Clinical trial results:
A Phase 3 Multicenter, Randomized, Double-Masked, Sham Controlled Clinical Trial to Assess the Safety and Efficacy of Intravitreal Administration of Zimura (Complement C5 Inhibitor) in Patients with Geographic Atrophy Secondary to Age-Related Macular Degeneration

Summary

EudraCT number	2020-000676-38
Trial protocol	GB FR DE HU EE LV PL CZ ES IT SK BE HR
Global end of trial date	22 August 2023

Results information

Result version number	v2 (current)
This version publication date	11 December 2024
First version publication date	11 August 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	ISEE2008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04435366
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Astellas Pharma Global Development, Inc
Sponsor organisation address	1 Astellas Way Northbrook, Illinois, United States, 60062
Public contact	Clinical Transparency, Astellas Pharma Global Development, Inc, +1 8008887704, astellas.resultsdisclosure@astellas.com
Scientific contact	Clinical Transparency, Astellas Pharma Global Development, Inc, +1 8008887704, astellas.resultsdisclosure@astellas.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	22 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial was to evaluate the safety and efficacy of avacincaptad pegol IVT administration when administered in patients with geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

Protection of trial subjects:

This clinical study was written, conducted and reported in accordance with the protocol, International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) Guidelines, and applicable local regulations, including the European Directive 2001/20/EC, on the protection of human rights, and with the ethical principles that have their origin in the Declaration of Helsinki. Astellas ensures that the use and disclosure of protected health information (PHI) obtained during a research study complies with the federal, national and/or regional legislation related to the privacy and protection of personal information.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 June 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	Argentina: 19
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	Austria: 11
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Canada: 16
Country: Number of subjects enrolled	Colombia: 23
Country: Number of subjects enrolled	Czechia: 8
Country: Number of subjects enrolled	Germany: 25
Country: Number of subjects enrolled	Estonia: 29
Country: Number of subjects enrolled	France: 51
Country: Number of subjects enrolled	Hungary: 15
Country: Number of subjects enrolled	Croatia: 7
Country: Number of subjects enrolled	Israel: 14
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Latvia: 3
Country: Number of subjects enrolled	Poland: 2

Country: Number of subjects enrolled	United States: 181
Worldwide total number of subjects	448
EEA total number of subjects	184

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)	39
From 65 to 84 years	320
85 years and over	89

Subject disposition

Recruitment

Recruitment details:

Participants ≥ 50 years of age diagnosed with GA that was at least partly within 1.5 mm radius from the foveal center were enrolled in the study.

Pre-assignment

Screening details:

Participants who met all inclusion criteria and none of the exclusion criteria were enrolled in the study.

Period 1

Period 1 title	Year 1 (12 months)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Avacincaptad Pegol

Arm description:

Participants received avacincaptad pegol (ACP) 2 milligram (mg)/eye via intravitreal (IVT) injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT injections monthly from month12 through month 23 (Year 2). Participants were followed up until month 24.

Arm type	Experimental
Investigational medicinal product name	Avacincaptad pegol
Investigational medicinal product code	ARC1905
Other name	Zimura (previous name) IZERVAY
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg/eye via IVT injections

Arm title	Sham

Arm description:

Participants received sham injections; through Month 11 (Year 1). At month 12, participants continued to receive monthly sham injection from month 12 through month 23 (Year 2). Participants were followed up until month 24.

Arm type	Active comparator
Investigational medicinal product name	Sham
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

IVT injections

Number of subjects in period 1	Avacincaptad Pegol	Sham
Started	225	223
Treated	225	222
Completed	200	205
Not completed	25	18
Adverse event, serious fatal	2	1
Consent withdrawn by subject	17	13
Adverse event, non-fatal	3	2
Patient non-compliance	1	-
Lost to follow-up	2	1
Not treated	-	1

Period 2

Period 2 title	Year 2 (12 months)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Data analyst

Arms

Are arms mutually exclusive?	Yes
Arm title	Avacincaptad Pegol

Arm description:

Participants received avacincaptad pegol (ACP) 2 milligram (mg)/eye via intravitreal (IVT) injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT injections monthly from month12 through month 23 (Year 2). Participants were followed up until month 24.

