)
occurrences (all)	4	5	2
General disorders and administration site conditions			
Injection site pain			
subjects affected / exposed	1 / 74 (1.35%)	4 / 73 (5.48%)	4 / 69 (5.80%)
occurrences (all)	1	5	9
Injection site erythema			
subjects affected / exposed	0 / 74 (0.00%)	6 / 73 (8.22%)	8 / 69 (11.59%)
occurrences (all)	0	14	24
Fatigue			
subjects affected / exposed	5 / 74 (6.76%)	2 / 73 (2.74%)	3 / 69 (4.35%)
occurrences (all)	5	2	4
Injection site pruritus			
subjects affected / exposed	0 / 74 (0.00%)	2 / 73 (2.74%)	6 / 69 (8.70%)
occurrences (all)	0	3	9
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 74 (5.41%)	4 / 73 (5.48%)	5 / 69 (7.25%)
occurrences (all)	4	4	7
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 74 (5.41%)	0 / 73 (0.00%)	1 / 69 (1.45%)
occurrences (all)	4	0	1
Diarrhoea			
subjects affected / exposed	11 / 74 (14.86%)	3 / 73 (4.11%)	7 / 69 (10.14%)
occurrences (all)	11	4	10
Abdominal pain upper			

subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 1	6 / 73 (8.22%) 7	1 / 69 (1.45%) 1
Abdominal pain subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 3	0 / 73 (0.00%) 0	7 / 69 (10.14%) 8
Abdominal distension subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 4	1 / 73 (1.37%) 2	0 / 69 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	6 / 74 (8.11%) 7	1 / 73 (1.37%) 1	1 / 69 (1.45%) 1
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all)	1 / 74 (1.35%) 2	4 / 73 (5.48%) 13	2 / 69 (2.90%) 8
Rash subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	2 / 73 (2.74%) 2	4 / 69 (5.80%) 4
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 5	2 / 73 (2.74%) 5	4 / 69 (5.80%) 5
Back pain subjects affected / exposed occurrences (all)	6 / 74 (8.11%) 7	6 / 73 (8.22%) 8	3 / 69 (4.35%) 3
Pain in extremity subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	4 / 73 (5.48%) 5	0 / 69 (0.00%) 0
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all)	2 / 74 (2.70%) 2	8 / 73 (10.96%) 11	7 / 69 (10.14%) 8
Upper respiratory tract infection subjects affected / exposed occurrences (all)	4 / 74 (5.41%) 5	7 / 73 (9.59%) 8	5 / 69 (7.25%) 5

Pharyngitis			
subjects affected / exposed	5 / 74 (6.76%)	1 / 73 (1.37%)	1 / 69 (1.45%)
occurrences (all)	7	1	1
Gastroenteritis			
subjects affected / exposed	3 / 74 (4.05%)	5 / 73 (6.85%)	3 / 69 (4.35%)
occurrences (all)	3	6	3
Influenza			
subjects affected / exposed	4 / 74 (5.41%)	1 / 73 (1.37%)	3 / 69 (4.35%)
occurrences (all)	4	1	3
Nasopharyngitis			
subjects affected / exposed	11 / 74 (14.86%)	6 / 73 (8.22%)	9 / 69 (13.04%)
occurrences (all)	15	7	10
COVID-19			
subjects affected / exposed	3 / 74 (4.05%)	4 / 73 (5.48%)	7 / 69 (10.14%)
occurrences (all)	3	4	7
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	4 / 74 (5.41%)	1 / 73 (1.37%)	0 / 69 (0.00%)
occurrences (all)	4	3	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 February 2023	CSP v2.0; Current data supports removing the pre-dose platelet count visit (local lab, within 1 week of dosing to have a fresh platelet count) after Visit 11 and onwards, to reduce the participant visit burden in the study. After Visit 11 and onwards, the monthly ongoing safety surveillance and review of the independent Safety Monitoring Committee would be considered sufficient to detect any drop in platelet count. Actions in case of development of thrombocytopenia are described in Appendix F.
04 August 2023	CSP V3.0; The Clinical Study Protocol (CSP), version 3.0, was updated to exclude the 50 mg exploratory heterozygous cohort. Heterozygous safety data had been reviewed during safety review committee (SRC) prior to the start of the Ph2b study, with no safety stopping criteria met and PK analysis in line with expectations. Efficacy data (liver fat content) is now available from the global multiple ascending dose study (GMAD) in the heterozygote participant cohort. The participants received 25 mg, 3 monthly doses and were followed for 16 weeks after the last dose. Review of the data from the ongoing study demonstrate a change in the benefit:risk ratio because there is not sufficient evidence of potential treatment benefit to support continued inclusion of this population in the D7830c00004 study.
01 July 2024	CSP v4.0; Current data supports removing the pre-dose platelet count visit (local lab, within 1 week of dosing to have a fresh platelet count) after Visit 11 and onwards, to reduce the participant visit burden in the study. After Visit 11 and onwards, the monthly ongoing safety surveillance and review of the independent Safety Monitoring Committee would be considered sufficient to detect any drop in platelet count. Actions in case of development of thrombocytopenia are described in Appendix F.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported