



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 | v1 |
| This version publication date | 11 August 2024 |
| First version publication date | 11 August 2024 |

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, Data analyst, Carer |

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, Data analyst, Carer |

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 month 12 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 | 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 injections monthly or ACP 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 month 12 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 month 12 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 injections monthly or ACP 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: Mean rate of change from Baseline in GA area as measured by autofluorescence (FAF) at 12 months

| | |
|--|---|
| End point title | Mean rate of change from Baseline in GA area as measured by autofluorescence (FAF) at 12 months |
| 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 from baseline to month 12 was measured by FAF. LS mean & SE at 12 month was based on square-root transformed data. 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 and 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 (\pm 0.032) | 0.392 (\pm 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 | Avacincaptad Pegol v Sham |
| 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: Mean rate of change in GA area as measured by FAF at 6 months

| End point title | Mean rate of change in GA area as measured by FAF at 6 months ^[2] |
|---|--|
| 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. Mean rate of change in GA area from baseline to month 6 was measured by FAF. 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 with available data was analyzed. | |
| End point type | Primary |
| End point timeframe: | |
| Baseline and month 6 | |

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not planned for this endpoint.

| End point values | Avacincaptad Pegol | Avacincaptad pegol and Sham | Sham | |
|--------------------------------------|--------------------|-----------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 92 | 91 | 195 | |
| Units: mm ² | | | | |
| arithmetic mean (standard deviation) | 1.146 (± 0.6972) | 1.104 (± 0.7048) | 1.317 (± 0.8958) | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean rate of change in GA area as measured by FAF at 18 months

| | |
|-----------------|---|
| End point title | Mean rate of change in GA area as measured by FAF at 18 months ^[3] |
|-----------------|---|

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. Mean rate of change in GA area from baseline to month 18 was measured by FAF.

Re rand analysis set with available data was analyzed.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Baseline and month 18

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not planned for this endpoint.

| End point values | Avacincaptad Pegol | Avacincaptad pegol and Sham | Sham | |
|--------------------------------------|--------------------|-----------------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 74 | 76 | 175 | |
| Units: mm ² | | | | |
| arithmetic mean (standard deviation) | 3.362 (± 1.9113) | 3.135 (± 1.5957) | 3.894 (± 2.0838) | |

Statistical analyses

No statistical analyses for this end point

Primary: Mean rate of GA growth (slope) as measured by FAF at 24 months

| | |
|-----------------|--|
| End point title | Mean rate of GA growth (slope) as measured by FAF at 24 months |
|-----------------|--|

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) from baseline to month 24 was measured by FAF.

LS mean & SE at 24 month was based on untransformed data.

Re-rand analysis set

| | |
|-----------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Baseline and 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 ^[4] |
| 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:

[4] - 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 ^[5] |
| 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:

[5] - 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 ^[6] |
| 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:

[6] - 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 ^[7] |
| 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:

[7] - 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

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 (\pm 0.950) | -7.023 (\pm 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:

Analysis population for all-cause, serious adverse events (SAEs), & non-SAEs (NSAEs) consisted of all participants who received at least one dose of study treatment. Participants who received an injection of avacincaptad pegol during this study were analyzed in the avacincaptad pegol treatment group according to the actual injections received.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|-------|
| Dictionary version | v24.1 |
|--------------------|-------|

Reporting groups

| | |
|-----------------------|------|
| Reporting group title | Sham |
|-----------------------|------|

Reporting group description:

Participants who received sham injections through month 23. Participants were followed up until month 24.

| | |
|-----------------------|--------------------|
| Reporting group title | Avacincaptad pegol |
|-----------------------|--------------------|

Reporting group description:

Participants who received ACP 2 mg/eye via IVT injections through month 23. Participants were followed up until month 24.

| Serious adverse events | Sham | Avacincaptad pegol | |
|---|-------------------|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 51 / 222 (22.97%) | 60 / 225 (26.67%) | |
| number of deaths (all causes) | 7 | 9 | |
| number of deaths resulting from adverse events | 5 | 4 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Acute leukaemia | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon cancer | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 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 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinonasal papilloma | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Squamous cell carcinoma of lung | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vascular disorders | | | |
| Aortic aneurysm | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Aortic stenosis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 | 1 / 222 (0.45%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypertensive emergency | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neurogenic shock | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Peripheral arterial occlusive disease | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 / 225 (0.44%) | |
| 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 / 225 (0.89%) | |
| 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 / 225 (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%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Emphysema | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| 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%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Product issues | | | |
| Device dislocation | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Device lead damage | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 | | | |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Joint injury | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Facial bones fracture | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Exposure to toxic agent | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ankle fracture | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Multiple fractures | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Radius fracture | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal fracture | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tibia fracture | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Traumatic intracranial haemorrhage | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Procedural intestinal perforation | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| 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 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac failure chronic | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |

| | | | |
|---|-----------------|-----------------|--|
| Cardiac failure | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | |
| Atrial tachycardia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial flutter | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 222 (1.35%) | 3 / 225 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 | 2 / 222 (0.90%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Atrioventricular block second degree | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinus arrest | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 / 225 (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 | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracardiac thrombus | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery insufficiency | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary artery disease | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 222 (0.00%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cerebral infarction | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 4 / 222 (1.80%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intracranial aneurysm | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolic encephalopathy | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Neuromyelitis optica spectrum disorder | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |

| | | | |
|---|-----------------|-----------------|--|
| Microcytic anaemia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Normocytic anaemia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| 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 | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 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 / 225 (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%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Choroidal neovascularisation | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Visual acuity reduced transiently | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Rectal haemorrhage | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Large intestine polyp | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (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 / 225 (0.44%) | |
| 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 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Barrett's oesophagus | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| 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 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pancreatitis chronic | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Biliary obstruction | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Cholecystitis acute | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatic cirrhosis | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Tenosynovitis | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Osteoarthritis | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 2 / 225 (0.89%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| COVID-19 | | | |
| subjects affected / exposed | 3 / 222 (1.35%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| COVID-19 pneumonia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Postoperative abscess | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 3 / 225 (1.33%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Listeria sepsis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis intestinal perforated | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulitis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis bacterial | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 225 (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 | 1 / 222 (0.45%) | 0 / 225 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Endophthalmitis | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| 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%) | 1 / 225 (0.44%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Sham | Avacincaptad pegol | |
|---|--------------------|--------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 135 / 222 (60.81%) | 155 / 225 (68.89%) | |
| Investigations | | | |
| Intraocular pressure increased | | | |
| subjects affected / exposed | 4 / 222 (1.80%) | 30 / 225 (13.33%) | |
| occurrences (all) | 6 | 68 | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 26 / 222 (11.71%) | 30 / 225 (13.33%) | |
| occurrences (all) | 35 | 32 | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 14 / 222 (6.31%) | 16 / 225 (7.11%) | |
| occurrences (all) | 15 | 16 | |
| Nervous system disorders | | | |

| | | | |
|--|-------------------------|-------------------------|--|
| Headache subjects affected / exposed occurrences (all) | 12 / 222 (5.41%) 12 | 6 / 225 (2.67%) 7 | |
| Eye disorders | | | |
| Conjunctival haemorrhage subjects affected / exposed occurrences (all) | 20 / 222 (9.01%) 40 | 41 / 225 (18.22%) 93 | |
| Choroidal neovascularisation subjects affected / exposed occurrences (all) | 29 / 222 (13.06%) 34 | 38 / 225 (16.89%) 42 | |
| Cataract subjects affected / exposed occurrences (all) | 18 / 222 (8.11%) 26 | 16 / 225 (7.11%) 21 | |
| Eye pain subjects affected / exposed occurrences (all) | 8 / 222 (3.60%) 9 | 15 / 225 (6.67%) 17 | |
| Dry eye subjects affected / exposed occurrences (all) | 14 / 222 (6.31%) 15 | 11 / 225 (4.89%) 11 | |
| Conjunctival hyperaemia subjects affected / exposed occurrences (all) | 15 / 222 (6.76%) 44 | 14 / 225 (6.22%) 36 | |
| Vitreous detachment subjects affected / exposed occurrences (all) | 12 / 222 (5.41%) 14 | 14 / 225 (6.22%) 15 | |
| Punctate keratitis subjects affected / exposed occurrences (all) | 16 / 222 (7.21%) 46 | 20 / 225 (8.89%) 39 | |
| Retinal haemorrhage subjects affected / exposed occurrences (all) | 7 / 222 (3.15%) 8 | 14 / 225 (6.22%) 17 | |
| Infections and infestations | | | |
| Urinary tract infection subjects affected / exposed occurrences (all) | 27 / 222 (12.16%) 35 | 19 / 225 (8.44%) 22 | |
| Nasopharyngitis | | | |

| | | | |
|-----------------------------|-------------------|-------------------|--|
| subjects affected / exposed | 9 / 222 (4.05%) | 13 / 225 (5.78%) | |
| occurrences (all) | 11 | 16 | |
| COVID-19 | | | |
| subjects affected / exposed | 33 / 222 (14.86%) | 31 / 225 (13.78%) | |
| occurrences (all) | 34 | 32 | |

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