Arm type	Experimental
Investigational medicinal product name	Avacincaaptad pegol
Investigational medicinal product code	ARC1905
Other name	Zimura (previous name) IZERVAY
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg/eye via IVT injections

Arm title	Avacincaptad pegol and Sham

Arm description:

Participants received ACP 2 mg/eye via IVT injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT every other month (EOM) at months 13, 15, 17, 19, 21, and 23 and sham injections at months 12, 14, 16,18, 20, and 22 (Year 2). Participants were followed up until month 24.

Arm type	Experimental

Investigational medicinal product name	Avacincaptad pegol
Investigational medicinal product code	ARC1905
Other name	Zimura (previous name) IZERVAY
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

2 mg/eye via IVT injections

Arm title	Sham

Arm description:

Participants received sham injections; through Month 11 (Year 1). At month 12, participants continued to receive monthly sham injection from month 12 through month 23 (Year 2). Participants were followed up until month 24.

Arm type	Active comparator
Investigational medicinal product name	Sham
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravitreal use

Dosage and administration details:

IVT injections

Number of subjects in period 2[1]	Avacincaptad Pegol	Avacincaptad pegol and Sham	Sham
Started	96	93	203
Completed	89	83	184
Not completed	7	10	19
Adverse event, serious fatal	1	4	6
Consent withdrawn by subject	4	3	7
Adverse event, non-fatal	2	1	6
Lost to follow-up	-	2	-

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: The participants were further divided into three arms in period 2, hence the participants that completed the first period do not match the participants that started period 2

Baseline characteristics

Reporting groups	
Reporting group title	Avacincaptad Pegol
Reporting group description:	
Participants received avacincaptad pegol (ACP) 2 milligram (mg)/eye via intravitreal (IVT) injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT injections monthly from month12 through month 23 (Year 2). Participants were followed up until month 24.	
Reporting group title	Sham
Reporting group description:	
Participants received sham injections; through Month 11 (Year 1). At month 12, participants continued to receive monthly sham injection from month 12 through month 23 (Year 2). Participants were followed up until month 24.	

Reporting group values	Avacincaptad Pegol	Sham	Total
Number of subjects	225	223	448
Age categorical Units: Participants			
Age Units: years			
arithmetic mean	76.3	76.7	
standard deviation	± 8.6	± 8.8	-
Sex Units: Participants			
Female	154	156	310
Male	71	67	138
Ethnicity Units: Subjects			
HISPANIC OR LATINO	27	23	50
NOT HISPANIC OR LATINO	168	179	347
NOT REPORTED	30	21	51
Race Units: Subjects			
AMERICAN INDIAN OR ALASKA NATIVE	1	0	1
ASIAN	1	1	2
BLACK OR AFRICAN AMERICAN	0	1	1
NOT REPORTED	31	21	52
More than one race	10	13	23
WHITE	182	187	369

End points

End points reporting groups

Reporting group title	Avacincaptad Pegol
Reporting group description:	
Participants received avacincaptad pegol (ACP) 2 milligram (mg)/eye via intravitreal (IVT) injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT injections monthly from month12 through month 23 (Year 2). Participants were followed up until month 24.	
Reporting group title	Sham
Reporting group description:	
Participants received sham injections; through Month 11 (Year 1). At month 12, participants continued to receive monthly sham injection from month 12 through month 23 (Year 2). Participants were followed up until month 24.	
Reporting group title	Avacincaptad Pegol
Reporting group description:	
Participants received avacincaptad pegol (ACP) 2 milligram (mg)/eye via intravitreal (IVT) injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT injections monthly from month12 through month 23 (Year 2). Participants were followed up until month 24.	
Reporting group title	Avacincaptad pegol and Sham
Reporting group description:	
Participants received ACP 2 mg/eye via IVT injections monthly through Month 11 (Year 1). At month 12, participants were re-randomized to receive ACP 2 mg/eye via IVT every other month (EOM) at months 13, 15, 17, 19, 21, and 23 and sham injections at months 12, 14, 16,18, 20, and 22 (Year 2). Participants were followed up until month 24.	
Reporting group title	Sham
Reporting group description:	
Participants received sham injections; through Month 11 (Year 1). At month 12, participants continued to receive monthly sham injection from month 12 through month 23 (Year 2). Participants were followed up until month 24.	

Primary: The mean rate of growth (slope) estimated based on GA area measured by autofluorescence (FAF) at 3 time points: Baseline, Month 6, and Month 12

End point title	The mean rate of growth (slope) estimated based on GA area measured by autofluorescence (FAF) at 3 time points: Baseline, Month 6, and Month 12
End point description:	
GA was associated with age-related macular degeneration (AMD) and caused bilateral, progressive, and irreversible loss of retinal tissue (photoreceptors, retinal pigment epithelium, and choriocapillaris) leading to a permanent loss of visual function and blindness. The least squares mean used to determine mean rate of change in GA growth (slope) was measured by FAF. LS mean & SE were based on square-root transformation. Intent to Treat (ITT) analysis set consisted of all randomized participants who received at least 1 dose of study drug.	
End point type	Primary
End point timeframe:	
Baseline to month 12	

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	222		
Units: millimeters (mm)/year				
least squares mean (standard error)	0.336 (± 0.032)	0.392 (± 0.033)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Difference in least squares mean between groups calculated as (sham) minus (avacincaptad pegol). Mixed Model for repeated measures (MMRM) was used to compare the treatment groups.

Comparison groups	Sham v Avacincaptad Pegol
Number of subjects included in analysis	447
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0064 [1]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.056
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.016
upper limit	0.096
Variability estimate	Standard error of the mean
Dispersion value	0.02

Notes:

[1] - Nominal p-value was used for the comparison between avacincaptad pegol versus sham.

Primary: The mean rate of growth (slope) estimated based on GA area measured by FAF at 5 timepoints: Baseline, Month 6, Month 12, Month 18, and Month 24

End point title	The mean rate of growth (slope) estimated based on GA area measured by FAF at 5 timepoints: Baseline, Month 6, Month 12, Month 18, and Month 24

End point description:

GA was associated with AMD and caused bilateral, progressive, and irreversible loss of retinal tissue (photoreceptors, retinal pigment epithelium, and choriocapillaris) leading to a permanent loss of visual function and blindness. The least square mean rate of GA growth (slope) was measured by FAF. LS mean & SE were based on untransformed data.
Re-randomized (Re-rand) analysis set- the subset of the ITT analysis set who were re-randomized at month 12 and who were on sham and completed the month 12 visit.
Re-rand analysis set-The subset of the ITT analysis set who were re-randomized at Month 12 and who were on sham and completed the Month 12 visit

End point type	Primary

End point timeframe:

Baseline to month 24

End point values	Avacincaptad Pegol	Avacincaptad pegol and Sham	Sham	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	96	93	203	
Units: mm^2/year				
least squares mean (standard error)	2.23 (± 0.124)	2.10 (± 0.126)	2.59 (± 0.085)	

Statistical analyses

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

Difference in least squares mean between groups calculated as (sham) minus (avacincaptad pegol and sham).

Comparison groups	Avacincaptad pegol and Sham v Sham
Number of subjects included in analysis	296
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0015 [2]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.488
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.189
upper limit	0.788
Variability estimate	Standard error of the mean
Dispersion value	0.152

Notes:

[2] - Nominal p-value was used for the comparison between avacincaptad pegol and sham versus sham

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Difference in least squares mean between groups calculated as (sham) minus (avacincaptad pegol).

Comparison groups	Avacincaptad Pegol v Sham
Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0165 [3]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	0.362
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.066
upper limit	0.657
Variability estimate	Standard error of the mean
Dispersion value	0.15

Notes:

[3] - Nominal p-value was used for the comparison between avacincaptad pegol versus sham.

Secondary: Change from Baseline in Best Corrected Visual Acuity (BCVA) using early treatment diabetic retinopathy study (ETDRS) letters at 24 months

End point title	Change from Baseline in Best Corrected Visual Acuity (BCVA) using early treatment diabetic retinopathy study (ETDRS) letters at 24 months

End point description:

BCVA was assessed using ETDRS visual acuity testing charts. The ETDRS Visual Acuity Score (VAS) is defined as the number of letters read on the ETDRS chart. Minimum and maximum possible scores are 0-100. A higher score represented better visual functioning. A positive change from baseline indicates an improvement and a negative change from baseline indicates a worsening.

ITT analysis set

End point type	Secondary

End point timeframe:

Baseline and month 24

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	222		
Units: score on a scale				
least squares mean (standard error)	-7.31 (± 1.07)	-6.48 (± 1.05)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Difference in least squares mean between groups calculated as (sham) minus (avacincaptad pegol).

Comparison groups	Avacincaptad Pegol v Sham
Number of subjects included in analysis	447
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58 [4]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	-0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.79
upper limit	2.12
Variability estimate	Standard error of the mean
Dispersion value	1.5

Notes:

[4] - Nominal p-value was used for the comparison between avacincaptad pegol versus sham.

Secondary: Change from Baseline in Low Luminance (LL) BCVA using ETDRS letters at 24 months

End point title	Change from Baseline in Low Luminance (LL) BCVA using ETDRS letters at 24 months

End point description:

BCVA was assessed using ETDRS visual acuity testing charts. The ETDRS VAS is defined as the number of letters read on the ETDRS chart. Minimum and maximum possible scores are 0-100. A higher score represented better visual functioning. A positive change from baseline indicates an improvement and a negative change from baseline indicates a worsening. LL BCVA was measured by placing a 2.0 log unit neutral density filter over the best correction for that eye and having the participant read the normally illuminated ETDRS chart.
ITT analysis set

End point type	Secondary

End point timeframe:

Baseline and month 24

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	222		
Units: score on a scale				
least squares mean (standard error)	-10.58 (± 1.20)	-9.10 (± 1.18)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Difference in least squares mean between groups calculated as (sham) minus (avacincaptad pegol).

Comparison groups	Avacincaptad Pegol v Sham
Number of subjects included in analysis	447
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38 [5]
Method	MMRM
Parameter estimate	Least Squares Mean Difference
Point estimate	-1.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.79
upper limit	1.81
Variability estimate	Standard error of the mean
Dispersion value	1.68

Notes:

[5] - Nominal p-value was used for the comparison between avacincaptad pegol versus sham.

Secondary: Change from Baseline in Visual Function Questionnaire (VFQ-25) Composite Scores at 6,12 and 18 months

End point title	Change from Baseline in Visual Function Questionnaire (VFQ-25) Composite Scores at 6,12 and 18 months

End point description:

The National Eye Institute Visual Function Questionnaire-25 (VFQ-25) measured the influence of visual disability and visual symptoms on general health domains. The VFQ-25 consisted of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. A higher score represented better visual functioning. Each item was then converted to a 0 to 100 scale so that the lowest and highest possible scores were set at 0 and 100 points, respectively. Each subscale score had a range of 0 to 100 inclusive and were calculated from the re-scaled raw data. A composite score was derived based on the average of the 11 vision-related subscales.

ITT analysis set with available data was analyzed

End point type	Secondary

End point timeframe:

Baseline, months 6, 12 and 18

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	206	215		
Units: score on a scale				
arithmetic mean (standard deviation)				
Change at 6 months (n = 206, 215)	-1.2 (± 10.56)	-1.6 (± 9.98)		
Change at 12 months (n = 196,199)	-3.4 (± 11.05)	-3.6 (± 11.01)		
Change at 18 months (n = 173,187)	-5.4 (± 12.80)	-4.7 (± 11.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Visual Function Questionnaire (VFQ-25) Composite Scores at 24 months

End point title	Change from Baseline in Visual Function Questionnaire (VFQ-25) Composite Scores at 24 months

End point description:

The National Eye Institute Visual Function Questionnaire-25 (VFQ-25) measured the influence of visual disability and visual symptoms on general health domains. The VFQ-25 consisted of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. A higher score represented better visual functioning. Each item was then converted to a 0 to 100 scale so that the lowest and highest possible scores were set at 0 and 100 points, respectively. Each subscale score had a range of 0 to 100 inclusive and were calculated from the re-scaled raw data. A composite score was derived based on the average of the 11 vision-related subscales. ITT analysis set

End point type	Secondary

End point timeframe:

Baseline and month 24

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	222		
Units: score on a scale				
least squares mean (standard error)	-7.735 (± 0.950)	-7.023 (± 0.931)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Avacincaptad Pegol v Sham
Number of subjects included in analysis	447
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5929
Method	MMRM
Parameter estimate	Least square mean difference
Point estimate	-0.712
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.326
upper limit	1.903
Variability estimate	Standard error of the mean
Dispersion value	1.33

Secondary: Number of Participants with Categorical one-level loss in VFQ-25 Subscale

End point title	Number of Participants with Categorical one-level loss in VFQ-25 Subscale

End point description:

The National Eye Institute VFQ-25 measured the influence of visual disability and visual symptoms on general health domains. The VFQ-25 consisted of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question. A higher score represented better visual functioning. Each item was then converted to a 0 to 100 scale so that the lowest and highest possible scores were set at 0 and 100 points, respectively.Categorical one-level loss in each item was defined as decline of one or more levels at Month 24 on the original scale from Baseline (equivalently 20 points for general vision and 25 points for other vision items in a 0 to 100 scale).
ITT analysis set with available data was analyzed

End point type	Secondary

End point timeframe:

Baseline up to month 24

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	175	182		
Units: participants				
Color Vision	45	35		
Distance Vision	56	43		
Near Vision	61	49		
Peripheral Vision	58	65		
General Vision	58	58		
Dependency	55	55		
Driving	27	26		
General Health	45	67		
Mental Health	35	42		
Ocular Pain	27	20		
Role Difficulties	60	59		
Social Function	52	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Persistent Vision Loss

End point title	Time to Persistent Vision Loss

End point description:

Vision loss event was defined as a loss of ≥ 15 letters (equivalent to a loss of 3 lines on the ETDRS chart) in BCVA from Baseline measured at any two or more consecutive visits up to Month 24. These parameters were chosen as a 3-line BCVA loss (equivalent to doubling of visual angle) is widely recognized as a significant deterioration in vision and a minimum of two consecutive visits was representative of persistent disease progression. BCVA was assessed using ETDRS visual acuity testing charts. The ETDRS VAS was defined as the number of letters read on the ETDRS chart. Min and max possible scores are 0-100. A higher score represents better visual functioning. Kaplan-Meier method was used for analysis. Participants with an event were reported and not the median time to event.

ITT analysis set

End point type	Secondary

End point timeframe:

Baseline up to month 24

End point values	Avacincaptad Pegol	Sham		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225	222		
Units: months				
median (full range (min-max))	17.02 (2.8 to 23.0)	13.93 (1.3 to 23.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Avacincaptad Pegol v Sham
Number of subjects included in analysis	447
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6424
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.42

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose up to 24 months

Adverse event reporting additional description:

ACM: All randomized participants.
Serious & non-SAEs: Those who received at least 1 dose of treatment.
Those who received injection of ACP were analyzed in ACP group according to actual injections. 1 participant randomized to sham didn't receive treatment & was included in denominator for ACM only & not for other outcomes.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	v24.1

Reporting groups

Reporting group title	Avacincaptad Pegol only (up to 12 months)

Reporting group description:

Participants received ACP 2 mg/eye via IVT injections monthly through Month 11 (Year 1).

Reporting group title	Avacincaptad Pegol only (12 to 24 months)

Reporting group description:

Participants were re-randomized at month 12 to receive ACP 2 mg/eye via IVT injections monthly from month 12 through month 23 (Year 2). Participants were followed up until month 24.

Reporting group title	Sham only (12 to 24 months)

Reporting group description:

Participants continued to receive monthly sham injection from month 12 through month 23 (Year 2). Participants were followed up until month 24.

Reporting group title	Sham only (up to 12 months)

Reporting group description:

Participants received sham injections through Month 11 (Year 1).

Reporting group title	Avacincaptad Pegol and Sham only (12 to 24 months)

Reporting group description:

Participants were re-randomized at month 12, to receive ACP 2 mg/eye via IVT injections every other month at months 13, 15, 17, 19, 21, and 23 and sham injections at months 12, 14, 16,18, 20, and 22 (Year 2). Participants were followed up until month 24.

Serious adverse events	Avacincaptad Pegol only (up to 12 months)	Avacincaptad Pegol only (12 to 24 months)	Sham only (12 to 24 months)
Total subjects affected by serious adverse events			
subjects affected / exposed	31 / 225 (13.78%)	18 / 96 (18.75%)	25 / 203 (12.32%)
number of deaths (all causes)	4	1	7
number of deaths resulting from adverse events	2	1	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute leukaemia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Breast cancer			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Sinonasal papilloma			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Non-small cell lung cancer stage IIIA			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Meningioma			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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			
Aortic aneurysm			

subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Aortic stenosis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Circulatory collapse			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypertension			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Hypertensive emergency			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Neurogenic shock			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Peripheral artery occlusion			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Pleural effusion			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Emphysema			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Dyspnoea exertional			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Pulmonary embolism			
subjects affected / exposed	2 / 225 (0.89%)	0 / 96 (0.00%)	0 / 203 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Device lead damage			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Exposure to toxic agent			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Facial bones fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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

Fall			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Femur fracture			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Humerus fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Lumbar vertebral fracture			
subjects affected / exposed	1 / 225 (0.44%)	1 / 96 (1.04%)	0 / 203 (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
Multiple fractures			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Procedural intestinal perforation			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Joint injury			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Procedural pain			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			

subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Rib fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Subdural haematoma			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Tibia fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Wrist fracture			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Upper limb fracture			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Traumatic intracranial haemorrhage			

subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Congenital, familial and genetic disorders			
Mobile caecum syndrome			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	2 / 225 (0.89%)	1 / 96 (1.04%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Atrial tachycardia			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardio-respiratory arrest			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure congestive			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Cardiac failure chronic			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Cardiac failure			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Coronary artery disease			
subjects affected / exposed	1 / 225 (0.44%)	1 / 96 (1.04%)	0 / 203 (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
Coronary artery insufficiency			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Intracardiac thrombus			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus arrest			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Myocardial ischaemia			

subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Myocardial infarction			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular extrasystoles			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	3 / 203 (1.48%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebral haemorrhage			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Metabolic encephalopathy			

subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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			
Normocytic anaemia			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Microcytic anaemia			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Retinal haemorrhage			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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

Choroidal neovascularisation			
subjects affected / exposed	2 / 225 (0.89%)	0 / 96 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Visual acuity reduced transiently			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Gastrointestinal disorders			
Barrett's oesophagus			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Enterovesical fistula			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Oesophageal spasm			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Inguinal hernia			
subjects affected / exposed	1 / 225 (0.44%)	1 / 96 (1.04%)	0 / 203 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Gastric haemorrhage			

subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Pancreatitis chronic			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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			
Biliary obstruction			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Hepatic cirrhosis			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Cholecystitis acute			

subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Lumbar spinal stenosis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Osteoarthritis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	2 / 203 (0.99%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tenosynovitis			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
COVID-19 pneumonia			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Cystitis bacterial			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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

Clostridium difficile infection			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Postoperative abscess			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Pneumonia bacterial			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Herpes zoster			
subjects affected / exposed	1 / 225 (0.44%)	0 / 96 (0.00%)	0 / 203 (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
Listeria sepsis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Pneumonia			

subjects affected / exposed	2 / 225 (0.89%)	0 / 96 (0.00%)	0 / 203 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Urosepsis			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	0 / 203 (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
Wound infection			
subjects affected / exposed	0 / 225 (0.00%)	0 / 96 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endophthalmitis			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 225 (0.00%)	1 / 96 (1.04%)	0 / 203 (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	Sham only (up to 12 months)	Avacincaptad Pegol and Sham only (12 to 24 months)	
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 222 (16.22%)	16 / 93 (17.20%)	
number of deaths (all causes)	1	4	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute leukaemia			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinonasal papilloma			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer stage IIIA			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	2 / 222 (0.90%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurogenic shock			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			

subjects affected / exposed	0 / 222 (0.00%)	2 / 93 (2.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 222 (0.45%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 222 (0.45%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			

subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
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	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device lead damage			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exposure to toxic agent			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fall			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural pain			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			

subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			

subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Mobile caecum syndrome			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (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	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardio-respiratory arrest			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	1 / 222 (0.45%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac thrombus			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 222 (0.45%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	2 / 222 (0.90%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			

subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuromyelitis optica spectrum disorder			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Normocytic anaemia			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Visual acuity reduced			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Choroidal neovascularisation			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced transiently			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Barrett's oesophagus			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal spasm			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (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 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary obstruction			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cirrhosis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			

subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tenosynovitis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
COVID-19			
subjects affected / exposed	2 / 222 (0.90%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis bacterial			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Clostridium difficile infection			
subjects affected / exposed	0 / 222 (0.00%)	1 / 93 (1.08%)	
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	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal perforated			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative abscess			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Listeria sepsis			
subjects affected / exposed	1 / 222 (0.45%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	2 / 222 (0.90%)	1 / 93 (1.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	2 / 222 (0.90%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 222 (0.00%)	0 / 93 (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: 5 %

Non-serious adverse events	Avacincaptad Pegol only (up to 12 months)	Avacincaptad Pegol only (12 to 24 months)	Sham only (12 to 24 months)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 225 (44.44%)	51 / 96 (53.13%)	77 / 203 (37.93%)
Investigations			
Intraocular pressure increased			

subjects affected / exposed	22 / 225 (9.78%)	9 / 96 (9.38%)	1 / 203 (0.49%)
occurrences (all)	43	18	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	14 / 225 (6.22%)	9 / 96 (9.38%)	12 / 203 (5.91%)
occurrences (all)	15	9	17
Eye disorders			
Choroidal neovascularisation			
subjects affected / exposed	21 / 225 (9.33%)	11 / 96 (11.46%)	19 / 203 (9.36%)
occurrences (all)	21	13	21
Cataract			
subjects affected / exposed	6 / 225 (2.67%)	7 / 96 (7.29%)	10 / 203 (4.93%)
occurrences (all)	8	8	13
Conjunctival haemorrhage			
subjects affected / exposed	31 / 225 (13.78%)	14 / 96 (14.58%)	5 / 203 (2.46%)
occurrences (all)	55	22	8
Punctate keratitis			
subjects affected / exposed	14 / 225 (6.22%)	5 / 96 (5.21%)	5 / 203 (2.46%)
occurrences (all)	25	8	14
Conjunctival hyperaemia			
subjects affected / exposed	12 / 225 (5.33%)	1 / 96 (1.04%)	5 / 203 (2.46%)
occurrences (all)	34	1	6
Retinal haemorrhage			
subjects affected / exposed	8 / 225 (3.56%)	2 / 96 (2.08%)	2 / 203 (0.99%)
occurrences (all)	9	2	3
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 225 (3.11%)	11 / 96 (11.46%)	26 / 203 (12.81%)
occurrences (all)	7	11	27
Nasopharyngitis			
subjects affected / exposed	4 / 225 (1.78%)	4 / 96 (4.17%)	3 / 203 (1.48%)
occurrences (all)	4	6	3
Urinary tract infection			
subjects affected / exposed	14 / 225 (6.22%)	3 / 96 (3.13%)	18 / 203 (8.87%)
occurrences (all)	17	3	22

Non-serious adverse events	Sham only (up to 12 months)	Avacincaptad Pegol and Sham only (12 to 24 months)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	83 / 222 (37.39%)	41 / 93 (44.09%)	
Investigations			
Intraocular pressure increased			
subjects affected / exposed	4 / 222 (1.80%)	5 / 93 (5.38%)	
occurrences (all)	5	7	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	17 / 222 (7.66%)	8 / 93 (8.60%)	
occurrences (all)	18	8	
Eye disorders			
Choroidal neovascularisation			
subjects affected / exposed	11 / 222 (4.95%)	8 / 93 (8.60%)	
occurrences (all)	13	8	
Cataract			
subjects affected / exposed	9 / 222 (4.05%)	4 / 93 (4.30%)	
occurrences (all)	13	5	
Conjunctival haemorrhage			
subjects affected / exposed	18 / 222 (8.11%)	9 / 93 (9.68%)	
occurrences (all)	32	16	
Punctate keratitis			
subjects affected / exposed	15 / 222 (6.76%)	5 / 93 (5.38%)	
occurrences (all)	32	6	
Conjunctival hyperaemia			
subjects affected / exposed	13 / 222 (5.86%)	1 / 93 (1.08%)	
occurrences (all)	38	1	
Retinal haemorrhage			
subjects affected / exposed	5 / 222 (2.25%)	5 / 93 (5.38%)	
occurrences (all)	5	6	
Infections and infestations			
COVID-19			
subjects affected / exposed	7 / 222 (3.15%)	14 / 93 (15.05%)	
occurrences (all)	7	14	
Nasopharyngitis			

subjects affected / exposed	6 / 222 (2.70%)	6 / 93 (6.45%)	
occurrences (all)	8	6	
Urinary tract infection			
subjects affected / exposed	13 / 222 (5.86%)	2 / 93 (2.15%)	
occurrences (all)	13	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 September 2020	Amendment contained clarifications on assessments, inclusion/exclusion criteria, and pregnancy urine/serum samples.
18 December 2020	Amendment added monthly optical coherence tomography, clarification on assessments, and inclusion/exclusion criteria.
24 May 2021	Amendment clarified the primary endpoint and analysis and minor administrative items.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported